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2024 KALAS International Symposium

JULY 24 |WED| – 27 |SAT|

ICC JEJU, Jeju Island, KOREA

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KOREAN ASSOCIATION
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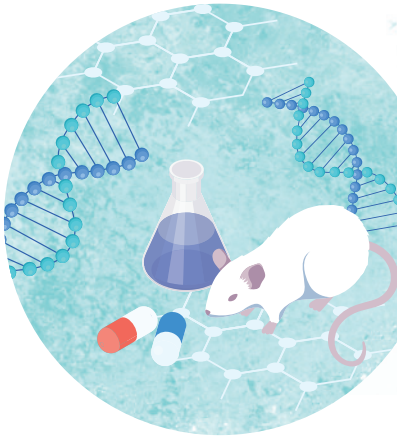
2025 한국실험동물학회
동계심포지엄

2025. 2. 5.(수) - 2. 8.(토)

강원도 평창 알펜시아 컨벤션센터



한국실험동물학회

중앙실험동물(주)
Central Lab.Animal Inc.

• Humanized Model

	STRAIN		STRAIN		STRAIN		STRAIN
면역부전	BRGSF	Double ICP	hCTLA4-hLAG3 (B6N)	당뇨	hGLP1R	Reporter Cell Line	EL4 LZ
인간화마우스	BRGSF-HIS	Double ICP	hGITR-hGITR-L (B6N)	PK:PD	hSA/hFcRn	Single Target Cell Line	MC38 mPdl1KO hPDL1
Single ICP	hPD1 / hCTLA-4 / hVISTA	Double ICP	hCD3ε/HCD28	면역부전 PK:PD	hSA/hFcRn/Rag1-KO	Single Target Cell Line	MC38 mPdl1KO hPDL1 LucGreen
Single ICP	hOX40 / hGITR / hSTING	Double ICP	hGITR/Foxp3	Reporter	Foxp3-mRFP	Single Target Cell Line	CT26 mPdl1KO hPDL1
Single ICP	hCD28 / cGAS / hCD39	Triple ICP	hPD1-hGITR-hGITR-L	Reporter	IL4-Get	Single Target Cell Line	CT26 mCD39KO hCD39 LucGreen
Double ICP	hPD1-hVISTA (B6N)	T-cell engager	hCD3epsilon	Reporter	hGITR-Foxp3-mRFP	Single Target Cell Line	CT26 mEpCAMKO hEpCAM LucGreen
Double ICP	hPD1-hCTLA4 (B6N)	T-cell engager	panCD3	Knockout Cell Line	MC38 mPdl1 KO (CMC1)	Single Target Cell Line	El4 hCD20 LZ
Double ICP	hPD1-hTIM3 (B6N)	Inflammation & Allergy	hCD4+	Knockout Cell Line	CT26 mPdl1 KO (CCT1)	Double Target Cell Line	MC38 mPdl1KO hPDL1 hHER2 LZ
Double ICP	hPD1-hLAG3 (B6N)	Inflammation & Allergy	hIgE/hFcεR1	Reporter Cell Line	MC38 LZ	Double Target Cell Line	MC38 mPdl1KO hPDL1 hCD47 LZ
Double ICP	hPD1-hPDl-1 (B6N)	Inflammation & Allergy	hTNF-α	Reporter Cell Line	CT26 LZ	개 발 중	

• Inbred/Outbred/Disease Model

종		STRAIN	종		STRAIN	종		STRAIN
MOUSE	비근교계	Slc:ddY (생약, 내분비, 백신)	MOUSE	질환모델	C57BL/6HamSlc-ob/ob (비만)	RAT	비근교계	Iar:Long-Evans (간손상, 신경독성)
MOUSE	비근교계	Iar : Ivcs (ddn)(Tangier Disease)	MOUSE	질환모델	C57BL/6HamSlc-+/+ (ob 대조군)	RAT	비근교계	Iar:Wistar-Imamichi (생리연구)
MOUSE	근교계	A/JmsSlc (폐암)	MOUSE	질환모델	C57BL/6JmsSlc-lpr/lpr (자가면역질환)	RAT	비근교계	Slc:SD
MOUSE	근교계	AKR/NSlc (혈액암)	MOUSE	질환모델	C57BLKS/Jlar-+Leprdb/+Leprdb (2형당뇨)	RAT	비근교계	Slc:Wistar/ST
MOUSE	근교계	BALB/cCrSlc	MOUSE	질환모델	C57BLKS/J lar-m+/+Leprdb (db 대조군)	RAT	근교계	BN/SsNSlc (천식,안과, Male)
MOUSE	근교계	C3H/HeNSlc (LPS 민감)	MOUSE	질환모델	C57BLKS/J lar-m+/m+ (db 대조군)	RAT	근교계	DA/Slc (관절염)
MOUSE	근교계	C3H/HeSlc (유방암)	MOUSE	질환모델	HIGA/NscSlc (신부전증, Female)	RAT	근교계	F344/NSlc (장기발암성)
MOUSE	근교계	C3H/HeYokSlc (LPS저민감, Tlr4 KO)	MOUSE	질환모델	Hos:HR-1 (피부, albino)	RAT	근교계	LEW/SsNSlc (관절염)
MOUSE	근교계	C57BL/6JmsSlc	MOUSE	질환모델	Hos:HRM2 (피부, 멜라닌有)	RAT	질환모델	DIR/Eis (식염감수성고혈압)
MOUSE	근교계	C57BL/6NCrSlc	MOUSE	질환모델	MRL/MpJmsSlc-lpr/lpr (자가면역질환)	RAT	질환모델	DIS/Eis (식염감수성고혈압, DIR 대조군)
MOUSE	근교계	CBA/NSlc (청력관련)	MOUSE	질환모델	MRL/MpJmsSlc-+/+ (MRL 대조군)	RAT	질환모델	GK/Slc (Type II 당뇨모델, Male)
MOUSE	근교계	DBA/1JmsSlc (관절염)	MOUSE	질환모델	NSY.B6-Tyr+ Ay (Type II 당뇨, Male)	RAT	질환모델	Hos:OLETF (Type II 당뇨, Male)
MOUSE	근교계	DBA/2CrSlc (청력관련)	MOUSE	질환모델	NSY/Hos (Type II 당뇨, Male)	RAT	질환모델	Hos:LETO (OLETF 대조군, Male)
MOUSE	근교계	NC/NgaSlc (아토피)	MOUSE	질환모델	NZBWF1/Slc (자가면역질환)	RAT	질환모델	Hos:ZFDM-(fa/fa) (Type II 당뇨,비만, Male)
MOUSE	근교계	NZB/N Slc (루프스)	MOUSE	질환모델	SAMP1/SkuSlc (일반노인성질환, Male)	RAT	질환모델	Hos:ZFDM-(+/fa) (ZFDM 대조군, Male)
MOUSE	근교계	NZW/N Slc (루프스)	MOUSE	질환모델	SAMP6/TaSlc (노인성골다공증, Male)	RAT	질환모델	HWY/Slc(Hairless) (피부연구)
MOUSE	근교계	129×1/SvJmsSlc (줄기세포관련)	MOUSE	질환모델	SAMP8/TaSlc (학습기억장애, Male)	RAT	질환모델	Long-Evans-rnu/rnu (면역부전, Male)
MOUSE	congenic	B10.A/SgSnSlc (H2:a)	MOUSE	질환모델	SAMP10/TaIdrSlc	RAT	질환모델	SHR/Izm (고혈압, Male)
MOUSE	congenic	B10.BR/SgSnSlc (H2:k)	MOUSE	질환모델	SAMP10-ΔSglt2 (노인성뇌퇴화, Male)	RAT	질환모델	WKY/Izm (SHR 대조군, Male)
MOUSE	congenic	B10.D2/nSnSlc (H2:d)	MOUSE	질환모델	SAMR1/TaSlc (SAM 대조군, Male)	RAT	질환모델	SHRSP/Ezo(ADHD, Male)
MOUSE	congenic	B10.S/SgSlc (H2:s)	MOUSE	질환모델	TSOD® (Type II 당뇨)	RAT	질환모델	SHRSP/Izm (뇌졸증)
MOUSE	congenic	C57BL/10SnSlc (H2:b)	MOUSE	질환모델	TSNO® (TSOD 대조군)	RAT	질환모델	SHRSP5/Dmcr (NASH, Male)
MOUSE	교잡군	B6C3F1/Slc	MOUSE	질환모델	WBB6F1/Kit-Kitw/KitW-v (비만세포결핍,빈혈)	RAT	질환모델	Slc:Zucker-fa/fa (비 만)
MOUSE	교잡군	B6D2F1/Slc (EPO)	MOUSE	질환모델	WBB6F1-+/+/Slc (WBB6F1 대조군)	RAT	질환모델	Slc:Zucker-+/+ (Zucker 대조군)
MOUSE	교잡군	CB6F1/Slc	MOUSE	Tg	APPOSK-Tg (알츠하이머, Male)	RAT	질환모델	Slc:Zucker-+/+ (대조군)
MOUSE	교잡군	CD2F1/Slc	MOUSE	Tg	APPwt-Tg (APPosk 대조군, Male)	RAT	Tg	SD-Tg (CAG-EGFP, Male)
MOUSE	돌연변이	BALB/cSlc-nu/nu (T cell 결핍-면역부전)	MOUSE	Tg	C57BL/6-BALB/c-nu/nu-EGFP	RAT	Tg	Slc:SD-Tg(SOD1H46R-4)
MOUSE	돌연변이	KSN/Slc	MOUSE	Tg	C57BL/6JmsSlc-Tg (gpt delta, Male)	RAT	Tg	F344／N -Tg(gpt delta) (Male)
MOUSE	질환모델	AKITA/Slc (Type I, II 당뇨)	MOUSE	Tg	C57BL/6-Tg (CAG-EGFP,Male)	G.P.		Slc:Hartley (Female)
MOUSE	질환모델	B6.KOR/StmSlc-Apoeshl (고지혈, Male)	MOUSE	Tg	OSK – KI (알츠하이머)	Hamster		Slc:Syrian (Male)
MOUSE	질환모델	C.KOR/StmSlc-Apoeshl (고지혈, Male)	MOUSE	Tg	Tau264 -Tg (Tau 대조군, Male)	Hamster		J2N-k (특발성 심근증, Male)
MOUSE	질환모델	BXSB/MpJmsSlc-Yaa (자가면역질환)	MOUSE	Tg	Tau609–Tg (알츠하이머, Male)	Hamster		J2N-n (대조군, Male)
MOUSE	질환모델	C3H/HeJmsSlc-lpr/lpr (자가면역질환)	MOUSE	Tg	Tau784–Tg (알츠하이머, Male)	Gerbil		MON/JmsGbsSlc (Male)

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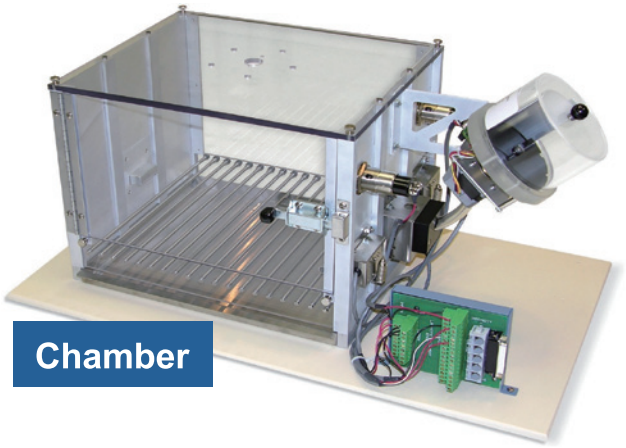
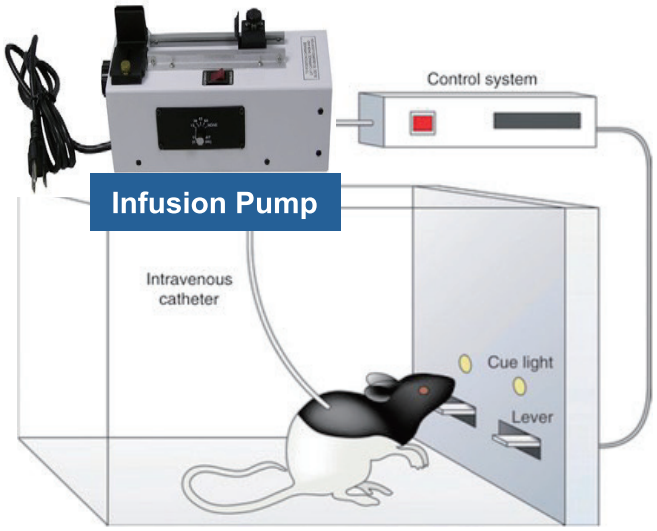
Operant Control and Conditioning for Rodents

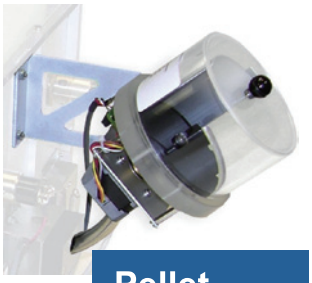


Chamber

White Stimulus Light



Infusion Pump



Pellet Dispenser

Peristaltic Pump for Liquid Reward

Infusion Pump for Drug Self Administration

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실험동물장비 및 기자재 산업의 선두주자 **럭키싸이언텍**은
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Korea Model animal Priority Center

INVITATION

Dear KALAS members,

It is our great pleasure to warmly invite you to the 2024 KALAS International Symposium, entitled 'IMPACT (Innovative Models for Predictive And Comparative Translational research)' at Jeju International Convention Center (Jeju ICC) in Jeju island from July 24 (Wed) to 27 (Sat) in 2024.

The International Symposium is composed with 2 plenary lectures: 'Insights from rodent models for understanding Diabetic Retinopathy' (Prof. Jesús Ruberte Paris, Autonomous University of Barcelona) and 'The current insights into Alzheimer's disease research and advancements in therapeutic development' (Prof. Inhee Mook, Seoul Natl. Univ.), and 16 program sessions including Brain development and disease models, Vision and hearing defect models, Laboratory rodent health monitoring, Humanized animal models, Xenotransplantation in nonhuman primate models, Gasrointestinal disease models, Metabolic disease therapy, Stem cell and organoid, IACUC, Research ethics, KLAT educational sessions, etc.

The symposium will be supported by several institutions, agencies and organizations including KOFST, NIFDS, JCVB, KIT, KMPC, etc. and I would like to thank all those concerned in this symposium.

We hope that all participants will enjoy this KALAS international symposium that gives an opportunity to broaden your academic knowledge, and carry back with you fond memories from Jeju island. Once again, I sincerely appreciate for those who support and contribute to this international symposium.

Je Kyung Seong

President, KALAS

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	부회장	서준교	한림대학교
	부회장	송시환	㈜코아스템켐온
	부회장	진희경	경북대학교
	부회장	천병년	㈜우정바이오
감사	감사	강병철	서울대학교
	감사	남기택	연세대학교
편집위원회	**위원장**	**성제경**	서울대학교
	부위원장	복진웅	연세대학교
	위원(ME간사)	고혁완	연세대학교
	위원(ME간사)	김경미	고려대학교
	위원(ME간사)	문창종	전남대학교
	위원(ME간사)	박만성	고려대학교
	위원(ME간사)	박종환	전남대학교
	위원(ME간사)	부혜진	제주대학교
	위원(ME간사)	서원효	이화여자대학교
	위원(ME간사)	서준교	한림대학교
	위원(ME간사)	성영훈	울산대학교
	위원(ME간사)	윤상선	연세대학교
	위원(ME간사)	이근욱	한림대학교
	위원(ME간사)	이대기	이화여자대학교
	위원(ME간사)	이정수	가톨릭대학교
	위원(ME간사)	이주영	가톨릭대학교
	위원(ME간사)	이 호	국립암센터
	위원(ME간사)	정주희	덕성여자대학교
	위원(ME간사)	정호성	연세대학교
	위원(ME간사)	조성대	서울대학교
	위원(ME간사)	조종기	서울대학교
	위원(ME간사)	최재훈	한양대학교
	위원(ME간사)	현영민	연세대학교
	위원(ME간사)	홍정주	한국생명공학연구원
	위원(ME간사)	황인구	서울대학교
	위원(RE간사)	황성순	연세대학교
	위원	구승희	고려대학교
	위원	김용환	숙명여자대학교
	위원	김항래	서울대학교
	위원	박성규	서울대학교
	위원	박한수	광주과학기술원
	위원	윤경아	건국대학교
	위원	이창훈	동국대학교
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	위원	김명석	강릉KIST
	위원	김상화	강원대학교
	위원	신태훈	제주대학교

직책		성명	소속
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	위원(하계간사)	최재훈	한양대학교
	위원(동계간사)	정호성	연세대학교
	위원	권호근	연세대학교
	위원	민혜영	중앙대학교
	위원	박해철	고려대학교
	위원	배옥남	한양대학교
	위원	부혜진	제주대학교
	위원	서준영	연세대학교
	위원	이은정	아주대학교
	위원	이정수	한국생명공학연구원
	위원	이현지	고려대학교
	위원	이희영	가천대학교
	위원	정수명	성균관대학교
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	위원	서원효	이화여자대학교
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	위원(간사)	황성순	연세대학교
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	위원(간사)	김성대	경북대학교
	위원	임 용	동의대학교
	위원	조현무	가톨릭대학교
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	위원(간사)	김경미	고려대학교
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	위원(간사)	신태훈	제주대학교
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	위원	구준서	기초과학연구원
	위원	서진수	대구경북과학기술원
	위원	윤성진	한국생명공학연구원
	위원	이기현	이화여자대학교
	위원	이미니	한국생명공학연구원
	위원	이은우	한국생명공학연구원
	위원	이진수	충남대학교
	위원	최동욱	고려대학교
	위원	최진욱	광주과학기술원
전산위원회	**위원장**	**이근욱**	한림대학교
	위원(간사)	박준원	서울대학교
	위원	진영배	경상대학교
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	위원	강경수	㈜아퓨어스
	위원	김재길	한신메디칼㈜
	위원	김찬수	베트컴코리아㈜
	위원	박천귀	㈜쓰리샤인
	위원	서일수	㈜테크노마트
	위원	유병천	㈜아이티스텐다드
	위원	이 오	㈜오리엔트바이오
	위원	이현주	㈜샘타코바이오코리아
	위원	천병년	㈜우정바이오
	위원	한남욱	㈜코아텍
인증위원회	**위원장**	**제정환**	서울대학교병원
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	부위원장(총무)	전현정	식품연구원
	위원(교육 및 교재간사)	김동재	대구경북과학기술원
	위원(교육 및 교재간사)	나이랑	서울대학교
	위원(소통간사)	허승호	서울아산병원
	위원(인증간사)	양세란	강원대학교
	위원(인증간사)	안재범	오산대학교
	위원(전산간사)	황지연	분당서울대병원
	위원(전산간사)	이정민	삼성병원
	위원(총무간사)	김지영	이화여자대학교
법제위원회	**위원장**	**김배환**	계명대학교
	위원(간사)	김기석	안전성평가연구소
	위원	정세훈	대구보건대
연구윤리위원회	**위원장**	**석승혁**	서울대학교
	위원(간사)	이지민	서울대학교
동물복지위원회	**위원장**	**이상래**	아주대학교
	위원(간사)	김종성	아주대학교
	위원	양인숙	연세대학교
	위원	전채은	동물을 위한 행동 대표
	위원	박준석	대구경북첨단의료산업진흥재단
포상위원회 (학술상위원회)	**위원장**	**이 호**	국립암센터
	위원	오한슬	충북대학교
지회	서울/경기지회장	송문용	한국건설생활환경시험연구원
	강원지회장	양세란	강원대학교
	경상지회장	김배환	계명대학교
	전라지회장	김종춘	전남대학교
	제주지회장	지영흔	제주대학교
	충청지회장	정재황	충북도립대학

KALAS COUNCIL MEMBERS

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성명	소속
강경선	서울대학교
강병철	서울대학교
강부현	㈜켐온
강종구	㈜바이오톡스텍
강종순	한국생명공학연구원
강진석	남서울대학교
고필옥	경상대학교
고혁완	연세대학교
구재형	대구경북과학기술원
권동락	대구가톨릭대학교병원
권명상	강원대학교
권중기	전북대학교
김곤섭	경상대학교
김근형	충북대학교
김길수	경북대학교
김대중	충북대학교
김동재	DGIST
김동환	건양대학교
김명옥	경북대학교
김무강	충남대학교
김배환	계명대학교
김옥진	원광대학교
김용범	안전성평가연구소
김윤배	충북대학교
김정훈	서울대학교
김종성	아주대학교의료원
김종춘	전남대학교
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김천호	강원대학교
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김태완	경북대학교
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김형식	부산대학교
김형진	한국생명공학연구원
김환묵	가천대학교
나이랑	서울대학교병원
남기택	연세대학교
남기환	한국생명공학연구원
남상윤	충북대학교
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류재웅	경북대학교
박대훈	동신대학교
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박종환	전남대학교
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박천귀	㈜쓰리샤인
배재성	경북대학교
배춘식	전남대학교
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서준교	한림대학교
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성제경	서울대학교
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송시환	㈜켐온
송창선	건국대학교
송창우	안전성평가연구소
신영수	신구대학교
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양만표	충북대학교
양세란	강원대학교
오경진	한국생명공학연구원
오구택	이화여자대학교
오승현	서울대학교
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이국현	서울대학교
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이현주	㈜샘타코 바이오코리아
이 호	국립암센터
이희영	가천대학교
장인석	경상국립대학교
장자준	서울대학교
장재진	㈜오리엔트바이오
전경희	연세대학교
전현정	한국식품연구원
정기원	㈜엠제이엘티디
정용현	H&H 호서대 안전성평가센터
정은주	안전성평가연구소
정자영	오송첨단의료산업진흥재단
정재황	충북도립대학
정지윤	공주대학교
정태천	영남대학교
제정환	서울대학교병원
조규혁	안전성평가연구소
조성대	서울대학교
조재진	서울대학교
조정식	(전) 식약처 실험동물자원실
진희경	경북대학교
차신우	안전성평가연구소
차지영	가천대학교
천병년	㈜우정바이오
최경철	충북대학교
최병인	가톨릭대학교 성의교정
최양규	건국대학교
최연식	한국폴리텍대학 바이오캠퍼스
최영석	건국대학교
최우성	(주)메디키나바이오
최재훈	한양대학교
한남옥	(주) 코아텍
한범석	호서대학교
한상섭	전북대학교
허승호	서울아산병원
허 용	대구가톨릭대학교
현병화	KAIST
황대연	부산대학교
황종익	고려대학교

발전기금 납입 회원

2024.07.01. 기준

성명	소속	금액(단위:원)
Alan Lee Chedester	NIH	300,000
Toru Takeo	Kumamoto University	USD 1,000
강병철	서울대학교	2,311,200
강종구	㈜바이오톡스텍	1,000,000
강진석	남서울대학교	200,000
권구범	NTCV Vaccine Co.	300,000
권중기	전북대학교	200,000
김길수	경북대학교	200,000
김대용	서울대학교	350,000
김대중	충북대학교	517,000
김덕원	삼양약화학	50,000
김배환	계명대학교	802,280
김윤배	충북대학교	267,680
김종성	삼성생명과학연구원	267,680
김종춘	전남대학교	300,000
김형식	부산대학교	300,000
남정석	광주과학기술원	869,950
박재학	서울대학교	5,955,525
박충권	녹십자 EM	300,000
서경덕	천안연암대학	100,000
서준교	한림대학교	1,769,950
석승혁	서울대학교	2,100,000
성제경	서울대학교	300,000
성하정	크로엔리서치	200,000
손우찬	울산대학교	100,000
송시환	㈜코아스템켐온	100,000
송창우	안전성평가연구소	3,650,000
신영수	신구대학교	467,680
신재호	을지대학교	200,000
안병우	충북대학교	200,000
염수청	서울대학교	200,000
오승현	서울대학교	200,000
오양석	한림대학교	1,791,299
원무호	강원대학교	3,000,000
위명복	강원대학교	391,200

성명	소속	금액(단위:원)
유영춘	건양대학교	200,000
이민재	강원대학교	500,000
이범준	충북대학교	200,000
이병한	오송첨단의료산업진흥재단	367,680
이상구	㈜바이오스텍	200,000
이상필	㈜한주씨엠아이	4,000,000
이수해	식품의약품안전처	100,000
이정규	㈜중앙실험동물	1,000,000
이철호	한국생명공학연구원	200,000
이한웅	연세대학교	5,000,000
인증위원회	인증위원회	3,000,000
인증위원회	동물실험길잡이 인세	36,587,000
장동덕	국군의학연구소	200,000
장자준	서울대학교	882,400
정기원	㈜엠제이엘티디	1,000,000
정재황	충북도립대학	100,000
정지윤	공주대학교	200,000
제정환	서울대학교병원	837,630
조기행	서울대학교	300,000
조윤주	서정대학교	200,000
조재진	서울대학교	10,000,000
차신우	안전성평가연구소	200,000
천병년	㈜우정비에스씨	2,000,000
최경철	충북대학교	1,000,000
최양규	건국대학교	2,769,950
최연식	한국폴리텍바이오대학교	200,000
최우성	대구경북첨단의료산업진흥재단	200,000
한남욱	㈜코아텍	30,000,000
한범석	건양대학교	2,200,000
허용	대구가톨릭대학교	200,000
현병화	오송첨단의료산업진흥재단	30,300,000
황대연	부산대학교	200,000
황인구	서울대학교	1,900,000
(재)한국건설생활환경시험연구원		2,000,000

학술상·편집위·실험동물연구장학생 후원금 납입 내역

2024.07.01. 기준

소속	금액(단위:원)	년도
㈜쓰리싸인	25,000,000	2005~2009
㈜코아텍	10,000,000	2016
중앙실험동물㈜	224,000,000	2007~2023

2024 한국실험동물학회 평생회비 납입회원

2024.07.01. 기준

성명	소속
강경수	신구대학교
강병철	서울대학교
강종구	충북대학교
강진주	경북대학교
고은아	제주대학교
곽동미	경북대학교
구재형	대구경북과학기술원(DGIST)
권구범	우정BSC
권동락	대구가톨릭대학교병원
권명상	강원대학교
권은아	서울대학교병원
권재성	연세대학교
권태준	대구경북첨단의료산업진흥재단
김건아	을지대학교
김경원	서울아산병원
김근형	충북대학교
김길수	대구경북첨단의료산업진흥재단
김대원	강릉원주대학교
김대중	충북대학교
김명옥	경북대학교
김무강	(재)충남동물자원센터
김배환	계명대학교
김보라	국립암센터
김상아	서울대학교 약학대학
김상운	한국생명공학연구원
김상현	대구경북첨단의료산업진흥재단
김선호	㈜폴라스
김성곤	대구경북첨단의료산업진흥재단
김옥진	원광대학교
김용안	충남대학교
김우석	한림대학교
김유용	서울대학교
김종남	서울대학교
김종춘	전남대학교
김주완	대구한의대학교
김중현	오송첨단의료산업진흥재단
김진만	㈜오리엔트바이오
김철규	오송첨단의료산업진흥재단
김충수	대구경북첨단의료산업진흥재단
김충용	대구경북첨단의료산업진흥재단
김태완	경북대학교
김태환	경북대학교
김형식	부산대학교
김혜진	한국한의학연구원
김희정	대구경북첨단의료산업진흥재단
김희진	농림축산검역본부
나운성	전남대학교
나이랑	서울대학교병원
남기택	연세대학교
남병수	한국한의학연구원
남상윤	충북대학교
남정석	광주과학기술원
노재일	연세대학교
류동렬	GIST
류정주	대구경북첨단의료산업진흥재단
박대훈	동신대학교
박민경	대구경북첨단의료산업진흥재단
박부환	인하대학교
박승춘	경북대학교
박인선	인하대학교
박재학	서울대학교
박종환	전남대학교
박준석	대구경북첨단의료산업진흥재단
박진성	서울대학교 병원
박천귀	㈜쓰리샤인
배재성	경북대학교
배춘식	전남대학교
백인정	서울아산병원 의생명연구소
복진웅	연세대학교
서병부	대구대학교
서준교	한림대학교
서진희	한국원자력의학원
석승혁	서울대학교
성영훈	아산병원
성제경	서울대학교
성하정	크로엔리서치
손성향	아주대학교
손화영	충남대학교
송승우	Harlan Korea Ltd
송창우	안전성평가연구소
신재호	을지대학교
신태훈	제주대학교
신형철	한림대학교
오구택	이화여자대학교
오미경	한양대구리병원
오승현	서울대학교
오연수	강원대학교
오은석	서울대학교병원
우계형	세명대학교
원무호	강원대학교
위갑인	대구경북첨단의료산업진흥재단
유대영	서울대학교
윤기영	신구대학교
윤준원	서울대학교
이경선	오송첨단의료산업진흥재단
이공현	인제대학교 부산백병원
이광훈	대구경북첨단의료산업진흥재단
이국현	서울대학교
이근식	강원대학교
이만휘	경북대학교
이민재	강원대학교
이범준	충북대학교
이병한	오송첨단의료산업진흥재단
이상래	한국생명공학연구원
이상필	㈜한주씨엠아이
이순신	순천향대학교
이윤재	한양대학교 구리병원
이재형	바이오지노케어
이재훈	연세대학교
이정규	㈜중앙실험동물
이정범	순천향대학교
이종권	식품의약품안전처
이준호	㈜바이오피아
이철호	한국생명공학연구원
이충현	단국대학교
이학모	서울대학교병원
이한웅	연세대학교
이현웅	㈜대종기기산업
이현주	㈜샘타코바이오코리아
임재향	이화여자대학교
장용기	㈜베르나바이오텍코리아
장윤성	전북대학교병원
장자준	서울대학교
장재진	㈜오리엔트바이오
전현정	한국식품연구원
정기원	㈜엠제이엘티디
정민재	한림대학교
정원일	한국과학기술원(KAIST)
정의숙	대구경북첨단의료산업진흥재단
제정환	서울대학교
조성대	서울대학교
조우리	대구경북첨단의료산업진흥재단
조익준	오송첨단의료산업진흥재단
조재진	서울대학교
조정식	호서대학교
조준휘	강원대학교병원
진희경	경북대학교
채갑용	식품의약품안전처
천병년	㈜우정바이오
최경철	충북대학교
최병태	부산대학교
최양규	건국대학교
최영석	건국대학교
최영현	동의대학교
최우성	대구경북첨단의료산업진흥재단
최은화	강원대학교
최정훈	강원대학교
최준영	대구경북첨단의료산업진흥재단
최혜윤	대구경북첨단의료산업진흥재단
한남옥	㈜코아텍
한덕주	건일제약㈜
한진주	건국대학교
한태원	한국식품연구원
홍성근	경상대학교
홍의주	충남대학교
황인구	서울대학교
황종익	고려대학교

2024 한국실험동물학회 국제학술대회 협력기관

회사명	대표자	전화번호	홈페이지
AAALAC International	AAALAC	031-696-9626	www.aaalac.org
Cyagen	Lanqing Han	+86-20-31601779	www.cyagen.kr
DBL Co., Ltd.	주재훈	070-4242-1546	www.dbl.kr
SABLESYSTEMS(미래stc)	Lars Breuer	042-822-9801~2	www.miraestc.co.kr
(재)국가모델동물연구소	성제경	02-885-8372	mousephenotype.kr
뉴텍	표광선	042-862-9848	www.new-tech.kr
대구경북첨단의료산업진흥재단(KMEDI)	양진영	053-790-5798	www.kmedihub.re.kr
라온바이오㈜	나종성	031-283-4197	www.raonbio.co.kr
라온시큐어㈜	이순형, 이정아	02-561-4545	www.raonsecure.com
럭키싸이언텍㈜	김철용	032-623-0899	
레비티	강신재	02-868-5313	revvity.co.kr
로킷제노믹스	권태우, 길윤기	1644-7203	rokitgenomics.com
마이크로바이옴핵심연구지원센터	이승우	054-279-2355	
㈜메디코어스	윤귀영	031-698-2008	www.medikors.com
㈜바이오덱	홍찬형	031-928-6412	www.biodech.com
㈜바이오톡스텍	강종구	043-210-7771	www.biotoxtech.com
베트컴㈜	김찬수	02-573-9669	www.vetcom.co.kr
브이에스팜㈜	한준택	02-3436-8252	www.vspharm.co.kr
㈜샘타코바이오코리아	이현주	031-372-3901	www.samtoko.com
㈜싸이텍코리아	박찬승	02-986-4413~5	scitechkorea.com

회사명	대표자	전화번호	홈페이지
㈜쓰리샤인	박천귀	042-933-3361	www.threeshin.com
에이알	한영모	1855-0561	www.arp.co.kr
에이치엘비바이오스텝㈜	문정환	031-523-2002	www.hlbbiostep.com
영바이오	송영종	031-759-9931	www.youngbio.kr
㈜오리엔트바이오	장재진	031-730-6100	www.orientbio.co.kr
오송첨단의료산업진흥재단 비임상지원센터	차상훈	043-200-9823	www.kbiohealth.kr
㈜오스테오시스	안영복	1551-5099	www.osteosys.com
㈜옵티팜	김현일	043-249-7593	www.optipharm.co.kr
㈜우정바이오	천병년	031-280-5220	www.woojungbio.kr
정도비엔피	정병도	02-952-8214	www.jeungdo.co.kr
제주컨벤뷰로	변덕승	064-739-1809	www.jejucvb.or.kr
준바이오텍	박신영	031-307-2792	notatum@hanmail.net
중앙실험동물㈜	이정규	02-3461-5255	www.labanimal.co.kr
㈜코아텍	한남옥	031-611-8221~2, 8224	www.koatech.co.kr
㈜퍼블랩	이재성	02-2081-5693	blog.naver.com/publecorp
포스트바이오	천두성	031-523-2731	www.postbio.com
한국생명공학연구원 실험동물자원센터-모델동물중앙은행	남기환	043-240-6524	mouse.kribb.re.kr
한국생명공학연구원 영장류자원지원센터	김장성	063-570-5312	portal.kribb.re.kr/prc
한신메디칼주식회사	김정열	032-500-8800	www.hanshinmed.co.kr

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TIME TABLE

July 24 (Wed)					
HALL	Halla Hall A	Halla Hall B	Samda Hall	Meeting Room (5F)	Lobby
11:30–13:00			**Council Meeting** (11:30~13:00)		
13:00–14:00	Registration				
14:00–15:40	**(ENG) Symposium 1** Zebrafish animal model to study in vivo mechanisms of disease	**(KOR) Symposium 2 [IACUC]** Post-experiment management of laboratory animals for 3R	**(ENG) AAALAC International** Part 1: Our Journey Balancing the Animal Welfare and Good Science by Voluntary Accreditation		**Booth Installation** Space Only : 10:00~ Shell Scheme (Space+Frame): 16:00~
15:40–16:00	Refreshment				
16:00–17:40	**(KOR) Symposium 3** Unraveling Immune Networks: Insights from Animal Models	**(KOR) Symposium 4 [KLAT Education 1 with KIT]** Anatomy and practical Methods for Animal Testing I	**(ENG) AAALAC International** Part 2: One-point Lesson to Achieve AAALAC International Accreditation		
17:40–19:00					

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<tr><td>09:00–09:40</td><td colspan="3">Registration</td><td></td><td rowspan="3">Poster
부착시간
(09:00~11:00)</td></tr>
<tr><td>09:40–10:00</td><td colspan="2">Opening</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>10:00–11:00</td><td colspan="2">(ENG)
Plenary Lecture 1</td><td>식품의약품안전평가원
/KCLAM 회의
(10:00~11:00)
[301호]</td></tr>
<tr><td>11:00–12:40</td><td>(ENG)
Symposium 5
Frontiers in Metabolic Regulation:
Paving the Way for Therapeutic Insights in Metabolic Diseases and Beyond</td><td>(KOR)
Symposium 6
Precised Animal Care for Disease Model</td><td>(KOR)
Symposium 7
Utility of the Minipigs as Laboratory Animals</td><td>Board Meeting
(11:00~12:00)</td><td rowspan="4">Poster
&
Booth</td></tr>
<tr><td>12:40–13:00</td><td colspan="3">Refreshment & Exhibition visit</td><td rowspan="2">40주년 준비위원회
(12:40~13:10)
[301호]</td></tr>
<tr><td>13:00–13:20</td><td>Luncheon Seminar 1
(SABLESYSTEMS/
㈜미래에스티씨)</td><td>Luncheon Seminar 2
(NEWTECH)</td><td>Luncheon Seminar 3
(포스트바이오)</td><td rowspan="4"></td></tr>
<tr><td>13:20–14:00</td><td colspan="3">Lunch Break</td><td rowspan="2">Poster
Presentation1
(13:20~14:20)</td></tr>
<tr><td>14:00–14:40</td><td>Academy Award Presentation</td><td></td><td></td><td rowspan="3">Poster
&
Booth</td></tr>
<tr><td>14:40–14:50</td><td colspan="3">Refreshment</td></tr>
<tr><td>14:50–16:30</td><td>(KOR)
Symposium 8
[KMPC]
Liver diseases in animal models</td><td>(ENG)
Symposium 9
[NIFDS 1]
Recent Trends in Stem Cell & Organoid Research</td><td>(KOR)
Symposium 10
Exploring Sensory Impairments: In Vivo Studies on Animal Models with Vision and Hearing Defects</td><td>AAALAC Int'
Meeting
(15:00~17:00)
[301호]</td></tr>
<tr><td>16:30–17:00</td><td colspan="3">Refreshment</td><td colspan="2"></td></tr>
<tr><td>17:00–19:00</td><td colspan="4">General Meeting & Welcome Reception (Tamna Hall 5F)</td><td></td></tr>
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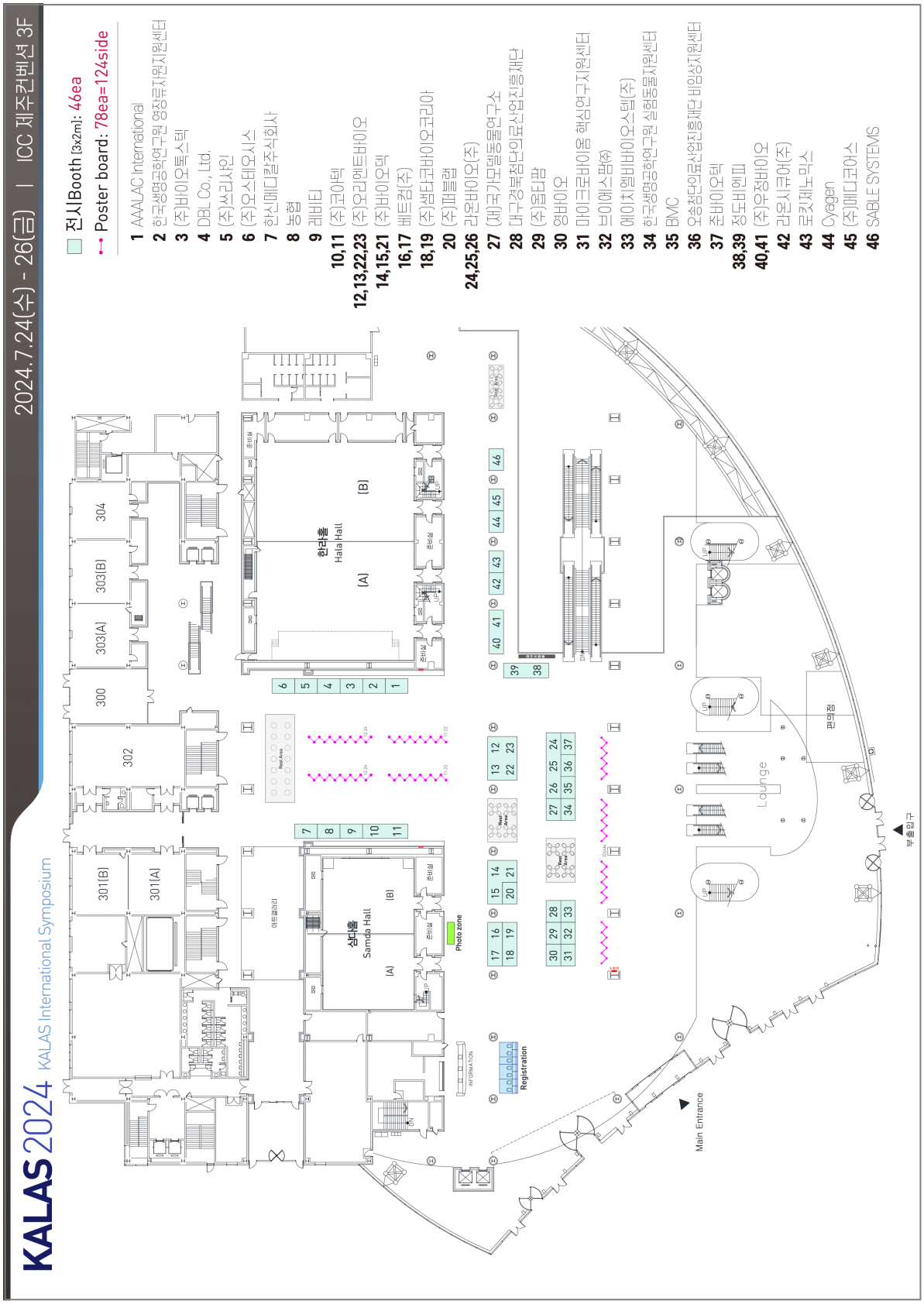
July 26 (Fri)

HALL	Halla Hall A	Halla Hall B	Samda Hall	Meeting Room (3F)	Lobby
08:30–09:00	Registration				
09:00–10:40	(ENG) **Symposium 11** **[NIFDS 2]** Revolution of laboratory rodent health monitoring	(ENG) **Symposium 12** Cell-Gene Immunotherapy using Humanized Animal Models	(ENG) **Symposium 13** Modeling Human Brain Development and Diseases	**산학협력 간담회** (10:00~10:30) [301호]	**Poster** **부착시간** (09:00–11:00)
10:40–11:00	Refreshment & Exhibition visit				
11:00–12:00	(ENG) **Plenary Lecture 2**				**Poster** **&** **Booth**
12:00–12:10	Refreshment				
12:10–12:30	**Luncheon Seminar 4** (한신메디칼)	**Luncheon Seminar 5** (GemPharmatech)	**Luncheon Seminar 6** (WoojungBio)		
12:30–14:00	Lunch Break				**Poster** **Presentation 2** (13:00–14:00)
14:00–15:30	(ENG) **Symposium 14** Immunosuppressive treatment and immune monitoring protocol for the preclinical NHP study of xeno solid organ transplantation	(KOR) **Symposium 15** **[KLAT Education 2]** Anatomy and practical Methods for Animal Testing II	(KOR) **Symposium 16** Research trends and perspectives of animal models for functional gastrointestinal disease		**Poster** **&** **Booth**
15:30–15:50		**기술원 QUIZ EVENT**			
15:50–16:20	**Giveaway &** **Closing Ceremony**				

July 27 (Sat)

HALL	Halla Hall A
09:30–11:10	Satellite meeting

HALL INFORMATION



PROGRAM

July 24 (Wed)

Symposium 1 ENG

Halla Hall A (14:00–15:40)

Zebrafish animal model to study in vivo mechanisms of disease

Organizer / Chair : **Jeong-Soo Lee** (KRIBB), **Hae Chul Park** (Korea Univ.)

Uncovering the secrets of tissue regeneration: From gene discovery to elucidating the mechanisms	**Junsu Kang**	Univ. of Wisconsin
Zebrafish model to study muscle development and regeneration	**Seong-Kyu Choe**	Wonkwang Univ.
Application of zebrafish model to study peripheral nervous system disorders	**Ji Eun Lee**	Sungkyunkwan Univ.
Neurotoxic effects of β-citronellol via KYN to 3-HK metabolic activation	**Suhyun Kim**	Korea Univ.

Symposium 2 [IACUC] KOR

Halla Hall B (14:00–15:40)

Post-experiment management of laboratory animals for 3R

Organizer / Chair : **Seung Hyeok Seok** (Seoul Natl. Univ.)

Considerations for end-experimental animals	**Ji Min Lee**	Seoul Natl. Univ.
Sharing and utilization of animal biological resources	**So Young Yune**	Ministry of Food and Drug Administration
Laboratory animal rehoming	**Jae-Hun Ahn**	Seoul Natl. Univ. Hospital
Advancing the 3Rs principle: scientific and ethical considerations for responsible reuse of laboratory animals	**Seung Hyeok Seok**	Seoul Natl. Univ.

AAALAC International ENG

Samda Hall (14:00–15:40)

Part 1: Our Journey Balancing the Animal Welfare and Good Science by Voluntary Accreditation

Organizer / Chair : **Montip Gettayacamin** (AAALAC International), **Young-Shin Joo** (The Catholic Univ. of Korea)

Animal care and use program management	**Hae-Jin Yoon**	KIT
Personnel and research management	**Jungmin Lee**	Samsung Medical Center
Internal oversight of the animal care and use program	**Ji Yeon Hwang**	Seoul Natl. Univ.
Overall veterinary care provision and communication	**Young-Shin Joo**	The Catholic Univ. of Korea
KOATECH facility applying 'The Guide'	**Jeong Hee Park**	Korean Animal Technology (KOATECH)

Symposium 3 KOR

Halla Hall A (16:00–17:40)

Unraveling Immune Networks: Insights from Animal Models

Organizer: **Hyeyoung Min** (Chung-Ang Univ.), **Jae-Hoon Choi** (Hanyang Univ.), **Ho-Keun Kwon** (Yonsei Univ.), **Jun-Young Seo** (Yonsei Univ.)
Chair : **Ho-Keun Kwon** (Yonsei Univ.), **Jae-Hoon Choi** (Hanyang Univ.)

Post-COVID pulmonary injury in hACE2 mice shows persistent neutrophils and neutrophil extracellular trap formation	**Juwon Park**	University of Hawai'i at Mānoa
Regulation of macrophage activation in cardiovascular diseases	**Sungho Park**	UNIST
Transgenic mouse models: invaluable tools for humoral immunity	**Youn Soo Choi**	Seoul Natl. Univ.
Microglial inflammasome-dependent regulation of blood-brain barrier integrity	**Jewook Yu**	Yonsei Univ.

PROGRAM

Symposium 4 [KLAT Education 1 with KIT] KOR	Halla Hall B (16:00–17:40)	
Anatomy and practical Methods for Animal Testing I		
Organizer / Chair : **Jeong-Hwan Che** (Seoul Natl. Univ. Hospital)		
Assessment of rodent respiratory toxicity and respiratory function	**Se Ran Yang**	Kangwon Natl. Univ.
Experimental technique in gastrointestinal research using rodents	**Jong Hwang Park**	Chonnam Natl. Univ.
Assessment of brain and nervous system function	**Jae Ho Shin**	Eulji Univ.
Characteristics and key research methods of the hematopoietic system	**Yi Rang Na**	Seoul Natl. Univ. Hospital

AAALAC International ENG	Samda Hall (16:00–17:40)	
Part 2: One-point Lesson to Achieve AAALAC International Accreditation		
Organizer : **Montip Gettayacamin** (AAALAC International), **Young-Shin Joo** (The Catholic Univ. of Korea) Chair : **Montip Gettayacamin** (AAALAC International), **Seung Hyeok Seok** (Seoul Natl. Univ.)		
Overview and update of AAALAC international accreditation program	**Montip Gettayacamin**	AAALAC International
Step 1: Preparing the program description and site visit	**Young-Shin Joo**	The Catholic Univ. of Korea
Step 2: Expectation of the post site visit communication and council deliberations	**Seung Hyeok Seok**	Seoul Natl. Univ.
Q&A Session	**All speaker and participants**	

July 25 (Thu)

Plenary Lecture 1 ENG	Halla Hall (10:00–11:00)	
Organizer / Chair : **Je Kyung Seong** (Seoul Natl. Univ.)		
Insights from rodent models for understanding diabetic retinopathy	**Jesús Ruberte Paris**	Autonomous University of Barcelona

Symposium 5 ENG	Halla Hall A (11:00–12:40)	
Frontiers in Metabolic Regulation: Paving the Way for Therapeutic Insights in Metabolic Diseases and Beyond		
Organizer: **Su Myung Jung** (Sungkyunkwan Univ.), **Hui-Young Lee** (Gachon Univ.), **Hyunji Lee** (Korea Univ.) Chair : **Su Myung Jung** (Sungkyunkwan Univ.), **Seung-Hoi Koo** (Korea Univ.)		
Elucidating adipocytes functions through development	**Joan Sanchez-Gurmaches**	Cincinnati Children's Hospital
Role of CRTC2 in metabolic disorders	**Seung-Hoi Koo**	Korea Univ.
Targeting immunometabolic functions of adipose tissue macrophages: therapeutic perspectives from animal model studies	**Yun-Hee Lee**	Seoul Natl. Univ.
Fibrotic niche-enriched single-cell transcriptomics uncovers novel age-associated cell type in liver	**Chuna Kim**	KRIBB

Symposium 6 KOR	Halla Hall B (11:00–12:40)	
Precised Animal Care for Disease Model		
Organizer: **Seung Hyun Oh** (Seoul Natl. Univ.) / Chair : **Hee Jin Kim** (WoojungBio)		
Advancing vivarium efficiency and animal welfare through digitalization: the scientific advantages of the DVC system	**Guglielmo Vismara**	Tecniplast
Good care and use laboratory animals in ABSL3 facility	**Sung-Hee Kim**	Yonsei Univ.
Animal experiments in germ free condition	**Hye Jin Kim**	KMPC

Symposium 7 KOR		Samda Hall (11:00–12:40)
Utility of the Minipigs as Laboratory Animals		
Organizer: **Jong Ki Cho** (Seoul Natl. Univ.) / Chair : **Byeong-Cheol Kang** (Seoul Natl. Univ.)		
Development of wound healing agents using minipigs	**Sokho Kim**	Kunsan Natl. Univ.
The use of miniature swine for preclinical modeling in cardiovascular research	**Se-Il Park**	Yonsei Univ.
Dermal toxicity and efficacy study using yucatan minipig	**Jeong Ho Hwang**	KIT
Trends in the development of bio-resources using miniature pigs	**Hyunil Kim**	Optipharm Inc.

Luncheon Seminar 1		Halla Hall A (13:00–13:20)
Organizer / Chair : **Dae Youn Hwang**		
Sable Systems社의 대사 비만 측정 분석 시스템 소개	**Lars Breuer**	SABLE SYSTEMS

Luncheon Seminar 2		Halla Hall B (13:00–13:20)
Organizer: **Je Kyung Seong** / Chair : **Sungsoon Fang**		
Validation of operations, facilities, and equipment for animal (marmoset) biosafety level 3 facility approval	**Yong Sub Byun**	오송첨단의료산업진흥재단 (KBIOhealth)

Luncheon Seminar 3		Samda Hall (13:00–13:20)
Organizer / Chair : **Byeong-Cheol Kang**		
Practical approach of point of care qPCR to monitor infectious pathogens for laboratory animals and facilities	**Doo-Sung Cheon**	POSTBIO

Poster Presentation 1	Lobby (13:20–14:20)
Chair : **Jae-Hoon Choi** (Hanyang Univ.)	

Academy Award Presentation		Halla Hall A (14:00–14:40)
Chair : **Je Kyung Seong** (Seoul Natl. Univ.)		
Development of the mammalian cochlea capable of frequency discrimination	**Jinwoong Bok**	Yonsei Univ.
SARS-CoV-2 Omicron variant causes brain infection with lymphoid depletion in a mouse COVID-19 model	**Na Yun Lee**	Seoul Natl. Univ.

PROGRAM

Symposium 8 [KMPC] KOR		Halla Hall A (14:50–16:30)
Liver diseases in animal models		
Organizer: **Je Kyung Seong** (Seoul Natl. Univ.) / Chair : **Jun-Won Yun** (Seoul Natl. Univ.)		
RORα-GABP-TFAM axis alleviates myosteatosis with fatty atrophy through reinforcement of mitochondrial capacity	**Mi-Ock Lee**	Seoul Natl. Univ.
Hepatic steatosis and steatohepatitis through immunometabolic synapse	**Won-Il Jeong**	KAIST
Altered hepatotoxic properties of SARS-CoV-2 mRNA vaccine in an animal model for type 2 diabetes	**Jun-Won Yun**	Seoul Natl. Univ.
Emerging insights: MASH-associated HCC progression	**Kyoung-Jin Oh**	KRIBB

Symposium 9 [NIFDS 1] ENG		Halla Hall B (14:50–16:30)
Recent Trends in Stem Cell & Organoid Research		
Organizer: **Hye-Jin Boo** (Jeju Natl. Univ.), **Ok Nam Bae** (Hanyang Univ.), **Jun Won Yun** (Seoul Natl. Univ.) Chair : **Jae-Jin Cho** (Seoul Natl. Univ.)		
Hair follicle stem cell and tissue regeneration	**Hanseul Yang**	KAIST
Organoid modelling of human fetal lung development	**Kyungtae Lim**	Korea Univ.
Biomaterials and devices for advanced organoid engineering	**Seung-Woo Cho**	Yonsei Univ.
Salivary gland organoids for investigating the etiology of xerostomia	**Hyung-Sik Kim**	Pusan Natl. Univ.

Symposium 10 KOR		Samda Hall (14:50–16:30)
Exploring Sensory Impairments: In Vivo Studies on Animal Models with Vision and Hearing Defects		
Organizer: **Dong Hyun Jo** (Seoul Natl. Univ.) / Chair : **Jinwoong Bok** (Yonsei Univ.)		
Establishing patient-mimicking mutant mice for the development of gene editing therapy	**Young Hoon Sung**	Ulsan Natl. Univ.
Therapeutic application on angiogenesis-related ocular diseases	**Seok Jae Lee**	Seoul Natl. Univ. Hospital
Allele-specific antisense oligonucleotide ameliorates KCNQ4-related autosomal dominant hearing loss	**Seung Hyun Jang**	Yonsei Univ.
In vivo base editing in humanized mice mimicking patients with retinoschisis	**Dong Hyun Jo**	Seoul Natl. Univ.

General Meeting & Welcome Reception	Tamna Hall 5F (17:00–19:00)

July 26 (Fri)

Symposium 11 [NIFDS 2] ENG

Halla Hall A (09:00–10:40)

Revolution of laboratory rodent health monitoring

Organizer: **Byeong-Cheol Kang** (Seoul Natl. Univ.)
Chair : **Byeong-Cheol Kang** (Seoul Natl. Univ.), **Jong Kwon Lee** (Ministry of Food and Drug Administration)

Health monitoring of laboratory rodent colonies-talking about (R)evolution	**Byeong-Cheol Kang**	Seoul Natl. Univ.
Prevalence of parvovirus in rodent: how can we deal with chappavovirus in SPF rodent?	**Yang-Kyu Choi**	Konkuk Univ.
Validation of a newly developed laboratory animal microbiological monitoring kit	**Ki Taek Nam**	Yonsei Univ.

Symposium 12 ENG

Halla Hall B (09:00–10:40)

Cell-Gene Immunotherapy using Humanized Animal Models

Organizer / Chair : **Kyung-Sun Kang** (Seoul Natl. Univ.)

In vivo and *in vitro* studies for evaluation of tumorigenicity of cell therapy product	**Yoji Sato**	National Institute of Health Sciences
Development of CD19 CAR-NK therapy targeting pericytes in the tumor microenvironment using a glioblastoma-blood vessel assembloid xenograft model	**Kyung-Sun Kang**	Seoul Natl. Univ.
Assessing the impact of CRISPR/Cas9 based *ex vivo* HSC gene therapy: insights from rhesus macaque competitive repopulation model	**Byung-Chul Lee**	Sookmyung Women's Univ.
Humanized mice are essential tools for evaluation of cell and gene therapies to move towards a clinical trial	**Sang-Nyun Kim**	Orient Genia
Regenerative approaches for off-the-shelf hypoimmunogenic stem cells	**Da-Hyun Kim**	Sung Shin Women's Univ.

Symposium 13 ENG

Samda Hall (09:00–10:40)

Modeling Human Brain Development and Diseases

Organizer / Chair : **Hosung Jung** (Yonsei Univ.), **Hyuk-Wan Ko** (Yonsei Univ.)

Modeling neurodevelopmental disorders using human pluripotent stem cells	**Hyunsoo Shawn Je**	Duke-NUS Medical School
Deciphering the neural epitranscriptome: the roles of mRNA modification in neurodevelopment	**Ki-Jun Yoon**	KAIST
Human spinal cord organoids as a model system for human neurodevelopment and disease	**Ju-Hyun Lee**	KIST
Decoding immune-microbiome-brain axis in a neurodevelopmental disorder mouse model	**Eunha Kim**	Korea Univ.

Plenary Lecture 2 ENG

Halla Hall (11:00–12:00)

Organizer / Chair : **Hyuk-Wan Ko** (Yonsei Univ.)

The current insights into Alzheimer's disease research and advancements in therapeutic development	**Inhee Mook**	Seoul National University

PROGRAM

Luncheon Seminar 4		**Halla Hall A** (12:10–12:30)
		Organizer: **Dae Youn Hwang**
의료용 멸균기 전문기업 한신메디칼주식회사 후원		

Luncheon Seminar 5		**Halla Hall B** (12:10–12:30)
		Organizer / Chair : **Ki Taek Nam**
Humanized models for tumor research	**Joseph Seo**	GemPharmatech Co. Ltd.

Luncheon Seminar 6		**Samda Hall** (12:10–12:30)
		Organizer: **Je Kyung Seong** / Chair : **Hyung-Sik Kim**
동물실 병원체 감염 확산의 물리적 차단과 박멸	**Gyeong Geon Kim**	WoojungBio
동물실험실 Facility Management	**Chang Hun Lee**	WoojungBio

Poster Presentation 2		**Lobby** (13:00–14:00)
		Chair : **Jun-Won Yun** (Seoul Natl. Univ.)

Symposium 14 ENG		**Halla Hall A** (14:00–15:50)
Immunosuppressive treatment and immune monitoring protocol for the preclinical NHP study of xeno solid organ transplantation		
		Organizer: **Ik Jin Yun** (Konkuk Univ. Hospital) / Chair : **Ik Jin Yun** (Konkuk Univ. Hospital), **Hyun Il Kim** (OptiPharm)
Immune modulation and monitoring in the nonhuman primate xenotransplantation experiments	**Hidetaka Hara**	Hainan Medical University
Immunosuppressive treatment protocol for the xeno solid organ transplantation of NHP preclinical model in Japan	**Takashi Yokoo**	The Jikei University School of Medicine
Immunosuppression for solid organ xenotransplantation	**Jaeseok Yang**	Yonsei Univ.
Histocompatibility test for xenogenic solid organ transplantation in a preclinical model of NHP in Korea	**Eun-Jee Oh**	The Catholic Uinv. Seoul St. Mary's Hospital

Symposium 15 [KLAT Education 2] KOR		**Halla Hall B** (14:00–15:30)
Anatomy and practical Methods for Animal Testing II		
		Organizer: **Dong-jae Kim** (DGIST), **Yirang Na** (Seoul Natl. Univ. Hospital) / Chair : **Hyunjhung Jhun** (KFRI)
Anatomy and practical methods for Laboratory animal eyes	**Won Tae Kim**	Keyprime Research
Normal anatomy and evaluation methods of bone	**Jin Seok Kang**	Namseoul Univ.
Mouse models for liver cancer; anatomy, modeling, and histopathology	**Seung-Ho Heo**	Asan Medical Center

Symposium 16 KOR		Samda Hall (14:00–15:50)
Research trends and perspectives of animal models for functional gastrointestinal diseas		
		Organizer / Chair : **Chang-Woo Song** (KIT)
Animal models for functional dyspepsia (FD) and screening test for drug candidate	**Chang-Gue Son**	Daejeon Univ.
Effects of vagotomy on GI motility and evaluation as an animal model	**Young-Su Yang**	KIT
Development of gastrointestinal disease model animals using *Helicobacter pylori*	**Yung Choon Yoo**	Konyang Univ.
Use of human/animal-derived intestinal stem cells and their differentiated cells to mimic intestinal metabolism and physiology	**Kazuya Maeda**	Kitasato Univ.

Giveaway & Closing Ceremony	Halla Hall A (15:50–16:20)

July 27 (Sat)

Satellite meeting	Halla Hall A (09:30–11:10)

CONFERENCE AND EVENT INFORMATION

1. 개회식 (Opening Ceremony)

July 25 (Thu) 09:40 ~ 10:00 / Halla Hall A

- 개회사: 고혁완 학술위원장
- 인사말: 성제경 이사장

2. 총회 및 환영만찬 (General Meeting & Welcome Reception)

July 25 (Thu) 17:00~19:00 / Tamna Hall (5F)

- 개회사: 오승현 총무위원장

1) 총회 안건

2) 학술상 시상식

① 실험동물학술상(대상)

시상: 성제경 이사장

성 명	소 속
복진웅	연세대학교

② 젊은과학자상

성 명	소 속
이나윤	서울대학교

③ LAR 다수논문게재상

성 명	소 속
황대연	부산대학교

④ LAR 다수논문인용상

성 명	소 속
고필옥 김종춘 최영현	경상대학교 전남대학교 동의대학교

⑤ 실험동물연구장학생

시상 : 고혁완 학술위원장

구 분	성 명	소 속
그룹 I	김태렬 손현경 이연수	부산대학교 경상대학교 을지대학교

3) 환영만찬

3. 폐회식 (Closing Ceremony)

• July 26 (Fri) 15:50~16:20 / Halla Hall A
1) 우수포스터상 시상 – 시상: 고혁완 학술위원장
2) 경품추첨
3) 폐회사
– 인사말: 성제경 이사장
– 폐회사: 고혁완 학술위원장
4) 기념촬영

4. 관련위원회 회의 및 모임 (Commitee & Meeting)

• KALAS 평의원회 (Council Meeting)
July 24 (Wed) 11:30~13:00 / 3F 삼다홀 (Samda Hall)
참석대상: 한국실험동물학회 평의원

• KALAS 이사회 (Board Meeting)
July 25 (Thu) 11:00~12:00 / 3F 델리지아
참석대상: 한국실험동물학회 이사 9명 및 감사 2명

• KALAS 우수포스터상 선정 회의
July 26 (Fri) 14:00~14:30 / Room 300 (사무국)
참석대상: 학술위원회 및 포스터 심사위원

• AAALAC KALAS MEETING
July 25 (Thu) 15:00~17:00 / Room 301
참석대상: AAALAC 관계자 등

• 40주년 준비위원회
July 25 (Thu) 12:40~13:10 / Room 301
참석대상: 40주년 준비위원회 및 관계자

• 산학협력 간담회
July 26 (Fri) 10:00~10:30 / Room 301

• 식품의약품안전평가원 / KCLAM 회의
July 25 (Thu) 10:00~11:00 / Room 301

5. 점심식사 안내 (Luncheon Seminar)

런천세미나		기업명	장소	티켓 수령처
July 25 (Thu) 13:00~13:20	LS 1	SABLE SYSTEMS/㈜미래에스티씨	Halla Hall A	09:30부터 기업부스 (선착순 100명)
	LS 2	NEWTECH	Halla Hall B	09:30부터 등록대 (선착순 100명)
	LS 3	POSTBIO	Samda Hall	09:30부터 등록대 (선착순 100명)
July 26 (Fri) 12:10~12:30	LS 4	HANSHIN MEDICAL	Halla Hall A	09:30부터 기업부스 (선착순 100명)
	LS 5	GemPharmatech	Halla Hall B	09:30부터 등록대 (선착순 100명)
	LS 6	WoojungBio	Samda Hall	09:30부터 기업부스 (선착순 100명)

※ 런천 티켓은 한정 수량으로 조기 품절될 수 있습니다.

※ 런천 세미나 강연을 청취하신 후 퇴실 시 도장을 받고 식당에서 티켓 확인 후 식사가 제공되는 쿠폰입니다.
도장이 없는 경우 식사가 불가능한 점 참고 바랍니다.

※ 식사장소: 3F 델리지아

LS 1: SABLE SYSTEMS/㈜미래에스티씨
주제: Sable Systems社의 대사 비만 측정 분석 시스템 소개
연자: Lars Breuer (SABLE SYSTEMS)

LS 2: NEWTECH
주제: Validation of Operations, Facilities, and Equipment for Animal (Marmoset) Biosafety Level 3 Facility Approval
연자: Yong Sub Byun (오송첨단의료산업진흥재단(KBIOhealth))

LS 3: POSTBIO
주제: 실험동물 헬스모니터링을 위한 현장용 리얼타임 피씨알의 적용 (Practical Approach of Point of Care qPCR to Monitor Infectious Pathogens for Laboratory Animals and Facilities)
연자: Doo-Sung Cheon (POSTBIO)

LS 4: HANSHIN MEDICAL
주제: 의료용 멸균기 전문기업 한신메디칼주식회사가 후원

LS 5: GemPharmatech
주제: Humanized Models For Tumor Research
연자: Joseph Seo (GemPharmatech)

LS 6: WoojungBio
주제: 동물실 병원체 감염 확산의 물리적 차단과 박멸
연자: Gyeong Geon Kim (WoojungBio)

주제: 동물실험실 Facility Management
연자: Chang Hun Lee (WoojungBio)

6. 실험동물연구장학생 포스터 발표

발표시간	7월 25일(목) 13:20-14:20
발표장소	제주 국제컨벤션센터 3층 로비
포스터 번호	PS-R-001 (해부병리) PS-R-002 (독성병리) PS-R-003 (해부병리)
	총 3개
부착 시간	7월 25일(목) 09:00-11:00
철거 시간	7월 25일(목) 17:00

※ 철거 시간 이후의 포스터 분실은 책임지지 않습니다.

- 포스터 발표는 좌장의 진행에 따라 포스터당 7분 (5분 발표, 2분 질의응답)으로 진행되며, 발표시간에 포스터 앞에 대기하여 주시기 바랍니다.

7. 포스터 발표 (Poster Session)

발표시간	포스터 발표 1	포스터 발표 2
	7월 25일(목) 13:20-14:20	7월 26일(금) 13:00-14:00
발표장소	제주 국제컨벤션센터 3층 로비	
포스터 번호	PS-A-001~020 (해부병리) PS-B-001~030 (독성병리) PS-C-001~010 (미생물) PS-D-001~040 (유전자질환모델) PS-E-001~021 (시설운영 및 기타)	PS-A-021~048 (해부병리) PS-B-031~067 (독성병리) PS-C-011~019 (미생물) PS-D-041~070 (유전자질환모델) PS-E-022~041 (시설운영 및 기타)
	총121개	총124개
부착 시간	7월 25일(목) 09:00-11:00	7월 26일(금) 09:00-11:00
철거 시간	7월 25일(목) 17:00	7월 26일(금) 17:00

※ 철거 시간 이후의 포스터 분실은 책임지지 않습니다.

- 포스터 심사
  - 포스터 발표는 좌장의 진행에 따라 포스터당 4분(3분 발표, 1분 질의응답)으로 진행되며, 과학적 성과와 발표자의 발표력 등을 기준으로 우수포스터를 선정하여 시상하오니 반드시 발표시간에 포스터 앞에 대기해 주시기 바랍니다.
- 미부착 포스터: 포스터 보드에 2회 이상 (개수로 적용) 미부착 시, 교신저자(연구책임자)에게 향후 1년간 포스터 제출 불가의 제재가 주어집니다.
- 우수포스터상 시상
  - 우수포스터상 시상: 7월 26일 (금) 15:50-16:20/폐회식
  - 우수포스터의 경우 폐회식에서 선정자를 호명합니다. 호명 시 자리에 없으면 다음 우수자에게 상이 수여되오니, 학술대회 종료일까지 학술대회에 꼭 참석해 주시기 바랍니다. (상장과 상금 15만원 수여, 대리수상불가)

8. 이벤트 및 경품추첨 안내 (Event & Giveaway)

1) 환영만찬 노래자랑 이벤트

진행일시 | 7월 25일(목) 17:00 총회 및 환영만찬

참여방법 | 사전접수 및 현장접수

경　　품 | 백화점상품권 30/20/10/1만 원권, 기타 등

2) 실험동물기술원 교육강연 퀴즈이벤트

진행일시 | 7월 26일(금) 14:00~ Halla Hall B / KLAT Education Ⅱ 이후 진행

참여방법 | 스마트폰 앱/Play 스토어에서 퀴즈를 위한 **카훗(Kahoot) 앱 다운로드** 후 참여

경　　품 | 에어팟, 백화점상품권 10/5/3/1만 원권

3) 폐회식 경품추첨

진행일시 | 7월 26일(금) 15:50 폐회식에서 추첨 / 폐회식

참여방법 | ① KALAS2024하계 App 다운로드

② 하계심포지엄 설문지 작성

③ App 을 열어 34개 부스 스탬프 투어 달성

부스 투어 이벤트 마감 : 7/26(금) 14:30 까지

경　　품 | 갤럭시탭 S9, 상품권 30만원, 10만원, 5만원, 1만원 등

※ KALAS Exhibition Hall (전시장) 운영 규칙

전시장에 입장시에는 항상 명찰을 잘 보이도록 착용하여야 한다. 전시장에 참여한 단체의 활동은 배정된 구역 내에서 진행되어야 한다. 해당 소속 전시 부스 이외의 타사 부스에 허락 없이 들어갈 수 없다. 사진촬영은 금지한다. 해당 부스의 전시책임자의 허가 없이 타 참여사의 제품 혹은 장비를 사진, 동영상, 혹은 기타 방식으로 기록 보관할 수 없다. 전시장을 포함하여 컨벤션홀 내부 전체는 모두 금연이다.

Safety & Security

모든 참여사의 인원들은 전시장 내부에서 항상 명찰을 잘 보이도록 착용하여야 한다.
발급받은 명찰은 어떠한 방식으로든 변경하거나 삭제할 수 없다.
참여 단체의 전시에 참여하는 인원은 해당 전시사의 허가 없이 타사 부스에 들어갈 수 없다.

KALAS 규정

전시장에 참여하는 참여사 인원과 학회 참가자는 모두 KALAS의 규정에 따라야 한다. 규정에 어긋나거나 학술대회 및 전시장에 심각한 문제를 일으키는 경우, KALAS의 권한으로 전시사 및 참가자는 페널티를 부여 받을 수 있다. 페널티는 전시사나 참가자를 전시홀에서 퇴장시키거나 사전 공지없이 전시 권한을 즉각 종료 시키고 전시를 마감할 수 있으며, 위의 사항들은 중복되어 부여될 수도 있다. 모든 규정의 실행은 최종적으로 학회 섭외위원회의 결정에 의거한다.

TRANSPORTATION INFORMATION

[제주 국제컨벤션센터(ICC)]

- 주소 : 제주특별자치도 서귀포시 중문관광로 224 (중문동)
- 전화 : 064-735-1000
- 홈페이지 : iccjeju.co.kr

[교통안내]

1. 리무진 버스 (600번 제주공항 ↔ 중문관광단지)
   - 탑승장: 공항정문 1층 5번 게이트 왼쪽 리무진 버스 승차장
   - 운행표

공항→제주 썬호텔→삼무공원사거리/롯데시티호텔→한라병원→정존마을→동광환승정류소→창천리→
우남동→예래입구→중문관광단지입구→여미지식물원입구→그랜드 조선 제주→파르나스호텔→신라호텔→
스위트호텔→블룸호텔/한국관광공사→롯데호텔→켄싱턴리조트 중문점입구→플레이케이팝박물관→
씨 에스호텔→ 제주국제컨벤션센터 중문대포해안주상절리대→대포항→배튼개입구(히든호텔)→약천사→
월평마을→강정농협→왕대왓→켄싱턴리조트(약근천)→서건도→제주월드컵경기장→샛기정공원→
서귀포항(화인호텔)→서복전시관→파라다이스호텔입구→서귀포칼호텔

※ 항공기 이착륙 시간 변경. 기상이변, 행사관계 등으로 수송수요에 변동이 생길 경우에는
증회 또는 운행시간이 조정될 수 있음.
※ 공항 출발 22:20, 22:50분 차량은 테디벨리골프장 정류소 정차.
※ 공항 출발 22:40분 차량은 수모루 정류소 정차.

   - 운행시간 (매 16~40분 간격으로 운행)
     (1) 제주국제공항출발 (06:00-10:40)
     (2) 서귀포(칼호텔)출발 (06:37-22:15)
     ※ 전체 운영시간표 사이트 참고 → https://bus.jeju.go.kr/schedule/viewNew/600
   - 이용요금: 공항에서 ICC JEJU까지 편도(성인) 4,500원 (ICCJEJU까지 소요시간 약 1시간 소요)
   - 이용문의: 삼영교통 (064) 713-7000

2. 택시 (제주공항 ↔ 중문)
   - 택시승차장 장거리, 단거리 확인: 제주공항 택시승차장에서 이용시
     장거리 승차장에서 출발하여 오십시오. 요금은 미리 정해져 있으므로 승차전에 확인하세요.
   - 이용안내: 약 50분 (거리 42km)

2024

KALAS

International Symposium

www.kalas.or.kr

SYMPOSIUM 1 ENG

July 24 (Wed) 14:00–15:40 | Halla Hall A

Zebrafish animal model to study in vivo mechanisms of disease

Organizer / Chair : **Jeong-Soo Lee** (KRIBB), **Hae Chul Park** (Korea Univ.)

Uncovering the secrets of tissue regeneration:
From gene discovery to elucidating the mechanisms

Junsu Kang (Univ. of Wisconsin)

Zebrafish model to study muscle development and regeneration

Seong-Kyu Choe (Wonkwang Univ.)

Application of zebrafish model to study peripheral nervous system disorders

Ji Eun Lee (Sungkyunkwan Univ.)

Neurotoxic effects of β-citronellol via KYN to 3-HK metabolic activation

Suhyun Kim (Korea Univ.)

KOREAN ASSOCIATION
FOR LABORATORY ANIMAL SCIENCE

S1-1

Harnessing the regenerative potential of *interleukin11* to enhance heart repair

Junsu Kang

[1]*Department of Cell and Regenerative Biology, School of Medicine and Public Health, University of Wisconsin - Madison, Madison, WI, USA*
[2]*UW Carbone Cancer Center, School of Medicine and Public Health, University of Wisconsin - Madison, Madison, WI, USA*

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Balancing regenerative processes and fibrosis is crucial for heart repair, yet strategies to regulate this balance remain a barrier to developing an effective therapy for heart repair. Here, we uncovered that *interleukin11a* (*il11a*), an Il11 homolog in zebrafish, can initiate robust regenerative programs in the zebrafish heart, including cell cycle reentry of cardiomyocytes (CMs) and coronary expansion, even in the absence of injury. However, prolonged *il11a* induction in uninjured hearts causes persistent emergence of fibroblasts, resulting in cardiac fibrosis. While deciphering the regenerative and fibrotic effects of *il11a*, we found that il11-dependent fibrosis, but not il11-dependent regeneration, is mediated through ERK activity, implying that the dual effects of *il11a* on regeneration and fibrosis can be uncoupled. To harness the regenerative ability of *il11a* for injured hearts, we devised a combinatorial treatment that induces *il11a* while inhibiting ERK. This approach enhances CM proliferation and mitigates fibrosis, achieving a balance between regenerative processes and fibrosis. Thus, our findings unveil the mechanistic insights into the regenerative roles of il11 signaling, offering potential avenues to utilize a paracrine regenerative factor to foster cardiac repair without exacerbating the fibrotic responses.

Key words : Heart, regeneration, zebrafish, fibrosis, interleukin11

S1-2

Zebrafish model to study muscle development and regeneration

Seong-Kyu Choe

Department of Microbiology and Sarcopenia Total Solution Center, Wonkwang University School of Medicine

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Skeletal muscle accounts for 40% of total body weight and is a critical component influencing human health and disease. The integrity of skeletal muscle is dependent on a fine balance of molecular mechanisms that govern organelle homeostasis. In this talk, I will discuss the similarities in muscle structure between mammals and zebrafish, as well as the methods available for studying zebrafish skeletal muscle. In addition, I will introduce various gene knockout zebrafish and describe their skeletal muscle characteristics. Elucidating the genes that play essential roles in zebrafish skeletal muscle development and functional maintenance may help us comprehend molecular pathways in skeletal muscle biology and uncover new therapeutic approaches for treating muscle illnesses in humans.

Key words : Zebrafish, Muscle, Knockout, Phenotypes, Organelles

S1-3

Application of zebrafish model to study peripheral nervous system disorders

Ji Eun Lee

[1]*Dept. Health Sciences and Technology, SAIHST, Sungkyunkwan University*
[2]*Samsung Biomedical Research Institute, Samsung Medical Center, Seoul, Korea*

jieun.lee@skku.edu

In neuromuscular junction (NMJ)-related diseases, including Charcot-Marie-Tooth (CMT), pathological mechanisms are being revealed as various causative genes have been identified. However, there are still no targeted treatments for this disease, so multiple approaches are needed to develop treatments. Here, we apply the zebrafish animal model system to generate NMJ disease models and study disease mechanisms. We verify the relevance of the identified mutations in CMT disease mechanisms in vivo by introducing mutated human genes into zebrafish or modifying the disease genes in zebrafish. To determine whether 1) Schwann cell-derived extracellular vesicles (EVs) or 2) control of microtubule dynamics are important for the development or function of NMJs, we treated zebrafish larvae exhibiting NMJ defects with candidate chemicals and EVs. Our data reveal that Schwann cell-derived EVs or HDAC6 inhibitors are effective in restoring NMJ defects in zebrafish, suggesting that they can be considered as potential treatments for CMT with NMJ damage.

Key words : Zebrafish, Neuromuscular Junction, Charcot-Marie-Tooth, Extracellular Vesicle, HDAC6 inhibitor

S1-4

Neurotoxic effects of β-citronellol via KYN to 3-HK metabolic activation

Suhyun Kim

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The zebrafish model has been extensively employed to evaluate the developmental neurotoxic effects of chemicals due to the significant similarities between zebrafish and humans in neurodevelopmental processes and physiological functions. Zebrafish offer numerous advantages for toxicity studies, including high genetic and organ homology with humans, high fecundity, and external fertilization and development. Citronellol, a volatile fragrance compound with a floral scent, is widely used in various consumer products such as cosmetics, fragrances, and household items. Citronellol is known for its relaxing and calming effects and is generally considered a relatively safe chemical. However, there is a lack of comprehensive research on the health effects and underlying mechanisms of citronellol. Consequently, we conducted experiments exposing zebrafish larvae to citronellol post-early neurogenesis to elucidate its neurological effects. Our findings revealed that citronellol exposure induced behavioral abnormalities, increased reactive oxygen species (ROS), and inflammatory responses in zebrafish larvae, primarily through the activation of the 3-hydroxykynurenine (3-HK) pathway and subsequent neurosteroid activation. These metabolic alterations, including 3-HK, were corroborated not only in zebrafish but also in mouse models following oral administration and in brain organoids. Furthermore, utilizing animal and brain chip models, we confirmed that citronellol crosses the blood-brain barrier (BBB) and accumulates within the brain. Our results demonstrated the induction of 3-HK-mediated ROS production and neuroinflammatory cascades in the brain following citronellol exposure, underscoring the potential necessity for regulatory restrictions on its use.

Key words : Neurotoxicity, Zebrafish, Fragrance, Neuroinflammation, Blood-brain barrier

SYMPOSIUM 2 [IACUC] KOR

July 24 (Wed) 14:00–15:40 I Halla Hall B

Post-experiment management of laboratory animals for 3R

Organizer / Chair : **Seung Hyeok Seok** (Seoul Natl. Univ.)

Considerations for end-experimental animals **Ji Min Lee** (Seoul Natl. Univ.)
Sharing and utilization of animal biological resources **So Young Yune** (Ministry of Food and Drug Administration)
Laboratory animal rehoming **Jae-Hun Ahn** (Seoul Natl. Univ. Hospital)
Advancing the 3Rs principle: scientific and ethical considerations for responsible reuse of laboratory animals **Seung Hyeok Seok** (Seoul Natl. Univ.)

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FOR LABORATORY ANIMAL SCIENCE

S2-1

Considerations for end-experimental animals

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The end point of an animal experiment can vary. In some experiments, the end point is when the animal is euthanized, but in other cases, the animal may still be alive at the end of the experiment. In these situations, it is ethically important to consider what to do with the surviving animals, particularly in terms of the 3Rs principle (Replacement, Reduction, and Refinement).

For euthanized animals, we can achieve a reduction effect by sharing their carcasses as resources, thus preventing the use of additional animals. However, for surviving animals, we need to consider the ethical implications of how we decide their fate. One option is to give the animals a second chance at life, provided they are in good health when the experiment ends. Rehoming the animals to private homes can be considered. Many European countries have successful rehoming programs in place in response to EU Directives, providing laboratory animals with a second chance at life. Another option is to offer animals as resources for other research. This can reduce the production and sacrifice of additional animals. However, it is important to consider whether it is justifiable for one animal to continue to be placed in a distressing environment to reduce the sacrifice of another, and whether the reuse of animals compromises scientific validity.

In conclusion, finding a way to deal with surviving animals after an experiment in line with the 3Rs requires careful thought and effort. Whether rehoming or reuse, the welfare of the animals should be a top priority. This requires a comprehensive program that involves an IACUC, attending veterinarian, and relevant agencies. It is important that these programs continuously monitor the health of the animals, provide necessary medical care, and help the animals adapt to their environment. By doing so, we can strengthen the ethical aspects of animal testing and improve animal welfare.

Key words : 3Rs, Animal rehoming, Animal reuse, Program for End-Experimental Animals

S2-2

Sharing and utilization of animal biological resources

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Laboratory animals used in experiments are often treated as industrial waste despite the potential value of their biological resources such as organs, tissues, serum and cells. In response, the Laboratory Animal Resources Bank (LAREB) was established in 2018 at the National Institute of Food and Drug Safety Evaluation (NIFDS) in Korea to reduce the use of laboratory animals and promote the 3Rs (Reduction, Refinement, and Replacement) in laboratory animal research. LAREB collects a range of laboratory animal-derived resources, including frozen organs, cells, serum, wet tissues, and paraffin-embedded blocks, used in studies such as food and drug safety/efficacy evaluation and biological research and shares them for utilizing into newly other research purposes. Additionally, LAREB generates whole slide images (WSI) from toxicology, pharmacology, and biological studies, with a focus on herbal medicine toxicity studies conducted by the Korea National Toxicology Program (KNTP). Through collaborations with institutions like Seoul National University as a primate research partner and the K-MEDI hub as a laboratory animal resources partner, LAREB expands its reach and capabilities. Until now, LAREB has distributed approximately 8,000 laboratory animal-derived resources to researchers, facilitating new research endeavors. These efforts have resulted in the publication of four papers, the submission of nine patent applications, and one successful technology transfer. In summary, LAREB plays a crucial role in reducing laboratory animal usage and supporting the 3Rs in Korea.

Key words : Laboratory Animal Resources Bank, Non-clinical study

S2-3

Laboratory animal rehoming

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Laboratory animal rehoming means that the healthy animals previously used for scientific experiments and not used anymore are sent to a new home. As social demands for animal ethics increase, policies and guidelines for animal experimental ethics become stronger. Although, the latest version of Guide for the Care and Use of Laboratory Animals (which is a pivotal guideline for US and AAALAC-certificated animal facilities) does not mention laboratory animal rehoming, the European Parliament and Australian Code for the Care and Use of Animals for Scientific Purposes, emphasize the rehoming of the laboratory animals. The statute of the Republic of Korea also refers to the authority (Legal terminology), not the obligation, of rehoming for healthy laboratory animals. Recently, 9 healthy beagles which were used for a pharmacodynamics and pharmacokinetics study in our facility were successfully adopted by a private citizen and an animal welfare organization. This talk introduces the procedure for laboratory animal (Beagle) rehoming of our facility.

Key words : Animal rehoming, Beagle, IACUC, Animal experiment

S2-4

Advancing the 3Rs principle: scientific and ethical considerations for responsible reuse of laboratory animals

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The reuse of laboratory animals after the completion of their primary experimental role is an important issue from both scientific and ethical standpoints. Providing these animals with new opportunities can contribute to improved animal welfare and positive public perception of animal research. However, factors related to reuse or adoption must be thoroughly considered, as animals may face health risks and stress in new environments after undergoing experiments. Clear criteria should be established to determine suitability for reuse and adoption for each species, with subsequent case-by-case reviews conducted.

Especially in case of reuse, there are concerns about whether it is ethical for one animal to be placed in a constant state of distress to reduce the sacrifice of another animal. It also needs to be examined whether reusing an animal that has already been used compromises scientific validity by making it a variable in the experiment. To address this issue, care must be taken to ensure that animal suffering is not compounded and that information is transparent. For example, ensure that reused animals are in sufficient physical and mental health before they are used in new experiments, and Ensure that reused animals have a thorough experimental history, including information about what they have experienced in previous experiments and what medications they have received. The provisions in South Korea's Animal Protection Act prohibiting experimentation on animals that have served humans, and allowing for their adoption, represent a significant starting point for addressing these concerns.

This session aims to foster an open dialogue exchanging diverse perspectives on the scientific and ethical considerations for responsible reuse of laboratory animals in line with the 3Rs (replacement, reduction, refinement) principle of humane animal research.

Key words : 3Rs principle, Animal reuse, Animal adoption, Animal Protection Act, Animal welfare

AAALAC INTERNATIONAL ENG

July 24 (Wed) 14:00–15:40 | Samda Hall

Part 1: Our Journey Balancing the Animal Welfare and Good Science by Voluntary Accreditation Organizer / Chair : **Montip Gettayacamin** (AAALAC International), **Young-Shin Joo** (The Catholic Univ. of Korea)
Animal care and use program management **Hae-Jin Yoon** (Korea Institute of Toxicology)
Personnel and research management **Jungmin Lee** (Samsung Medical Center)
Internal oversight of the animal care and use program **Ji Yeon Hwang** (Seoul Natl. Univ.)
Overall veterinary care provision and communication **Young-Shin Joo** (The Catholic Univ. of Korea)
KOATECH facility applying 'The Guide' **Jeong Hee Park** (Korean Animal Technology (KOATECH))

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AAALAC International 1-1

Animal care and use program management

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Korea Institute of Toxicology (KIT), is one of government-funded institute, was designated as nation's first certified organization for GLP-compliant studies. Based on our global toxicology testing capabilities, we lead the development of source technologies for next-generation toxicity assessments, contributing to national industrial development and the improvement of public health and welfare.

KIT developed standard operation protocols for regulatory tests from 1988. As times have advanced, we have developed and implemented an animal care and use program that aligns with the principles of The Guide and domestic laws for all experiments involving laboratory animals.

Through these endeavors, KIT became the first institution in South Korea to achieve AAALAC accreditation in 1998 and maintained consecutive re-accreditations for eight terms until 2019.

Since 2023, significant efforts have been focused on improving the management, use, and welfare environment of laboratory animals based on the latest information from AAALAC. At the same time, there has been a strong emphasis on creating a safe working environment for animal care personnel.

The comprehensive details will be elaborated upon during the KIT's animal care and use program management presentation.

Key words : Animal care and use program, Animal welfare, Korea institute of toxicology

AAALAC International 1-2

Personnel and research management

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Proper animal care and handling is essential to ensure animal welfare and the prevention of diseases. In addition, personnel must be familiar with applicable regulations and guidelines to ensure compliance. Finally, institutions must be willing to provide ongoing training and assistance to their staff. Professional development should also include providing staff with the opportunity to gain new experiences, such as attending workshops and conferences, or shadowing colleagues in different laboratories. In addition, the institution should provide financial support for such activities. In addition, the occupational health and safety program (OHSP) should include measures to prevent injury, illness, and disease; provide appropriate training and education; and provide for regular inspections, reviews, and assessments. It should also include procedures to investigate accidents and incidents, and take corrective action if needed. Based on The Guide (8th), essential management factors will be considered.

Key words : Ongoing training, Occupational health and safety program (OHSP)

AAALAC International 1-3

Internal oversight of the animal care and use program

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Achieving a balance between animal welfare and scientific excellence necessitates comprehensive oversight of the animal care and use program. Program Oversight encompasses three major areas: 1) The Role of the IACUC, including protocol review and approval, facility inspection, program review, and the assessment of animal care and use; 2) Postapproval Monitoring; and 3) Disaster Planning and Emergency Preparedness. We will share insights and experiences from Seoul National University Bundang Hospital's journey toward enhancing their Internal Oversight of the Animal Care and Use Program through AAALAC International accreditation. One significant advancement is the improvement in the review and monitoring of humane endpoints. This includes requiring precise definitions of humane endpoints in protocols, criteria for assessment, frequency of animal observations, and the training of personnel responsible for recognizing humane endpoints. Specifically, researchers involved in tumor experiments must undergo humane endpoints training. We will also discuss the robust Postapproval Monitoring (PAM) operations, which include regular PAM conducted twice yearly by designated IACUC members with subsequent reporting to the IACUC, ongoing oversight by laboratory animal facility staff, and special PAM for monitoring and investigating issues of animal welfare or non-compliance, conducted by IACUC members or the Attending Veterinarian. Lastly, we will outline the establishment of comprehensive disaster planning and emergency preparedness programs. These include a triage plan, procedures for HVAC or electrical failures, general disaster response strategies, and staff training to ensure preparedness and effective response during emergencies. Through this presentation, we aim to provide valuable insights into achieving high standards of animal welfare while maintaining scientific integrity through systematic internal oversight and voluntary accreditation.

Key words : AAALAC international accreditation, Program oversight, Postapproval monitoring (PAM), Humane endpoints, Disaster planning

AAALAC International 1-4

Overall veterinary care provision and communication

Young-Shin Joo

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Veterinary care is an essential part of an animal care and use program which is mentioned The Guide for the care and use of laboratory animals, 8th edition. Not only does it takes as much time and effort as it is important, but it also requires communication between researchers, laboratory animal technicians and laboratory animal veterinarians.

'Veterinary Medical Record (VMR)' is used for providing appropriate and effective veterinary care for the animal at the Laboratory Animal Research Center (LARC), The Catholic University of Korea (CUK) after 2018.

Laboratory animal technicians (LATs) check the condition of animals every day and notify the veterinary medical record if they find any abnormalities. After that, the LAV examines the animals, informs researchers about the condition of animals, and explain how researchers care for the animals without affecting the results of the experiment through VMR, which is sent by email and text message. Researchers visit the LARC to check and confirm animals' conditions, proceed with appropriate treatment to relieve unnecessary pain and distress, and keep animals well until the experiment is over.

VMR helps researchers to keep animals healthier and also guides them to comply with the humane endpoint. Through this, researchers, LAV, and LATs are communicating about the condition of animals together and trying to reduce the unneeded discomfort in animals.

From 2018 to June 2023, a total of 16,132 VMRs were implemented. According to a survey conducted in 2022, 96.4% of researchers said this system was necessary and helpful to their research, also improve the welfare of laboratory animals. VMR is an important helper for researchers to improve ethical and scientific animal research and is used as not only an effective veterinary care program but also the archive and references for LAVs and LATs.

Key words : Veterinary care, Communication, Laboratory animal research, Animal care and use program

AAALAC International 1-5

KOATECH facility applying 'The Guide'

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The 'Physical Plant' section of 'The Guide' emphasizes the importance of facility design and maintenance for animal welfare and research integrity. Facilities are designed to minimize stress and contamination, maintain appropriate temperature and humidity, and prevent the spread of pathogens through regular sanitation and maintenance. Security measures prevent unauthorized access, and animal housing meets the specific requirements of each species. Koatech Co., Ltd. became the first in Asia to achieve AAALAC Full accreditation in 2010, and this presentation introduces Koatech's facility case studies based on 'The Guide'.

Key words : The Guide, Physical plant, AAALAC, animal facility, KOATECH

2024

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SYMPOSIUM 3 KOR

July 24 (Wed) 16:00–17:40 | Halla Hall A

Unraveling Immune Networks: Insights from Animal Models

Organizer: **Hyeyoung Min** (Chung-Ang Univ.), **Jae-Hoon Choi** (Hanyang Univ.),
Ho-Keun Kwon (Yonsei Univ.), **Jun-Young Seo** (Yonsei Univ.)
Chair : **Ho-Keun Kwon** (Yonsei Univ.), **Jae-Hoon Choi** (Hanyang Univ.)

Post-COVID pulmonary injury in hACE2 mice shows persistent neutrophils and neutrophil extracellular trap formation

Juwon Park (University of Hawai'i at Mānoa)

Regulation of macrophage activation in cardiovascular diseases

Sungho Park (UNIST)

Transgenic mouse models: Invaluable tools for humoral immunity

Youn Soo Choi (Seoul Natl. Univ.)

Microglial inflammasome-dependent regulation of blood-brain barrier integrity

Jewook Yu (Yonsei Univ.)

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S3-1

Post-COVID pulmonary injury in K18-hACE mice show persistent neutrophils and neutrophils extracellular trap formation

Juwon Park

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Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 is a major health concern with nearly one-third of patients showing long-term residual symptoms in a condition called Post-Acute Sequelae of SARS-CoV-2 infection (PASC). The alterations in circulating neutrophil functions, including up-regulation of neutrophil-associated inflammatory signatures, have already been shown in PASC individuals. However, direct in vivo evidence of neutrophil dysregulation in the lung after SARS-CoV-2 clearance is lacking. To better understand neutrophils' involvement in persistent lung injury and fibrosis seen in PASC individuals, relevant SARS-CoV-2 animal models are needed. In this study, we utilized survivor K18-hACE2 mice (approximately, 20% survival rate) after SASC-CoV-2 infection with 104 plaque forming units to understand the pathogenesis of post-COVID-19 pulmonary injury. Survivor K18-hACE2 mice exhibit sustained lung inflammation, injury, and neutrophil infiltration for up to 30 days of post-infection (dpi). Further analyses of neutrophil extracellular trap (NET) formation in lungs revealed the presence of NETs at 8 and 30 dpi, suggesting that infiltrating neutrophils are more likely to form NETs despite viral clearance. Our study provides the first evidence that survivor K18-hACE2 mice are an appropriate small animal model to study the involvement of neutrophils in post-COVID-19 pulmonary injury and allow to systematically dissect the underlying mechanisms of the role of neutrophils in long-term lung injury. Increased NET formation in survivor K18-hACE2 mice could exacerbate lung inflammation and promote thrombosis, leading to prolonged lung injury. Thus, the data provides a framework for future translational research including evaluation of the inhibitors targeting NET or neutrophil activation in preventing pulmonary PASC development.

Key words : K18-hACE2 mouse, COVID-19, PASC, Neutrophils, NET

S3-2

Regulation of macrophage activation in cardiovascular diseases

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Circulating Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) levels, known for regulating plasma cholesterol by degrading LDL receptors, correlate with acute myocardial infarction (AMI) risk. Recent studies suggest that PCSK9 improves cardiac function beyond LDL cholesterol levels after cardiac ischemic injury, but the precise role of PCSK9 in this process is not clarified yet. Our study reveals that PCSK9 deficiency induces heterogeneous changes in myeloid cells and macrophages, potentially protecting the heart in AMI regardless of LDL cholesterol homeostasis. Single-cell RNA sequencing identifies PCSK9-dependent cardiac macrophages (PDCMs) as reparative macrophages enriched in activator protein-1 (AP-1) transcription factor (TF)-related pathways. PDCMs enhance VEGF-C secretion and activate Akt signaling in cardiac endothelial cells, improving cardiac remodeling. Indeed, PCSK9 inhibitor-treated coronary artery disease (CAD) patients show increased myeloid cells with PDCM-like features. In sum, targeting myeloid-PCSK9 may offer cardio-protective effects through increased AP-1 activity and VEGF-C expression, providing a novel approach to prevent cardiac dysfunction in AMI.

Key words : Cardiac infarction, PCSK9, Macrophages, Cardiac remodeling

S3-3

Transgenic mouse models: invaluable tools to study humoral immunity

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Humoral immunity, mediated by secreted antibodies, is crucial for defending against extracellular pathogens and ensuring long-term immunity. Understanding the mechanisms that regulate humoral responses is essential for developing effective vaccines and therapeutic strategies. Transgenic mouse models have been fundamental in revealing these regulatory mechanisms due to their ability to mimic human immune responses and provide insights into the processes governing antibody production and function. In this talk, I will discuss several key transgenic mouse models that have been pivotal in advancing our knowledge of B cell development, activation, and differentiation. These models include mice with targeted mutations or transgenes that affect specific aspects of the humoral immune response, such as antigen receptor diversity, signaling pathways, and the role of helper T cells. Through these models, researchers have been able to dissect the contributions of various genes and molecular pathways to the overall humoral immune response. Additionally, I will present recent findings from studies utilizing these transgenic mice, showcasing how they have uncovered novel regulatory mechanisms and potential therapeutic targets. The talk will also cover the advantages and limitations of using transgenic mouse models, emphasizing the importance of selecting appropriate models for specific research questions. By providing a platform for in-depth analysis of immune responses, transgenic mouse models continue to be invaluable in unraveling the complexities of antibody-mediated protection and guiding the development of innovative immunotherapies.

Key words : Humoral immunity, B cells, Transgenic mouse models, Immune regulation, Vaccines

S3-4

Microglial inflammasome-dependent regulation of blood-brain barrier integrity

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Blood-brain barrier (BBB) disintegration emerges as a significant contributor to neuroinflammation; however, the biological processes governing BBB permeability under physiological conditions remain unclear. Here, we examined the potential role of NLRP3 inflammasome in BBB disruption following peripheral inflammatory challenges. Systemic lipopolysaccharide administration caused an NLRP3-dependent increase in BBB permeability and myeloid cell infiltration into the brain. Using a cell-specific, hyperactive NLRP3-expressing mouse model, we found that microglial NLRP3 activation is crucial for peripheral inflammation-induced BBB disruption. In contrast, NLRP3 and microglial gasdermin D (GSDMD) deficiency remarkably attenuated lipopolysaccharide-induced BBB breakdown. Notably, IL-1β was unnecessary for this NLRP3-GSDMD-mediated BBB disruption. Instead, single cell transcriptomic analysis of mouse brain revealed that microglial NLRP3-GSDMD axis specifically upregulates CXCL chemokine around BBB, recruiting Cxcr2-containing neutrophils into the brain. Neutrophil depletion and Cxcr2 blockade significantly reduced NLRP3-mediated BBB impairment. Collectively, our findings unveiled the significant role of NLRP3-driven chemokine production for BBB disintegration, suggesting a potential therapeutic target to mitigate neuroinflammation.

Key words : Blood-brain barrier (BBB), Microglia, Inflammasome, Gasdermin D, Neuroinflammation

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SYMPOSIUM 4 KOR

[KLAT Education 1 with KIT]

July 24 (Wed) 16:00–17:40 I Halla Hall B

Anatomy and practical Methods for Animal Testing I

Organizer / Chair : **Jeong-Hwan Che** (Seoul Natl. Univ. Hospital)

Assessment of rodent respiratory toxicity and respiratory function **Se Ran Yang** (Kangwon Natl. Univ.)
Experimental technique in gastrointestinal research using rodents **Jong Hwang Park** (Chonnam Natl. Univ.)
Assessment of brain and nervous system function **Jae Ho Shin** (Eulji Univ.)
Characteristics and key research methods of the hematopoietic system **Yi Rang Na** (Seoul Natl. Univ. Hospital)

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S4-1

Assessment of rodent respiratory toxicity and respiratory function

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Respiratory toxicity and deterioration of respiratory function are major features of various substances, including environmental pollutants, chemicals and even pharmaceutical compounds. To better understand the potential respiratory toxicity and the associated mechanisms, rodent models, particularly mice and rats, are widely applied with those substance to assess the potential respiratory toxicity and impaired lung function. In this session, rodent models used in respiratory toxicity studies will be discussed along with various routes of exposure, including inhalation, intratracheal instillation and non-respiratory route, as well as their physiological responses and limitations in recapitulating human exposure. Additionally, respiratory toxicity will be compared between acute or chronic exposure protocols, as the duration and frequency of exposure influencing the severity and phenotype of the respiratory injury.

Moreover, the key endpoints and techniques will be explored the respiratory toxicity assessment and function in rodent models. These measurements include histopathological examination of the respiratory tract, bronchoalveolar lavage fluid (BALF) for pro-inflammatory cytokines and accumulation of inflammatory immune cells in the alveoli of lung tissues, pulmonary function test such as plethysmography, and imaging analyses such as micro-computed tomography (micro-CT) for evaluating alveolar structure changes. Traditional biochemical biomarkers will also be highlighted, focusing on changes in the secretome and protein levels in response to respiratory toxicity.

Key words : Toxicity, BALF, Functional test, Secretome, Clinical correlation

S4-2

Experimental technique in gastrointestinal research using rodents

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Inflammatory Bowel Disease (IBD) is a term primarily used to describe two chronic conditions: Crohn's disease and ulcerative colitis. These disorders involve chronic inflammation of the gastrointestinal (GI) tract, leading to a variety of symptoms that can significantly influence an individual's quality of life. Animal models for IBD include chemical (DSS, TNBS, oxazolone, etc)-induced models, genetically-engineered mice, and T cell adoptive transfer model. Among chemical-induced models, dextran sodium sulfate (DSS)-induced colitis has been extensively used for screening therapeutic candidates or studying relevant molecular mechanisms. In this session, we will discuss the details of developing mice models for IBD, and the criteria and methods for evaluation.

S4-3

Assessment of brain and nervous system function

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Because the cerebrum is significantly developed in humans, it is very difficult to phenotypically assess the function of the human central nervous system in animals. However, animal models are essential for drug development for central nervous system diseases. Animal models are preferred for these experiments because they represent the pathological and neurochemical changes of human diseases and exhibit psychological and behavioral changes similar to those in humans. If an animal's behavior is specifically changed by an existing psychotropic drug, that behavior can be used as a model for a specific disease. Therefore, we would like to provide guidance on basic morphological and functional analysis methods to investigate changes in the brain and nervous system using animal models.

Key words : Brain, Nervous system, Assessment, Animal model

S4-4

Characterization and key research methods of the hematopoietic system

Yi Rang Na

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This lecture provides a comprehensive overview of the hematopoietic system in laboratory mice. It will start with an introduction to the basic anatomy and physiology of the hematopoietic system, covering the functions and components of blood, bone marrow, spleen, lymph nodes, and thymus. The main focus will be on the purposes and methodologies of hematopoietic system modulation, highlighting bone marrow transplantation (BMT) as a key example. This includes preconditioning treatments such as bulsilvex injections or irradiation, followed by donor marrow cell transplantation. Since preconditioning requires specific drugs or radiation equipment, it is crucial for laboratory animal technicians to grasp the mechanisms behind experimental protocols. Attendees will gain insight into the hematopoietic system's role in disease modeling and therapeutic studies, enhancing their comprehension of how and why researchers manipulate the hematopoietic system of mice in laboratory settings.

Key words : Hematopoietic system, Mice, Bone marrow, BMT, Irradiation

AAALAC INTERNATIONAL ENG

July 24 (Wed) 16:00–17:40 | Samda Hall

Part 2: One-point Lesson to Achieve AAALAC International Accreditation

Organizer : **Montip Gettayacamin** (AAALAC International), **Young-Shin Joo** (The Catholic Univ. of Korea)
Chair : **Montip Gettayacamin** (AAALAC International), **Seung Hyeok Seok** (Seoul Natl. Univ.)

Overview and update of AAALAC international accreditation program	**Montip Gettayacamin** (AAALAC International)
Step 1: Preparing the program description and site visit	**Young-Shin Joo** (The Catholic Univ. of Korea)
Step 2: Expectation of the post site visit communication and council deliberations	**Seung Hyeok Seok** (Seoul Natl. Univ.)
Q&A Session	**All speaker and participants**

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AAALAC International 2-1

Overview and update of AAALAC international accreditation program

Montip Gettayacamin

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AAALAC International is a private, non-profit organization that promotes the humane and ethical treatment of animals in science through voluntary program assessment, accreditation and education. AAALAC International's mission improves the welfare of animals in science and education through the accreditation of organizations meeting high standards of humane and responsible animal care and use. AAALAC International has been recognized around the world as a symbol of high-quality animal care and use for research, teaching and testing, as well as promoting animal welfare and maintaining safety. About 1,100 institutions in 50 countries have earned AAALAC accreditation. There are more than 250 accredited programs in Asia and Australia. The AAALAC International's Council on Accreditation evaluates overall performance and all aspects of any animal care and use program, involving an in-depth, multi layered, confidential peer-review process. The AAALAC International evaluators (site visitors) consider compliance with applicable local animal legislation of the particular country, institutional policies, and use a customized approach for evaluating overall program performance using principles outlines in The Three Primary Standards: *Guide for the Care and Use of Laboratory Animals* (National Research Council, 2011), *Guide for the Care and Use of Agricultural Animals in Research and Teaching* (2020), or European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes, Council of Europe (ETS 123), and supplemental Reference Resources as applicable. AAALAC International uses the same assessment process to evaluate animal programs in any country around the world. This presentation provides the overview and update of AAALAC International accreditation program.

Key words : AAALAC International, Accreditation, Peer-review, Animal welfare, Global standards

AAALAC International 2-2

Preparing the program description and site visit

Young-Shin Joo

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AAALAC International is a private, nonprofit organization that promotes the humane treatment of animal in science through voluntary accreditation and assessment program. Animal research facility in Korea are also being accredited to enhance the status of the institution along with ethical and scientific animal experiment. The title with "One-point Lesson to Achieve AAALAC International Accreditation" in 2024 KALAS International Symposium is organized by AAALAC International to help the understanding of institutions preparing or maintaining accreditation.

The first step in preparing for the accreditation is to create a Program Description (PD). It consist of Certification page, Section 1. Introduction, Section 2. Description including I. Animal Care and Use Program, II. Animal Environment, Housing and Management, III. Veterinary care, IV. Physical Plant which is followed in the Guide for the Care and Use of Laboratory Animal and Appendices 19 items. An accurate PD is necessary to provide Council on Accreditation with sufficient information to make an objective judgment concerning accreditation of unit. Writing tips for PD is like that; Don't change the content or delete any Appendix. Respond to each question about all items and indicate if "Not applicable", not used, not allowed, etc. Provide sufficient and accurate detail or to summarize and explain how your methods achieve quality animal care and use, and the rationale (if necessary). And do not refer to appendices or SOPs in lieu of providing a brief description in the PD and Make sure that current practices and PD match.

After submission of PD, Site Visit is implemented by site visitor with council members of Council on Accreditation and ad hoc specialists. It proceeds in the order of Entrance Briefing, Program Description Review, Facility tour, Lunch with IACUC member, Document Review, Executive Session and Exit Briefing.

Key words : AAALAC International, Accreditation, Program description, Site visit

AAALAC International 2-3

Expectation of the post site visit communication and council deliberations

Seung Hyeok Seok

Seoul National University

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AAALAC International employs a standardized assessment process to evaluate animal care and use programs in institutions worldwide. The evaluation process is conducted by AAALAC International site visitors who consider compliance with applicable local animal welfare legislation, institutional policies, and utilize a tailored approach to assess overall program performance based on the principles outlined in the following primary standards: *Guide for the Care and Use of Laboratory Animals* (National Research Council, 2011), *Guide for the Care and Use of Agricultural Animals in Research and Teaching* (2020), or the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes, Council of Europe (ETS 123). Supplemental reference resources are also used as applicable.

This presentation aims to provide an overview of the AAALAC International site visit process, highlighting common issues encountered during the evaluation. The presentation will also discuss how to effectively respond to the concerns raised during the site visit exit briefing and outline the expectations of the Council on Accreditation regarding the retained findings mentioned in the accreditation letters.

By adhering to AAALAC International's uniform assessment process, institutions can ensure that their animal care and use programs maintain high standards of animal welfare and promote the responsible use of animals in research, testing, and education. This, in turn, contributes to the scientific validity and reproducibility of research findings while fostering public trust in the scientific community.

Key words : AAALAC International, Animal welfare, Site visit, Assessment process, Accreditation

PLENARY LECTURE 1 ENG

July 25 (Thu) 10:00–11:00 | Halla Hall

Organizer / Chair : **Je Kyung Seong** (Seoul Natl. Univ.)

Insights from rodent models for understanding diabetic retinopathy

Jesús Ruberte Paris (Autonomous University of Barcelona)

Plenary Lecture 1

Insights from mouse models for understanding diabetic retinopathy

Jesús Ruberte Paris

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Despite many years of clinical and laboratory investigation, diabetic retinopathy remains the leading cause of vision impairment among working-aged people. Mouse models have been valuable tools in further understanding the pathophysiology of diabetic retinopathy and discovering and assessing new potential therapeutic agents. However, although numerous diabetic mouse models have been developed, none of these models replicates all the key features of human disease.

Diabetic retinopathy results in damage of vascular and nonvascular cells. Although microvascular changes serve as the basis for classification in non-proliferative and proliferative retinopathy, loss of ganglion cells and changes in glia have been also detected in human patients. Non-proliferative diabetic retinopathy is characterized by thickening of capillary basement membrane, pericyte and vascular smooth muscle cell loss, capillary occlusion, and formation of acellular capillaries and microaneurysms. In the proliferative phase new blood vessels appear as a consequence of retinal ischemia, giving rise to retinal detachment and sudden blindness. Here I present the work done in my laboratory for more than a decade to try to model the phases of diabetic retinopathy on the mouse, and although not a single mouse can display all the lesions observed in human patients, currently several models can reasonably recapitulate this devastating disease.

Key words : Diabetic retinopathy, Mouse models

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SYMPOSIUM 5 ENG

July 25 (Thu) 14:00–15:40 | Halla Hall A

Frontiers in Metabolic Regulation: Paving the Way for Therapeutic Insights in Metabolic Diseases and Beyond

Organizer: **Su Myung Jung** (Sungkyunkwan Univ.), **Hui-Young Lee** (Gachon Univ.), **Hyunji Lee** (Korea Univ.)
Chair : **Su Myung Jung** (Sungkyunkwan Univ.), **Seung-Hoi Koo** (Korea Univ.)

Elucidating adipocytes functions through development
Joan Sanchez-Gurmaches (Cincinnati Children's Hospital)

Role of CRTC2 in metabolic disorders
Seung-Hoi Koo (Korea Univ.)

Targeting immunometabolic functions of adipose tissue macrophages: therapeutic perspectives from animal model studies
Yun-Hee Lee (Seoul Natl. Univ.)

Fibrotic niche-enriched single-cell transcriptomics uncovers novel age-associated cell type in liver
Chuna Kim (KRIBB)

KOREAN ASSOCIATION
FOR LABORATORY ANIMAL SCIENCE

S5-1

Elucidating adipocytes functions through development

Joan Sanchez-Gurmaches

Cincinnati Children's Hospital

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Adipose tissue heterogeneity plays a crucial role in metabolic health, yet the mechanisms underlying this diversity remain poorly understood. Our research focuses on elucidating the developmental origins and molecular pathways that contribute to adipocyte heterogeneity and its impact on metabolic function. Using innovative lineage tracing techniques and mouse genetics, we have demonstrated that both brown and white adipocytes arise from multiple, distinct precursor populations. This heterogeneity extends not only between different fat depots but also within individual depots, revealing a complex landscape of adipocyte origins. Using this new developmental information, we can now decipher the roles of signaling, metabolic, and transcriptional pathways in particular adipocytes uncovering new layers of regulation relevant to health and disease. Here I will discuss our new discoveries in how distinct types of adipose tissue contribute to whole body metabolic homeostasis and new transcriptional networks regulating the formation of adipose tissue.

S5-1

Unraveling adipocyte heterogeneity: from developmental origins to metabolic implications

Joan Sanchez-Gurmaches

Cincinnati Children's Hospital

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Adipose tissue heterogeneity plays a crucial role in metabolic health, yet the mechanisms underlying this diversity remain poorly understood. Our research focuses on elucidating the developmental origins and molecular pathways that contribute to adipocyte heterogeneity and its impact on metabolic function. Using innovative lineage tracing techniques and mouse genetics, we have demonstrated that both brown and white adipocytes arise from multiple, distinct precursor populations. This heterogeneity extends not only between different fat depots but also within individual depots, revealing a complex landscape of adipocyte origins. Using this new developmental information, we can now decipher the roles of signaling, metabolic, and transcriptional pathways in particular adipocytes uncovering new layers of regulation relevant to health and disease. Here I will discuss our new discoveries in how distinct types of adipose tissue contribute to whole body metabolic homeostasis and new transcriptional networks regulating the formation of adipose tissue.

S5-2

Role of CRTC2 in metabolic disorders

Seung-Hoi Koo

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The cAMP signaling cascade is crucial in the regulation of metabolic homeostasis in mammals. CREB regulated transcription co-activator (CRTC) 2 is involved in the transcriptional regulation of genes involved in the metabolic processes in the peripheral tissues, thus playing a crucial role in the alteration of metabolic flux in response to cAMP signaling. Indeed, we and others have delineated the specific role of this protein in the regulation of glucose and lipid metabolism in the liver, pancreatic islets, intestinal L cells, and adipose tissues.

In this presentation, we would like to discuss our recent findings regarding the role of CRTC2 in the regulation of various metabolic processes in the liver and adipose tissues by using tissue-specific knockout mouse models.

Key words : CRTC2, Metabolic pathways, Liver, Adipose tissues, Transcriptional regulation

S5-3

Targeting immunometabolic functions of adipose tissue macrophages: therapeutic perspectives from animal model studies

Yun-Hee Lee

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Adipose tissue (AT) adapts to overnutrition in a complex process, wherein specialized immune cells remove and replace dysfunctional and stressed adipocytes with new fat cells. Among immune cells recruited to AT, lipid-associated macrophages (LAMs) have emerged as key players in obesity and in diseases involving lipid stress and inflammation. Here, we show that LAMs selectively express transmembrane 4 L six family member 19 (TM4SF19), a lysosomal protein that represses acidification through its interaction with Vacuolar-ATPase. Inactivation of TM4SF19 elevates lysosomal acidification and accelerates the clearance of dying/dead adipocytes in vitro and in vivo. TM4SF19 deletion reduces the LAM accumulation and increases the proportion of restorative macrophages in AT of male mice fed a high-fat diet. Importantly, male mice lacking TM4SF19 adapt to high-fat feeding through adipocyte hyperplasia, rather than hypertrophy. This adaptation significantly improves local and systemic insulin sensitivity, and energy expenditure, offering a potential avenue to combat obesity-related metabolic dysfunction.

Key words : Adipose tissue, Obesity, Lipid-associated macrophage, Tm4sf19

S5-4

Fibrotic niche-enriched single-cell transcriptomics uncovers novel age-associated cell type in liver

Chuna Kim

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Aging is associated with the accumulation of senescent cells, which are triggered by tissue injury response and often escape immune system clearance. The specific traits and diversity of these cells in aged tissues, along with their effects on the tissue microenvironment, remain largely unexplored. Despite the advance in single-cell and spatial omics technologies to understand complex tissue architecture, senescent cell populations are often neglected in general analysis pipelines due to their scarcity and the technical bias in current omics toolkits. In this study, we utilized the physical properties of tissue to enrich aged-associated fibrotic niche and subjected them to multi-omics analysis and named this novel method Fibrotic Niche enrichment sequencing (FiNi-seq). We profiled young and old livers using FiNi-seq, discovered novel mesenchymal cell populations showing senescent phenotypes, and investigated the early immune responses within this fibrotic niche. Spatial mapping techniques revealed that FiNi-seq-enriched cells are found around the portal vein and form interspersed patches, which expand upon chronic liver injury. Finally, FiNi-ATAC-seq reveals age-associated epigenetic changes enriched in fibrotic niche cells. Thus, our quasi-spatial single-cell profiling method allows the detailed analysis of initial aging microenvironments, providing potential therapeutic targets for aging prevention.

Key words : Aging, Senescence, scRNA-seq, scATAC-seq, Spatial transcriptomics

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SYMPOSIUM 6 KOR

July 25 (Thu) 11:00–12:40 I Halla Hall B

Precised Animal Care for Disease Model

Organizer: **Seung Hyun Oh** (Seoul Natl. Univ.) / Chair : **Hee Jin Kim** (WoojungBio)

Advancing vivarium efficiency and animal welfare through digitalization: the Scientific advantages of the DVC system	**Guglielmo Vismara** (Tecniplast)
Good care and use laboratory animals in ABSL3 facility	**Sung-Hee Kim** (Yonsei Univ.)
Animal experiments in germ free condition	**Hye Jin Kim** (KMPC)

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S6-1

Advancing Vivarium Efficiency and Animal Welfare through Digitalization: the Scientific advantages of the DVC® System

Guglielmo Vismara

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The integration of digital technologies in vivarium management has emerged as a pivotal strategy for enhancing both operational efficiency and animal welfare. This study presents a comprehensive analysis of the Digital Vivarium Cage (DVC®), a system designed to facilitate real-time tracking of laboratory animal cages, thereby addressing key challenges in vivarium operations. The DVC® system exemplifies a novel approach to vivarium management by leveraging digitalization to optimize task execution, reduce manual labor, and improve accuracy in the animal census and asset management.

By automating the calculation of cage per-diem costs and providing instantaneous access to data on rack occupancy levels and cage locations, the DVC® system significantly reduces the potential for human error and enhances the reliability of operational workflows. Additionally, the system incorporates dedicated LED indicators and sensors to assist in the identification and management of cages requiring attention, thereby streamlining caretaker tasks.

From a scientific perspective, the DVC® system's most noteworthy contribution is its capacity to elevate animal welfare through the continuous monitoring of activity patterns, environmental conditions, and behavioral indicators. Utilizing an advanced AI algorithm, the system offers a novel method for detecting behavioral anomalies such as aggression and stereotypic behaviors, providing critical insights that can inform welfare assessments and interventions. This continuous data collection, particularly of nocturnal activity patterns, enriches the traditional health check process by offering objective, data-driven insights into the well-being of the animals.

The integration of the DVC® system with existing Animal Management Systems (AMS) further exemplifies its scientific utility by ensuring a seamless workflow for colony management and facilitating the efficient allocation of resources.

In summary, the DVC® system represents a significant advancement in the scientific management of vivaria, offering a dual benefit of operational efficiency and enhanced animal welfare. By harnessing digital technology to support precise monitoring and management practices, the DVC® system aligns with the scientific community's ethical responsibilities towards laboratory animals and underscores the potential of digitalization in the pursuit of excellence in vivarium management.

S6-2

Good Care and Use Laboratory Animals in ABSL3 Facility

Sung Hee Kim

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Since handling live pathogens involves bio hazard, appropriate management and regulation are required. Biosafety is divided into four levels, known as Biosafety Levels (BSL) 1, 2, 3, and 4, based on the level of bio hazard. Among these, coronaviruses such as SARS-CoV, MERS-CoV, and SARS-CoV-2 are classified as BSL-3 pathogens because they can cause severe or fatal symptoms in humans, even though prevention or treatment is possible, and they can be transmitted through the air. Appropriate facility infrastructure is necessary for each BSL.

Our research team has been utilizing a BSL-3 research facility to study the pathogenic mechanisms and pathological characteristics of SARS-CoV-2 using mouse models since 2020. We developed infection model mice to identify the characteristics of viral infection for each model and advanced methods of respiratory virus infection such as intranasal inoculation and inhalational infection. Particularly, by developing and introducing inhalational infection methods in addition to the commonly used intranasal infection in mouse models, we were able to enhance the similarity of the lesions to those seen in human respiratory virus infections.

Furthermore, we conducted basic pathological analyses of SARS-CoV-2 infection and examined the transcriptome and protein expression in target organs such as the lungs and spleen during infection, thereby enhancing our understanding of the pathogenic mechanisms. Additionally, based on this fundamental research, we supported the development of new drugs for epidemic response by conducting preclinical studies on six vaccine candidates and twenty therapeutic candidates.

Key words : Biosafety Levels (BSL), SARS-CoV-2, Mouse model, Infection, Pathology

S6-3

Animal experiments in germ free condition

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Microbes produce beneficial metabolites through bacterial fermentation to enhance exercise performance and regulate the host's physiology and energy metabolism. In our study, we found that germ-free (GF) mice have reduced aerobic exercise capacity, lower oxygen consumption rates, and reduced glucose availability. Surprisingly, GF mice had lower body weight gain and lower body fat mass than specific pathogen-free (SPF) mice. We hypothesized that this paradoxical phenotype may be mediated by a compensatory increase in adipose tissue lipolysis due to impaired glucose utilization in skeletal muscle. This adaptation limits obesity in GF mice but impairs exercise performance by interfering with immediate fuel supply during exercise. Our findings highlight the unique physiological features of GF mice and emphasize considerations that should be taken into account when conducting experimental studies with these mice. Future studies should confirm the hypothesis that specific microbes influence exercise performance. At that time, we will discuss what needs to be considered experimentally.

Key words : Aerobic exercise, Germ-free, Glucose metabolism, Exercise capacity

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SYMPOSIUM 7 KOR

July 25 (Thu) 11:00–12:40 | Samda Hall

Utility of the Minipigs as Laboratory Animals

Organizer: **Jong Ki Cho** (Seoul Natl. Univ.) / Chair : **Byeong-Cheol Kang** (Seoul Natl. Univ.)

Development of wound healing agents using minipigs	**Sokho Kim** (Kunsan Natl. Univ.)
The use of miniature swine for preclinical modeling in cardiovascular research	**Se-Il Park** (Yonsei Univ.)
Dermal toxicity and efficacy study using yucatan minipig	**Jeong Ho Hwang** (KIT)
Trends in the development of bio-resources using miniature pigs	**Hyunil Kim** (Optipharm Inc.)

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S7-1

Development of wound healing agents using minipigs

Sokho Kim

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In the research and development of pharmaceuticals and medical devices, safety and efficacy must be evaluated. Recently, there has been a shift towards using appropriate experimental animals in the research and development of pharmaceuticals and medical devices involving rodents. Mini pigs generally refer to experimental animals weighing less than 100 kg, with adult mini pigs typically weighing between 20 and 40 kg. The various genetic and morphological characteristics of mini pigs are being studied by many veterinarians and genetic researchers. Additionally, the value of mini pigs as animals for producing xenotransplant organs has emerged, and related research is being conducted worldwide. Various preclinical studies leveraging the similarities between mini pigs and humans are being conducted globally, with significant research focused on wound healing agents and skin-related regenerative medicine. The physiological characteristics of mini pig skin tissue are remarkably similar to those of human skin tissue, and even their genetic traits are similar to humans, providing results that are closer to human responses than experiments using rodents. The development of new therapeutics for wound healing is currently ongoing in many pharmaceutical companies, expanding from traditional chemical and natural materials to cell therapies, extracellular vesicle therapies, gene therapies, and microbiome-based treatments. This presentation aims to provide a brief introduction to mini pigs and highlight their value and examples as a wound healing model used in pharmaceutical development.

S7-2

The use of miniature swine for preclinical modeling in cardiovascular research

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Cardiovascular (CV) diseases represent the leading cause of death and morbidity in most countries. This category of diseases encompasses a range of conditions affecting the heart and blood vessels, including coronary artery disease, heart attacks, stroke, heart failure, and hypertension-related complications. However, CV disease complications have complex multi-factorial pathologies, in which both physical and hemodynamic factors are implicated, there are limitations in reflecting the functional characteristics of the human heart.

Miniature swine models are increasingly recognized as an ideal model in CV research due to their physiological and anatomical similarities to humans as miniature swine have CV systems that closely resemble those of humans in terms of heart performances, coronary artery distribution, hemodynamic characteristics, and metabolic profiles for making them suitable for studying human-like disease progression and response to treatments.

Biomedical products for CV diseases should have durability, strength, and flexibility to withstand throughout their lifetime. The most important desirable factors are the material's biological properties, thromboresistance, anti-hemostasis, and endothelialization capability. For this reason, these models are ideal for evaluating the performance and safety testing for intravascular stents, valve replacement, pacemakers, and biomedical CV devices.

Miniature swine also has offered important models for investigating the safety and efficacy evaluation system for various new CV drugs before they proceed to human clinical trials. They can be used to develop a refractory disease model through dietary modifications and pharmacological induction for studying the progression of hypertension, plaque development, atherosclerosis, and lipid-related disease.

In particular, miniature swine models play a pivotal role in evaluating biomedical products to overcome acute and chronic myocardial injury, heart failure, and cardiomyopathy. Induced myocardial infarction models allow for the research of attack mechanisms, recovery processes, and the efficacy of interventions such as reperfusion therapies, regenerative treatments, and bioengineering to repair damaged heart tissue.

Key words : Preclinical safety and efficacy evaluation, Cardiovascular research, Miniature swine models

S7-3

Dermal toxicology and efficacy study using Yucatan minipig

Jeongho Hwang

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Minipig is a non-rodent animal model considered for studying human disease or pre-clinical study to evaluate novel candidate drug. Especially, porcine skin has similarities with human skin in terms of histology, physiology and immunological characteristics. In this session, we will introduce our previous research on the topics of minipig skin disease model and dermal toxicity and efficacy studies using biomaterial and therapeutic substrate. As a dermal animal model, we established atopic dermatitis model, burn wound model, and subcutaneous implant model. For the atopic dermatitis model, 1-fluoro-2,4-dinitrobenzene (DNFB) and ovalbumin (OVA) were applied to the minipig skin. As a result, inflammatory cytokines (IL-4, INF γ, IL-13) were increased in the serum and skin of atopic minipigs. In the histological assessment, hyperkeratosis, increased epidermal thickness and infiltration of immune cells were detected. For the burn wound model, wounds were induced using a soldering iron with a square-shaped tip at 180 ℃. In addition, a novel bentonite complex developed for therapeutic purpose of treating skin inflammation was evaluated for its efficacy through COX-2/PGE2 axis and cytokines. As a dermal toxicity study, Titanium ion (Ti)-infiltrated Polylactide (PLA/Ti) was evaluated using subcutaneous implant model. The dermal toxicity was determined using immunohistochemistry (IHC) and real-time qPCR. In H&E staining, mild immune infiltration around degraded PLA/Ti were detected, but no skin structure damage and activation of inflammatory cytokines were observed. In conclusion, the research suggested that a minipig is expected to become promising animal model in dermatological research for studying human skin disease and evaluating novel drug candidate and biomaterials.

Key words : Minipig, Dermatology, Biomaterial, Toxicity

S7-4

Trends in the development of bio-resources using miniature pigs

Hyunil Kim

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Miniature pigs have recently been receiving significant attention in the fields of laboratory animal research, translational medicine, and xenotransplantation. Miniature pigs are frequently used in non-clinical studies due to their genetic similarity to humans, their status as non-rodent experimental animals, and their comparable body weight. Additionally, the diameter and anatomical structure of their blood vessels are similar to those of humans, making them valuable for evaluating the safety of intravascular medical devices. Furthermore, recently, genetically modified pigs have been developed as source animals for xenotransplantation, in which four specific pig genes are knocked out and four human genes are knocked in. In the United States, this advancement has already progressed to the level of transplanting hearts and kidneys into humans, and non-clinical primate experiments are currently underway in South Korea.

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LUNCHEON SEMINAR 1~3

July 25 (Thu) 13:00–13:20

Luncheon Seminar 1

Halla Hall A

Organizer / Chair : **Dae Youn Hwang**

Sable Systems社의 대사 비만 측정 분석 시스템 소개 — **Lars Breuer** (SABLE SYSTEMS)

Luncheon Seminar 2

Halla Hall B

Organizer: **Je Kyung Seong** / Chair : **Sungsoon Fang**

Validation of operations, facilities, and equipment for animal (marmoset) biosafety level 3 facility approval

Yong Sub Byun (오송첨단의료산업진흥재단(KBIOhealth))

Luncheon Seminar 3

Samda Hall

Organizer / Chair : **Byeong-Cheol Kang**

Practical approach of point of care qPCR to monitor infectious pathogens for laboratory animals and facilities

Doo-Sung Cheon (POSTBIO)

KOREAN ASSOCIATION
FOR LABORATORY ANIMAL SCIENCE

LS1

Sable Systems社의 대사 비만 측정 분석 시스템 소개

Lars Breuer

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Sable Systems is dedicated to helping you push the boundaries of animal and human metabolism research. We design and manufacture leading-edge systems for metabolic and behavioral phenotyping, calorimetry, respirometry and gas analysis. We're driven to deliver you the most accurate and precise data, enabling you to see every aspect of metabolism and behavior more clearly.

The Promethion Core Mouse Metabolic System gives you the truest and most trustworthy results from your mouse phenotyping studies. At the heart of the system is the highest resolution metabolic measurement instrumentation, yielding accurate resting and active energy expenditure values.

Promethion Core tightly synchronizes all metabolic and behavioral data, allowing you to pinpoint and correlate metabolism changes with behavioral events. The Environmental Sensor Array (ESA) data is also available in real-time to correlate any changes in the environment with the metabolic and behavioral changes.

Key words : Metabolism, Obesity, Behavioral Phenotyping, Calorimetry, Respirometry

LS2

Validation of operations, facilities, and equipment for animal (marmoset) biosafety level 3 facility approval

Yong Sub Byun

오송첨단의료산업진흥재단 (KBIOhealth)

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Preparing for infectious disease research using experimental animals requires significant costs, time, and personnel. Regulatory standards from approval agencies vary depending on the type of animal used, leading to diverse operational policies and validation criteria for facilities and equipment. KBIOhealth has successfully obtained approval for South Korea's first Biosafety Level 3 facility utilizing small non-human primates (common marmosets). Here, I'll describe relevant details, focusing on operational policies for this unique facility and the validation processes for marmoset housing equipment, which are unprecedented in South Korea. Additionally, I'll provide a more detailed explanation of the newly introduced marmoset infection housing cage (NEWTECH).

Key words : Marmoset, NHP, ABL3

LS3

Practical approach of point of care qPCR to monitor infectious pathogens for laboratory animals and facilities

Doo-Sung Cheon

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Microbial monitoring of laboratory animals should be performed regularly to ensure the accuracy and reproducibility of animal experimental results and to prevent the spread of diseases due to the movement of animals within and between institutions, and the use of healthy animals is considered essential to ensure reliable and quality animal experimental results.

Health monitoring of various infectious pathogens in laboratory animals is performed by serologic tests, cultivation, PCR, microscopic observation and recent advances in molecular biology have led to the development and widespread application of technologies that rapidly and sensitively detect the genes of each pathogen. In particular, the real-time PCR method using fluorescently labeled probes has been widely used to detect infectious pathogens for the diagnosis of large-scale infectious diseases such as COVID-19, and is also widely used as a highly sensitive and multiplexed diagnostic method for diagnosing major infectious microorganisms in laboratory animals. The real-time PCR method has the advantage of not requiring electrophoresis after amplification of specific genes and enabling 3-4 multiple diagnoses in a single reaction using fluorescence of various wavelengths, so it is widely used for screening various pathogens at once or detection tests using multiple samples.

At the same time as the development and introduction of real-time PCR, point of care real-time PCR method, which integrates the process of extracting nucleic acids and amplifying specific nucleic acids, has been technically developed and is being used in human and veterinary clinical sites, and has recently been utilized in various genetic detection processes such as industrial animals, quality control of biological products, and food microbial monitoring. It is expected that the scope of utilization of real-time PCR for field use will be expanded in the future due to the advantage that the test can be easily performed in the field without the need for large-scale equipment and highly skilled experimenters.

This talk was prepared to review the development and performance evaluation process of point of care real-time PCR for major infectious diseases in various livestock species over the past five years, and to explore practical ways to apply it to the monitoring process of major infectious diseases in representative laboratory animals such as mice and rats.

It is expected that the real-time PCR-based laboratory animal health monitoring for field use, which will be developed in the future, will serve as a powerful diagnostic tool in the process of self-quality control and systematic periodic microbial monitoring in laboratory animal breeding facilities.

Key words : Laboratory animals, Point of care, Real time PCR, Microbial monitoring

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ACADEMY AWARD PRESENTATION

July 25 (Thu) 14:00–14:40 | Halla Hall A

Chair : **Je Kyung Seong** (Seoul Natl. Univ.)

Development of the mammalian cochlea capable of frequency discrimination

Jinwoong Bok (Yonsei Univ.)

SARS-CoV-2 Omicron variant causes brain infection with lymphoid depletion in a mouse COVID-19 model

Na Yun Lee (Seoul Natl. Univ.)

KOREAN ASSOCIATION
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A-1

Development of the mammalian cochlea capable of frequency discrimination

Jinwoong Bok

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The cochlea's ability to discriminate sound frequencies is facilitated by a special topography along its longitudinal axis known as tonotopy. Auditory hair cells located at the base of the cochlea respond to high-frequency sounds, whereas hair cells at the apex respond to lower frequencies. Gradual changes in morphological and physiological features along the length of the cochlea determine each region's frequency selectivity, but it remains unclear how tonotopy is established during cochlear development. Recently, sonic hedgehog (SHH) was proposed to initiate the establishment of tonotopy by conferring regional identity to the primordial cochlea. Here, using mouse genetics, we provide in vivo evidence that regional identity in the embryonic cochlea acts as a framework upon which tonotopy-specific properties essential for frequency selectivity in the mature cochlea develop. We found that follistatin (FST) is required for the maintenance of apical cochlear identity, but dispensable for its initial induction. In a fate-mapping analysis, we found that FST promotes expansion of apical cochlear cells, contributing to the formation of the apical cochlear domain. SHH, in contrast, is required both for the induction and maintenance of apical identity. In the absence of FST or SHH, mice produce a short cochlea lacking its apical domain. This results in the loss of apex-specific anatomical and molecular properties and low-frequency-specific hearing loss.

Key words : Cochlea, Frequency, Tonotopy, Hair cell, Follistatin

A-2

SARS-CoV-2 Omicron variant causes brain infection with lymphoid depletion in a mouse COVID-19 model

Na Yun Lee

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Preclinical murine models have been instrumental in advancing our understanding of SARS-CoV-2 pathogenesis and facilitating the development of therapeutic interventions. In our previous study, we found that the lethality of COVID-19 mouse models was characterized by severe lymphoid depletion related to fatal neuroinvasion. Although the Omicron, the most prevalent SARS-CoV-2 variant, is known to induce milder lesions compared to the original Wuhan strain, apparent infections into the brain by Omicron have not been reported in human adult cases or animal models. In this study, we investigated whether Omicron could spread to the brain using K18-hACE2 mice susceptible to SARS-CoV-2 infection. K18-hACE2 mice were intranasally infected with 1×105 PFU of the original Wuhan strain and the Omicron variant of SARS-CoV-2. At 7 days post infection (dpi), all Wuhan-infected mice exhibited lethal conditions, while two out of five Omicron-infected mice (40%) also reached a lethal state. Histopathological analyses revealed inflammatory responses with severe infection of neuron cells in the brains of these two Omicron-infected mice. Lymphoid depletion and apoptosis were observed in the spleen of Omicron-infected mice with brain infection. The lymphoid depletion was associated with a decreased number of antigen-presenting cells (APCs) and their suppressed functionality below basal levels. Our study reports, for the first time, that Omicron can induce brain infection with lymphoid depletion in the mouse COVID-19 model. These findings underscore the need for further research to elucidate the determinants, predisposing conditions, and mechanisms contributing to the severity of disease induced by the Omicron.

Key words : SARS-CoV-2, Animal model, Brain, Antigen-presenting cells

SYMPOSIUM 8 [KMPC] KOR

July 25 (Thu) 14:50–16:30 I Halla Hall A

Liver diseases in animal models

Organizer: **Je Kyung Seong** (Seoul Natl. Univ.) / Chair : **Jun-Won Yun** (Seoul Natl. Univ.)

RORα-GABP-TFAM axis alleviates myosteatosis with fatty atrophy through reinforcement of mitochondrial capacity

Mi-Ock Lee (Seoul Natl. Univ.)

Hepatic steatosis and steatohepatitis through immunometabolic synapse

Won-Il Jeong (KAIST)

Altered hepatotoxic properties of SARS-CoV-2 mRNA vaccine in an animal model for type 2 diabetes

Jun-Won Yun (Seoul Natl. Univ.)

Emerging insights: MASH-associated HCC progression

Kyoung-Jin Oh (KRIBB)

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S8-1

RORα-GABP-TFAM axis alleviates myosteatosis with fatty atrophy through reinforcement of mitochondrial capacity

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The pathogenesis of NAFLD, a prevalent metabolic disorder in liver, evidently involves a complex interplay between liver and multiple organ systems. Recent population-based studies have demonstrated that the severity of fat infiltration in skeletal muscles (known as myosteatosis) was more strongly reflective on the severity of human NAFLD than the decline of muscle mass. Despite the clinical significance of myosteatosis in NAFLD, the molecular regulator which has pathophysiologic link between NAFLD and myosteatosis still remains to be elucidated. Mitochondria are central to oxidative metabolism of lipid in muscles, and modulation of muscle mitochondrial activity in oxidative fibers may be a candidate for therapeutic approach to reduce myosteatosis. In previous studies, RORα has been reported to play protective roles in progression of NAFLD. However, there are few studies proving the role of RORα in the muscles of NAFLD-related myosteatosis to explain the alleviating effect of RORα in NAFLD. Here, we found that RORα reinforces the differentiation of oxidative muscle cells and regulates the expression of a group of genes related to mitochondrial biogenesis including the TFAM gene, suggesting that mitigation of myosteatosis of RORα may be a potential therapeutic strategy against NAFLD.

Key words : NAFLD, Myosteatosis, Fatty atrophy, RORα, Mitochondrial biogenesis

S8-2

Hepatic steatosis and steatohepatitis through immunometabolic synapse

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Traditionally, alcohol-related liver disease (ALD) is induced by multiple factors that occur during various metabolic processes of hepatocyte, diverse absorption of pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs) from intestine, and delivery of free fatty acids and pro-inflammatory cytokines from adipose tissue. These factors cause fat accumulation in hepatocyte at early stage but continuous drinking promotes more serious diseases such as inflammation, fibrosis and even tumor. However, interestingly, our research team recently discovered the existence of glutamatergic signaling pathways in the liver and reported that ALD can be occurred by them. Briefly, we have revealed that chronic alcohol consumption increases glutamate production especially by aldehyde dehydrogenase 4 family member A1 (ALDH4A1) enzyme in hepatocyte, and generated hepatic glutamate is stored within the hepatocytes, and then secreted through xCT or granules. Simultaneously, metabotropic glutamate receptor 5 (mGluR5) is expressed in various non-parenchymal cells (NPCs) and exerts pathophysiological effects through interaction with secreted glutamate. In addition, released glutamate is mainly absorbed by hepatocytes and NPCs. Today, I would like to briefly introduce the roles of hepatic glutamate, as a hepatotransmitter, in inducing and suppressing the development of ALD. In addition, adipose tissue could release glutamate release through xCT transporter as well to activate interferon-gamma production of natural killer cells. Here, I will briefly address hepatic glutamate production by non-canonical pathway and its function of double-edged sword in the development of liver diseases, including ALD. It is believed that our study will contribute to the discovery of therapeutic targets and development of treatments for liver diseases.

Key words : Glutamate, mGluR5, Alcohol, Liver disease, Steatohepatitis

S8-3

Altered hepatotoxic properties of SARS-CoV-2 mRNA vaccine in an animal model for type 2 diabetes

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Due to the high transmissibility of the SARS-CoV-2 virus, mRNA vaccines were initially developed as preventive tools against viral respiratory illness, based on their rapid development speed and high efficacy. Despite the widespread interest and potential efficacy of these mRNA vaccines, comprehensive investigations into their safety are essential. Several studies have reported a high rate of adverse events associated with COVID-19 vaccines among diabetic patients. Therefore, this study aimed to compare the toxicological profiles of a novel SARS-CoV-2 mRNA vaccine, CUK3/LNP128, between wild-type (WT) mice and db/db mice, an animal model for type 2 diabetes. For this purpose, mice were intramuscularly immunized with the mRNA vaccine twice, with an interval of two weeks between doses. Our findings indicated that db/db mice exhibited aggravated mRNA vaccine-induced hepatotoxicity compared to WT mice, as evidenced by serum biochemistry and histopathology. Importantly, biodistribution analysis using luciferase signals from mRNA expressing firefly luciferase and RT-PCR indicated that db/db mice exhibited a longer-lasting and greater signal at the injection site and in the liver compared to WT mice. Additionally, RNAseq analysis identified differentially expressed genes related to the complement activation, organ regeneration, and cell proliferation in vaccinated db/db mice, suggesting the involvement of these pathways in the exacerbation of mRNA vaccine-induced liver injury in this model. Taken together, our results demonstrate more severe hepatotoxicity in db/db mice following the administration of CUK3/LNP128, leading to the need for a more thorough evaluation of mRNA vaccine-related side effects, including liver injury, in individuals with type 2 diabetes mellitus.

Key words : Animal model, Type 2 diabetes, mRNA vaccine, Side effect, Liver injury

S8-4

Emerging insights: MASH-associated HCC progression

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Metabolic dysfunction-associated steatohepatitis (MASH), the severe manifestation of metabolic dysfunction- associated fatty liver disease (MAFLD), is emerging as a significant global health concern due to its role as a major risk factor for hepatocellular carcinoma (HCC). However, the molecular mechanisms underlying MASH-associated HCC remain unclear. This study aims to establish a rapid and reproducible murine model of MASH-associated HCC and identify specific signaling pathways responsible for the progression of MASH to HCC. Our study will increase understanding of the progression from MASH to HCC and provide a rapid and reliable MASH-associated HCC murine model to test drug candidates for prevention and treatment of MASH progression.

Key words : MASH, HCC, MASH-associated HCC, Rapid and reproducible murine model

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SYMPOSIUM 9 [NIFDS 1] ENG

July 25 (Thu) 14:50–16:30 | Halla Hall B

Recent Trends in Stem Cell & Organoid Research

Organizer: **Hye-Jin Boo** (Jeju Natl. Univ.), **Ok Nam Bae** (Hanyang Univ.), **Jun Won Yun** (Seoul Natl. Univ.)
Chair : **Jae-Jin Cho** (Seoul Natl. Univ.)

Hair follicle stem cell and tissue regeneration	**Hanseul Yang** (KAIST)
Organoid modelling of human fetal lung development	**Kyungtae Lim** (Korea Univ.)
Biomaterials and devices for advanced organoid engineering	**Seung-Woo Cho** (Yonsei Univ.)
Salivary gland organoids for investigating the etiology of xerostomia	**Hyung-Sik Kim** (Pusan Natl. Univ.)

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S9-1

Hair follicle stem cell and tissue regeneration

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Tissue regeneration relies on resident stem cells, whose activity and lineage choices are influenced by microenvironment. Once activated, stem cells typically give rise to short-lived progenitors, which then progress to differentiate into their lineages. Exploiting the synchronized cyclical bouts of tissue regeneration in hair follicles, we investigated when and how stem cell lineage choices take place. Using temporal single-cell RNA-seq and in vivo lineage tracing, we unearthed unexpected heterogeneity among stem cells and their progeny and found that the ability of stem cells to make lineage choices (plasticity) becomes restricted in a sequentially and spatially choreographed program. We traced the roots of lineage restriction to micro-niches located along epithelial-mesenchymal borders, each of which receive slightly different signaling inputs. Instructed by micro-niches signals, hair follicle stem cells reorganize their super-enhancer network to achieve lineage switches. In most mammals, wound-induced tissue regeneration is incomplete and results in fibrotic scarring. How adult stem cells lose their regenerative potential and the trade-off of incomplete regeneration remain unknown. Interestingly, the African spiny mouse (*Acomys* spp.) is a unique mammalian species that can autotomize its skin to escape from predators and completely regenerate it as with salamanders. The naturally-developed robust tissue recovery of *Acomys* spp. serves as a powerful model system to study complete tissue regeneration in mammals. I will briefly introduce some recent progresses of our study on tissue regeneration in *Acomys* spp.

Key words : Skin wound healing, Hair follicle regeneration, African spiny mice, Epigenetics, Single cell RNA-seq

S9-2

Orgranoid modelling of human fetal lung development

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In the developing human lung, alveolar development requires highly systemic, spatiotemporal interactions between subsets of differentiating progenitor cells of epithelial and mesenchymal lineages. Extensive studies have been performed to understand the underlying mechanisms which organise alveolar differentiation and cell patterning in the developing alveolar niche in human, however, it remains elusive. In this study, we have generated multiomic cell atlas of human lung development that combines single-cell RNA and ATAC sequencing, high-throughput spatial transcriptomics, and single-cell imaging. The atlas identifies alveolar-fated epithelial progenitors in late-stage distal lung regions that can be modelled as self-organising organoids in vitro. We functionally validate spatiotemporal cell-cell interaction between the alveolar-fated progenitors and surrounding multiple mesenchymal cells, showing that Wnt signaling from differentiating alveolar fibroblasts promotes alveolar-type-2 cell identity, whereas myofibroblasts secrete the Wnt inhibitor, NOTUM, providing spatial patterning. We also identify a Wnt-NKX2.1 axis controlling alveolar cell fate determination and differentiation and supporting novel human fetal lung-derived alveolar organoid model that is stable over long-term passaging, efficiently process and secrete surfactants, and can differentiate into AT1-like cells. Using this model, we finally reveal the underlying mechanisms of surfactant protein C maturation relevant to interstitial lung disease. Our single cell analysis in combination with lung organoid system revealed key aspects of human fetal lung stem cell biology, allowing mechanistic experiments to determine the cellular and molecular regulation of human alveolar development.

Key words : Human lung development, Alveolar development, Organoid, Singe-cell technology, Stem cell

S9-3

Biomaterials and devices for advanced organoid engineering

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Organoids have been highlighted for regenerative medicine and precision medicine. However, current organoid culture methods have several limitations due to a lack of tissue-specific microenvironments and well-controlled dynamic culture systems, leading to immature structural and phenotypic characters and limited functionality. Thus, we develop functional hydrogels and microfluidics for improving organoid development and functions. Combination of tissue-mimetic hydrogels and microfluidic devices with dynamic flow can successfully recapitulate in vivo-like microenvironments favorable for organoids, resulting in structural and functional maturation of several types of tissue organoids including brain, intestine, heart, and liver. Accordingly, the organoids generated with our engineering platforms exhibit improved metabolic activity and drug responses which are critical for the performance of drug testing platforms. They also show enhanced regenerative potential upon transplantation into injured tissues. Our bioengineering approaches would be able to facilitate the development of highly effective organoid platforms for advanced regenerative medicine. Acknowledgment: This work was supported by the National Research Foundation of Korea (NRF) (2021R1A2C3004262).

Key words : Organoid, Hydrogel, Microfluidic, Disease modeling, Tissue engineering

S9-4

Salivary gland organoids for investigating the etiology of xerostomia

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Despite the high incidence of dry mouth (termed xerostomia) in postmenopausal women, research addressing underlying mechanisms and therapeutic interventions remains underexplored. Expanding on our prior work which demonstrated the detrimental effects of estrogen deficiency on salivary gland (SG) function in ovariectomized (OVX) animal models, here we identified disruptions in redox signaling and ferroptosis, an iron-dependent programmed cell death, as central mechanisms driving postmenopausal SG dysfunction. The transcriptomic analysis pinpointed an elevated TGFβ signaling pathway, particularly with enhanced TGFβ2 expression, in the SG of OVX mice. TGFβ2 was primarily secreted by SG mesenchymal cells and impaired the viability of SG epithelial organoids (SGOs), which was reversed by either TGFβ inhibitor SB431542 or estrogen treatment. Intriguingly, SGO exposure to TGFβ2 resulted in iron-binding ferritin depletion paving the way for free iron-triggered ROS generation, lipid peroxidation and subsequent ferroptotic death. Mechanistically, TGFβ2 promoted the autophagy-mediated selective ferritin degradation, so-called ferritinophagy, while blockage of autophagy initiation preserved the ferritin level in TGFβ2-treated SGOs. Finally, treatment with the ferroptosis inhibitor liproxistatin-1 (Lip-1) alleviated the reduced saliva secretion in OVX mice. Our findings collectively unveil an unappreciated connection between TGFβ signaling, ferroptosis and SG injury, suggesting novel therapeutic strategies for postmenopausal xerostomia.

Key words : Xerostomia, Organoid, Estrogen, Ferroptosis

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SYMPOSIUM 10 KOR

July 25 (Thu) 14:50–16:30 | Samda Hall

Exploring Sensory Impairments: In Vivo Studies on Animal Models with Vision and Hearing Defects

Organizer: **Dong Hyun Jo** (Seoul Natl. Univ.) / Chair : **Jinwoong Bok** (Yonsei Univ.)

Establishing patient-mimicking mutant mice for the development of gene editing therapy
Young Hoon Sung (Ulsan Natl. Univ.)

Therapeutic application on angiogenesis-related ocular diseases
Seok Jae Lee (Seoul Natl. Univ. Hospital)

Allele-specific antisense oligonucleotide ameliorates KCNQ4-related autosomal dominant hearing loss
Seung Hyun Jang (Yonsei Univ.)

In vivo base editing in humanized mice mimicking patients with retinoschisis
Dong Hyun Jo (Seoul Natl. Univ.)

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S10-1

Establishing patient-mimicking mutant mice for the development of gene editing therapy

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To find a cure for a disease, understanding the cause of the disease must be preceded. The development of next-generation sequencing (NGS) technologies has allowed us to identify patient-specific genetic variants of unknown significance (VUS). Generation and subsequent phenotypic analysis of mutant mice carrying patient-derived mutations provide the direct evidence needed to determine whether these mutations cause disease or not. Furthermore, the mutant mice recapitulating the human diseases will be very useful for developing novel drugs including the gene-editing therapeutics. Here we will discuss how to use the CRISPR-Cas system to generate genetically humanized mice for retinitis pigmentosa (RP) and apply them to proof-of-concept studies for gene editing therapies.

Key words : Gene editing, CRISPR, Variants of unknown significance, Mouse model, Retinitis pigmentosa

S10-2

Therapeutic application on angiogenesis-related ocular diseases

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Aberrant growth of new blood vessels, known as angiogenesis, is a key feature in vision-threatening eye diseases such as retinopathy of prematurity, diabetic retinopathy, neovascular age-related macular degeneration, and corneal neovascularization-related diseases. Among the various pro-angiogenic factors, vascular endothelial growth factor (VEGF) is the main driver of ocular neovascularization supported by increased VEGF levels of ocular fluid, blood samples, and primary cells from patients or animal models with pathologic ocular diseases. While intraocular anti-VEGF treatment remains the gold standard therapy in various pathologic angiogenesis-related ocular diseases, its application poses challenges due to ocular and systemic side effects. This presentation aims to introduce the results of preclinical studies for drug development, including a novel compound and existing drugs, with the goal of supplementing or replacing conventional anti-VEGF agents. These studies utilize various mouse models of pathologic angiogenesis-related ocular diseases established in the FARB lab.

Key words : Choroidal neovascularization, Corneal neovascularization, Retinal neovascularization, Retinal pigment epithelium

S10-3

Allele-specific antisense oligonucleotide ameliorates KCNQ4-related autosomal dominant hearing loss

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Hearing loss is the most common sensory organ disorder. Genetic mutations are a significant cause of hearing loss, with over 150 genes identified as causative when mutated. KCNQ4, a voltage-gated potassium channel, is highly expressed in cochlear outer hair cells, and mutations in KCNQ4 have been reported to cause progressive hearing loss (DFNA2), making it the most common deafness-causing autosomal dominant gene among East Asians. Among the many pathogenic mutations in KCNQ4 responsible for hearing loss, KCNQ4 p.W276S (c.G830C) mutation is one of the frequent dominant-negative mutations associated with DFNA2. Despite this prevalence, there is no effective biological treatment for KCNQ4-associated hearing loss, highlighting an imperative clinical need for novel therapeutics. Here, we employed allele-specific antisense oligonucleotides (ASO) to target and develop novel therapeutics for the dominant-negative KCNQ4 mutation.

Through in vitro screening, we identified that two out of the nine ASOs (ASO-123 and -127) selectively targeted the mutant mouse Kcnq4, while sparing the wild type, in a dose-dependent manner. Considering toxicity profiles, we selected ASO-123 as the final candidate. For the in vivo experiment, we generated a Kcnq4 p.W277S knock-in mouse harboring a homologous mutation to human KCNQ4 p.W276S. This model successfully recapitulated progressive hearing loss and deterioration of outer hair cells, particularly at high frequencies. NGS and RT-PCR of ASO-123 injected cochleae in Kcnq4 p.W277S heterozygous mutant mice indicated preferential knockdown of wild-type transcripts over mutants, while the injection in wild-type mice did not induce hearing loss and maintained wild-type transcript levels, suggesting the safety of ASO-123. Serial audiological tests corroborated the observed efficiency in transcript levels, mitigating progressive hearing loss up to 7 weeks post-injection.

Our findings suggest that tailored ASO targeting a dominant-negative mutation can ameliorate progressive hearing loss. Further optimization is expected to increase safety and the potential for clinical translation.

Key words : Hearing loss, Inner ear, Autosomal dominant, Antisense oligonucleotides

S10-4

In vivo base editing in humanized mice mimicking patients with retinoschisis

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Base editing offers a promising therapeutic approach for genetic disorders lacking effective treatments. In our study, we focused on a specific mutation in the RS1 gene, identified in six related individuals with retinoschisis, an X-linked retinal condition that leads to progressive vision loss. We created a humanized mouse model carrying this specific variant, which exhibited a phenotype comparable to that seen in human patients. By testing various adenine base editors (ABEs) and single guide RNAs (sgRNAs), we determined the most effective combination, characterized by high editing efficiency and minimal off-target effects. Remarkably, intravitreal administration of adeno-associated viral (AAV) vectors encoding the selected ABE into 2-week-old mice resulted in approximately 40% correction of the target variant across all retinal cells. This treatment not only preserved the integrity of the retinal layers but also maintained visual function. Notably, these mice already displayed retinal layer splitting, a disease hallmark, by two weeks of age. Our findings demonstrate a clear strategy for identifying optimal base editing tools for clinical applications through preclinical studies using humanized mouse models with patient-specific mutations. This methodology has potential applications for the treatment of various genetic disorders.

Key words : Retinoschisis, Base editing, CRISPR, Humanized mouse, RS1

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SYMPOSIUM 11 [NIFDS 2] ENG

July 26 (Fri) 09:00-10:40 | Halla Hall A

Revolution of laboratory rodent health monitoring

Organizer: **Byeong-Cheol Kang** (Seoul Natl. Univ.)

Chair : **Byeong-Cheol Kang** (Seoul Natl. Univ.), **Jong Kwon Lee** (Ministry of Food and Drug Administration)

Health monitoring of laboratory rodent colonies-talking about (R)evolution

Byeong-Cheol Kang (Seoul Natl. Univ.)

Prevalence of parvovirus in rodent: how can we deal with chappavovirus in SPF rodent?

Yang-Kyu Choi (Konkuk Univ.)

Validation of a newly developed laboratory animal microbiological monitoring kit

Ki Taek Nam (Yonsei Univ.)

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S11-1

Health Monitoring of Laboratory Rodent Colonies-Talking about (R)evolution

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Health monitoring in the laboratory animals is essential process for the health care of laboratory animals and reproducibility of preclinical study. Microbiome compositions in laboratory animals affects disease phenotypes and the scientific value of research data, and many research communities became aware of the influence of pathogenic microbes and felt the needs of the fast treatment and progress in pathogen detection and elimination. So, there was much improvement of the microbiological quality of laboratory animals, but still, traditional health monitoring methods serve as powerful tools for the diagnostics of laboratory animal diseases. Recently, molecular methods with improved sensitivities developed rapidly, and also can analysis various types of samples. Recently, the Korean Ministry of Food and Drug Safety established the guideline for microbial quality control of experimental animals and invested the research grant "Study for establishment of quality control system for high quality care of laboratory animals (21184MFDS326)". Here, we suggest recapitulate common health monitoring concepts and outline strategies and measures on coping with microbiome variation in order to increase reproducibility and replicability. And, we will continue to monitor microbes for animal health care, accuracy of experimental results and strive to present eradication methods.

Key words : Health monitoring, Laboratory animals, Rodent pathogens, Monitoring methods, Quality control

S11-2

Prevalence of parvovirus in rodent: how can we deal with chapparvovirus in SPF rodent?

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The various parvoviruses are occasionally present in laboratory mice and rats. Mouse parvovirus (MPV), minute virus of mice (MVM) and murine chapparvovirus (MuCPV) can be infected in mice. Parvoviruses in rats include Toolan's H-1 virus (H-1), Kilham rat virus (KRV), rat minute virus (RMV), and rat parvovirus (RPV). Murine parvoviruses are transmitted primarily by direct contact or contact with fomites. MVM appears to be more pathogenic than MPV and MuCPV in mice. KRV can produce clinical disease with natural infection in young rats. H-1, KMV and RPV infection are usually subclinical in rats. Over the past five years in Korea, the incidence of MVM and MPV at laboratory animal facility were very low, and none of the samples were positive for MuCPV, H-1, KRV, RMV, or RPV. One of reasons for the low incidence of parvovirus in Korea is as follows. Institutions that maintain a maximum barrier and provide excellent veterinary care perform health monitoring for all pathogens, but institutions that maintain a standard barrier conduct health monitoring for major pathogens. Additionally, most institutions do not test for MuCPV infection. As a result of the above, it seems necessary to investigate the prevalence of parvovirus infection including MuCPV in institutions that maintain a standard barrier or do not provide veterinary management.

Key words : Parvovirus, Barrier, Veterinary care, Health monitoring

S11-3

Validation of a newly developed laboratory animal microbiological monitoring kit

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The accurate monitoring of microbial presence in laboratory animal facilities is crucial for ensuring animal health, maintaining experimental integrity, and upholding rigorous biosecurity standards. In this presentation, we examined the validation of a newly developed microbiological monitoring kit specifically designed for use in laboratory animal environments. This comprehensive evaluation includes an assessment of sensitivity, specificity, accuracy, precision, interference, user-friendliness, stability, and cost-effectiveness. We present the validation process of the newly developed ELISA kit and multiplex qPCR kit for monitoring laboratory animals and discuss the challenges encountered during the development and validation phases. In conclusion, the newly developed microbiological monitoring kit meets stringent validation criteria, offering a reliable, efficient, and user-friendly solution for monitoring microbial presence in laboratory animal facilities. This advancement supports the ongoing efforts to maintain high standards of animal welfare and experimental accuracy.

Key words : Microbiological monitoring kit, Animal welfare

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SYMPOSIUM 12 ENG

July 26 (Fri) 09:00–10:40 | Halla Hall B

Cell-Gene Immunotherapy using Humanized Animal Models

Organizer / Chair : **Kyung-Sun Kang** (Seoul Natl. Univ.)

In vivo and in vitro studies for evaluation of tumorigenicity of cell therapy product
Yoji Sato (National Institute of Health Sciences)

Development of CD19 CAR-NK therapy targeting pericytes in the tumor microenvironment using a glioblastoma-blood vessel assembloid xenograft model
Kyung-Sun Kang (Seoul Natl. Univ.)

Assessing the impact of CRISPR/Cas9 based *ex vivo* HSC gene therapy: insights from rhesus macaque competitive repopulation model
Byung-Chul Lee (Sookmyung Women's Univ.)

Humanized mice are essential tools for evaluation of cell and gene therapies to move towards a clinical trial
Sang-Nyun Kim (Orient Genia)

Regenerative approaches for off-the-shelf hypoimmunogenic stem cells
Da-Hyun Kim (Sung Shin Women's Univ.)

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S12-1

In vivo and *in vitro* studies for evaluation of tumorigenicity of cell therapy products

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One of the challenges in ensuring the safety of cell therapy products is the evaluation of the cells' ability to form tumors after clinical administration to patient, i.e., tumorigenicity. In particular, since the production of products derived from human pluripotent stem cells (hPSCs) requires long-term culture, including induction of differentiation into target cells, the possibility of cells being transformed is presumed to be higher than for somatic cell therapy products. In addition, because the raw material hPSCs themselves can inherently form teratomas, residual undifferentiated hPSCs in the final product should be avoided as much as possible. In other words, to ensure the safety of cell therapy products, technologies are needed to avoid and quantitate/detect the proliferative hazards, i.e., transformed cells and undifferentiated hPSCs. In Japan, a variety of new sensitive test methods have been developed for the detection of tumorigenic cells as impurities in cell therapy products. To validate these assays and a method for the assessment of non-clinical biodistribution, which is closely associated with tumorigenicity of cell therapy products, the National Institute of Health Sciences (NIHS) and the Committee for Non-Clinical Safety Evaluation of Pluripotent Stem Cell-Derived Therapeutic Products, the Forum for Innovation in Regenerative Medicine (FIRM-CoNCEPT) organized a public-private joint consortium (MEASURE) and have compared the performance of those assays across multiple institutions. In addition, through the Committee of Cell Therapy-Tracking, Circulation and Safety, the Health and Environmental Sciences Institute (HESI CT-TRACS), the MEASURE consortium is also working with foreign research institutes to promote international understanding of the tumorigenicity-associated tests by evaluating their reproducibility and issuing position papers on the need for international consensus building.

Key words : Cell therapy products, tumorigenicity, test method development, pluripotent stem cells

S12-2

Development of CD19 CAR-NK therapy targeting pericytes in the tumor microenvironment using a glioblastoma-blood vessel assembloid xenograft model

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High heterogeneity and metastatic potential are major challenges in the development of glioblastoma (GBM) therapeutics. Furthermore, such heterogeneity can cause off-target effects in targeted cancer cell therapies like chimeric antigen receptor (CAR)-T therapy. Therefore, this study aimed to generate CAR-NK cells targeting pericytes in the GBM tumor microenvironment to effectively eliminate highly metastatic GBM stem cells. We developed a GBM-blood vessel assembloid (GBVA) xenograft model by transplanting GBVAs into immunodeficient mice, thereby establishing a GBM tumor microenvironment with human pericytes. By fusing with blood vessel organoids, we recapitulated the perivascular niche of the GBM tumor microenvironment and observed the metastatic behavior of GBM cells. This GBM tumor microenvironment became vascularized in vivo after transplantation, allowing for the assessment of whether intravenously injected CD19 CAR expressing induced pluripotent stem cell-drived NK cells (CD19 CAR-iNK) cells could effectively target pericytes derived from GBM stem cells. The experimental results showed that, compared to the GBM spheroid xenograft model without pericytes, CD19 CAR-iNK cells in the GBVA xenograft model effectively suppressed GBM growth and infiltrated tumor tissues. This study suggests the potential for developing CAR-iNK cells targeting pericytes as a GBM cell-based immunotherapy.

Key words : Glioblastoma, Assembloid, Xenograft, CAR-NK therapy

S12-3

Assessing the impact of CRISPR/Cas9 based *ex vivo* HSC gene therapy: insights from rhesus macaque competitive repopulation model

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For clinical application of precision genome editing via CRISPR/Cas9 system, effective and safe editing of long-term engrafting hematopoietic stem cells (LT-HSCs) is required, resulting in successful hematopoietic reconstitution. Therefore, the clinical feasibility should be validated via an adequate preclinical model enabling long-term tracking. Although murine xenograft models have revealed that gene edited LT-HSCs could facilitate prolonged hematopoiesis, long-term analyses including potential malignant transformation, hematopoietic reconstitution, and immune dysfunction cannot be assessed. To track the competitive hematopoiesis of CRISPR-edited versus wild type HSPCs following autologous transplantation over time, we generated a rhesus macaque (RM) Familial Platelet Disorder with associated Myeloid Malignancies (FPDMM) competitive repopulation model using CRISPR/Cas9 NHEJ editing in the RUNX1 gene and the AAVS1 safe-harbor control locus. In the animals, RUNX1-edited cells expanded over time compared to AAVS1-edited cells. Bone marrows developed megakaryocytic dysplasia similar to human FPDMM, and $CD34^+$ HSPCs showed impaired megakaryocytic differentiation. Platelet counts remained below the normal range long-term, suggesting that gene correction approaches for FPDMM will be challenging. Given this challenging results, we next decided to track the clonal dynamics of CRISPR-edited cells, then ssODN barcode library structure was inserted at CD33 genetic locus of RM $CD34^+$ cells via CRISPR/HDR machinery, alongside competitive lentiviral barcodes. As seen in the AAVS1-edited cells, CD33 edited cells were rapidly decreased, while the drop off of LV-transduced GFP+ cells stabilized at 2 months. For further analysis, we retrieved embedded barcodes and revealed that various clones contributed to early hematopoietic reconstitution in CRISPR arm, then after limited number of dominant clones appeared at steady state, resulting in oligoclonal hematopoiesis. In conclusion, CRISPR-edited cells were found to disappear rapidly after the autologous transplantation in RM despite substantial gene editing outcome and clonality of CRISPR/HDR-edited cells drastically shrank at early stage and then relied on several dominant clones.

Key words : Precise genome editing, Homology directed repair, Rhesus macaque, Genetic barcoding, Ex vivo HSC gene therapy

S12-4

Humanized mice are essential tools for evaluation of cell and gene therapies to move towards a clinical trial

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Humanized mice became indispensable for preclinical testing of gene therapies using retroviral vectors or gene editing tools for many indications, allowing scientists to investigate therapeutic efficacy, toxicity, safety and stability of the therapy, which often constitutes the information required by regulatory agencies to proceed with a clinical trial. The most frequently used mouse model for CD34+ cell engraftment is the non-obese diabetic (NOD)/severe combined immunodeficiency (SCID), gamma c-/-mouse model (NSG). However, existing humanized mouse are unable to support development of human innate immune cells, including myeloid cells and NK cells and are thus not adapted for functional testing of genetic diseases affecting myeloid function or differentiation. Recently, c-Kit receptor-mutant mice (c-Kit mutant mice) on the NSG background support unprecedented levels of human engraftment including myelo-erythroid differentiation and become commercially available (NBSGW and NSGW41 mouse model). The MISTRG mouse model, in which human versions of four genes encoding cytokines important for innate immune cell development are knocked in to their respective mouse loci also support an improved development of an innate immune system compared to NSG mice. More robust T cell reconstitution, which provides a more relevant model for HIV infection and the study of T cell immunity, was subsequently developed and involved the intravenous injection of autologous CD34+ human hematopoietic cells from fetal liver tissues, which engraft in the bone marrow, along with the transplantation of human fetal liver and thymus tissue under the kidney capsule of the mice, which forms a recapitulated human thymus (the bone marrow–liver–thymus (BLT) mouse. In this presentation, several gene therapy applications that have benefited from evaluation in humanized mice such as chimeric antigen receptor (CAR) T cell therapies for cancer, anti-viral therapies and hematopoietic stem cell gene therapy for multiple monogenetic diseases is discussed.

Key words : Humanized Mouse, NSG, Gene therapy

S12-5

Regenerative approaches for off-the-shelf hypoimmunogenic stem cells

Da-Hyun Kim

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For treating the patients with organ failure, one of the best regenerative approach is to use primary cells for autologous transplantation, but the substantial time required for cell expansion has hindered its clinical application. In this regard, cells differentiated from human-induced pluripotent stem cells (hiPSCs) can be promising substitutes because they can be readily prepared. However, allogeneic transplantation of hiPSC-derived cells has the potential to elicit the immune responses in recipients, thereby leading to graft rejection. To address these challenges, we investigated strategies to obtain hypoimmunogenic stem cells by engineering the immune-related genes. First, to evade T cell-mediated responses, major histocompatibility complex (MHC) class I and II genes were inactivated. CD24, one of 'don't eat me signals', was inserted in the cells since depletion of MHC class renders cells susceptible to NK cell attack. Indeed, activation of not only T cells but also NK cells was markedly decreased in the universal hiPSC-derived endothelial cells (U-ECs) compared to wild type hiPSC-derived endothelial cells (WT-ECs), indicating the immune-evading capabilities of hypoimmunogenic stem cells. We confirmed that U-ECs survived for longer periods with better functions than WT-ECs after being transplanted into the humanized mice generated by injecting CD34+ human hematopoietic stem cells into NSG mice. These findings suggest that U-ECs produced from hypoimmunogenic iPSCs can be utilized as an off-the-shelf cell therapy for patients with ischemia. Beyond 2D-cultured cell therapy, we next aimed to develop 3D-engineered vascularized liver tissues assembled with hepatoblasts and endothelial cells, both differentiated from universal iPSCs. These off-the-shelf liver tissues also showed reduced immune rejection in vitro while maintaining their functionalities, suggesting that this approach can serve as a potential organ substitute for patients in need of transplants. Taken together, in this study, we lay the foundation for regenerative approaches with off-the-shelf hiPSCs, including cell and tissue therapy.

Key words : Rejection, Hypoimmunogenic, Angiogenesis, Liver, Humanized mice

2024

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SYMPOSIUM 13 ENG

July 26 (Fri) 09:00–10:40 | Samda Hall

Modeling Human Brain Development and Diseases

Organizer / Chair : **Hosung Jung** (Yonsei Univ.), **Hyuk-Wan Ko** (Yonsei Univ.)

Modeling neurodevelopmental disorders using human pluripotent stem cells
Hyunsoo Shawn Je (Duke-NUS Medical School)

Deciphering the neural epitranscriptome: the roles of mRNA modification in neurodevelopment
Ki-Jun Yoon (KAIST)

Human spinal cord organoids as a model system for human neurodevelopment and disease
Ju-Hyun Lee (KIST)

Decoding immune-microbiome-brain axis in a neurodevelopmental disorder mouse model
Eunha Kim (Korea Univ.)

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S13-1

Modeling neurodevelopmental disorders using human pluripotent stem cells

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The ability to generate functional neural cells from human pluripotent stem cells (hPSCs) provides a unique opportunity to study human brain development and neural disorders. In this seminar, I will present recent published and unpublished findings from our laboratory. First, I will present the direct induction and functional maturation of human forebrain glutamatergic and GABAergic neurons derived from hPSCs (Sun et al., Cell Reports, 2016) and their utility in modeling Angelman syndrome and identifying therapeutic targets for the treatment of Angelman syndrome (Kok et al., in preparation; Sun et al., Science, 2019).

Key words : Human pluripotent stem cells, human induced neurons, brain organoids, Angelman syndrome, Drug development

S13-2

Deciphering the neural epitranscriptome: the roles of mRNA modification in neurodevelopment

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Proper nervous system development is critical for its function, and deficits in neural development have been implicated in many brain disorders. Recent discoveries of widespread mRNA chemical modifications raise the question of whether this mechanism plays a post-transcriptional regulatory role in the development and function of the brain. Among various epitranscriptomic modifications, m^6A methylation is the most abundant internal mRNA modification in eukaryotes. m^6A methylation is remarkably prevalent in the brain compared to other organs and plays a critical role in regulating the cell cycle and differentiation of neural stem cells. On the other hand, mRNAs produced in the nucleus must be transported to distal axons and dendrites in differentiating neurons. We have discovered that m^6A modification in the 3'UTR of mRNAs related to cytoskeletal remodeling promotes mRNA transport to the axon terminal, facilitated by m^6A-specific binding proteins crucial for proper axonal development. Moreover, m^6A modification is frequently dysregulated in nervous system disorders. For instance, m^6A modification is significantly downregulated in postmortem tissues of ALS patients. Intriguingly, upon depleting m^6A modification in astrocytes, mice exhibited ALS-like motor impairment, motor neuron loss, and astrocyte hypertrophy. Profiling m^6A modification in astrocytes revealed its tagging on mRNAs associated with inflammatory signals and lipid metabolism, thereby limiting the stability of target mRNAs. These findings suggest that m^6A modification regulates the appropriate inflammatory response of astrocytes, and its dysregulation may contribute to the progression of neurodegenerative diseases, suggesting novel therapeutic potentials through m^6A modulation.

Key words : M6A RNA modification, RNA translocation, Epitranscriptomics, Neurodegeneration, Neuroinflammation

S13-3

Human spinal cord organoids as a model system for human neurodevelopment and disease

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The human spinal cord forms well-organized neural circuits for environmental sensing and motor behavior. Three-dimensional (3D) induction of spinal cord-like tissues from human pluripotent stem cells has been reported, but they often do not mimic the morphological features of neurulation, and their maturity is limited. Here, we report an advanced 3D culture system for producing human spinal cord-like organoids (hSCOs) suitable for scale-up and quantitative studies. The hSCOs exhibited many aspects of spinal cord development, including neurulation-like tube-forming morphogenesis, major spinal cord neuron and glial cell differentiation, and mature synaptic functional activities. We demonstrated that the hSCO platform allowed quantitative and systematic high-throughput examination of the potential risk of neural tube defects induced by antiepileptic drugs. Our findings show that hSCOs can be used to understand human spinal cord development, disease modelling, and toxicology screening.

Key words : Organoid, Spinal cord, Neurulation, Neural tube defects, Valproic acid

S13-4

Decoding immune-microbiome-brain axis in a neurodevelopmental disorder mouse model

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Children diagnosed with Autism Spectrum Disorder (ASD) commonly exhibit dysregulated immune responses. However, the underlying mechanisms contributing to the development of both neuro-developmental and immunological characteristics remain unclear. Our research revealed that offspring exposed to maternal immune activation (MIA), displaying neurodevelopmental traits, also show increased vulnerability to heightened inflammatory phenotypes upon later immune challenges. Maternally induced IL-17A during MIA contributes to prenatal neurodevelopmental phenotypes but postnatally triggers immune-primed traits in offspring, influenced by alterations in the maternal gut microbiota. Notably, transferring stool samples from pregnant mice with heightened IL-17A responses to germ-free dams was sufficient to enhance offspring's susceptibility to gut inflammation and induce changes in chromatin accessibility of $CD4^+$ T cells. This study offers mechanistic insights into how children exposed to heightened inflammation in the womb, whether due to viral infection or other inflammatory conditions, may face an elevated risk of developing both inflammatory diseases and neurodevelopmental disorders.

Key words : Neurodevelopment, Inflammatory bowel disease, Co-morbidity, Maternal immune activation

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PLENARY LECTURE 2 ENG

July 26 (Fri) 11:00–12:00 | Halla Hall

Organizer / Chair : **Hyuk-Wan Ko** (Yonsei Univ.)

The current insights into Alzheimer's disease research and advancements in therapeutic development

Inhee Mook (Seoul National University)

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Plenary Lecture 2

The current insights into Alzheimer's disease research and advancements in therapeutic development

Inhee Mook

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and a range of neuropsychiatric symptoms. Recent research has deepened our understanding of the pathophysiological mechanisms underlying AD, highlighting the roles of amyloid-beta plaques, tau neurofibrillary tangles, neuroinflammation, and synaptic dysfunction. Advances in genomic and proteomic technologies have identified novel biomarkers and potential therapeutic targets. Therapeutic development has seen significant strides with the advent of disease-modifying treatments aiming to slow or halt disease progression. Notable approaches include amyloid-beta targeting therapies, tau protein inhibitors, and agents modulating neuroinflammation and neuroprotection. Innovative drug delivery systems and personalized medicine strategies are also being explored to enhance treatment efficacy and reduce adverse effects. Despite these advancements, challenges such as drug efficacy, delivery, and patient heterogeneity remain. Ongoing clinical trials and interdisciplinary research are crucial for translating these scientific insights into effective therapies, with the ultimate goal of improving patient outcomes and quality of life. The entire process of drug development has been well supported by the development and utilization of disease-specific animal models. For research on sporadic Alzheimer's disease, further research with novel animal models in various directions will be necessary in the future.

Key words : Alzheimer's disease, Amyloid-beta, tau, Drug target, Animal model

LUNCHEON SEMINAR 4~6

July 26 (Fri) 12:10-12:30

Luncheon Seminar 4	Halla Hall A Organizer: **Dae Youn Hwang**
의료용 멸균기 전문기업 한신메디칼주식회사 후원	

Luncheon Seminar 5	Halla Hall B Organizer / Chair : **Ki Taek Nam**
Humanized models for tumor research	**Joseph Seo** (GemPharmatech Co. Ltd.)

Luncheon Seminar 6	Samda Hall Organizer: **Je Kyung Seong** / Chair : **Hyung-Sik Kim**
동물실 병원체 감염 확산의 물리적 차단과 박멸	**Gyeong Geon Kim** (WoojungBio)
동물실험실 Facility Management	**Chang Hun Lee** (WoojungBio)

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LS4

의료용 멸균기 전문기업 한신메디칼주식회사 후원

LS5

Humanized Models For Tumor Research

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Severely immunodeficient mice engrafted with human hematopoietic stem cells (HSC) have been extensively used in immuno-oncology studies to evaluate the efficacy of cancer therapies. However, because of species differences in the immune system between human and mouse, murine cytokines provide limited support to human immune cells, thus human immune system mice have limited human immune cell engraftment. Increasing evidence has shown that myeloid cells, especially macrophages and dendritic cells, are critical for the induction of anti-tumor immunity. We developed a mouse model, NCG-M, that can support human T, B, NK, and various myeloid and granulocyte cells such that in vivo evaluation of agents that require the interplay between these immune cells can be examined. This model was genetically engineered on the severely immunodeficient strain NCG and can produce human granulocyte/macrophage colony-stimulating factor 2 (GM-CSF, also known as CSF2), interleukin-3 (IL-3) and stem cell factor (SCF, also known as KITLG). Upon human CD34+ HSC cell engraftment, a significant increase in myeloid lineage cells, such as granulocytes, monocytes, neutrophils, macrophages, dendritic cells, and mast cells, was observed in the NCG-M cohort compared to NCG mice. The NCG-M mouse also supports the development of human T cells, and preliminary data showed increased B cells and NK cells. Importantly, the increased efficiency of immune cell reconstitution did not affect the morbitity and mortality of this mouse. The NCG-M is an appropriate mouse model for studying the efficacy of therapeutic agents that require human T cells and myeloid cells.

LS6

동물실 병원체 감염 확산의 물리적 차단과 박멸

Gyeong Geon Kim

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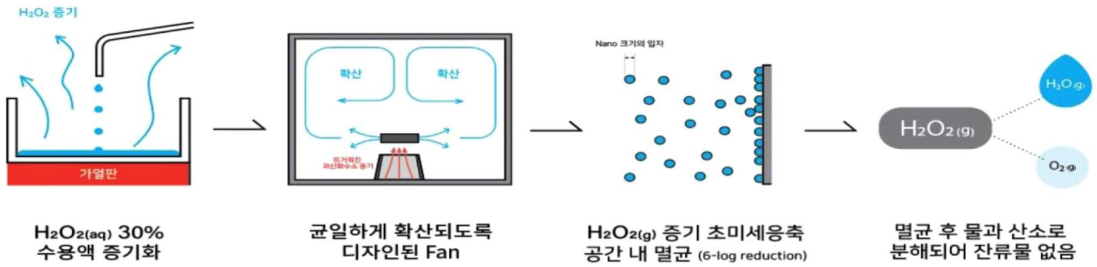
1. Hydrogen Peroxide Room Disinfection Technology Principle

Hydrogen peroxide room disinfection (HPV, Hydrogen Peroxide Vapor) uses a device to spray a 30% aqueous solution of ultra-pure hydrogen peroxide into a closed space with nanoscale vapor, making it supersaturated above the dew point. It can kill all surface and floating pathogens in the space to be sterilized and has the biological effect of inactivating all microorganisms by destroying cell walls, cell membranes, DNA & RNA.

In addition, it is an eco-friendly disinfection method that leaves no residue as it decomposes into water and oxygen through catalytic decomposition even after complete sterilization. It is the latest, efficiently upgraded disinfection and sterilization method that allows immediate entry without additional rinsing after completion.

2. Sterility Verification

General conventional disinfection methods cannot verify disinfection even after completion, but hydrogen peroxide room disinfection has the advantage of being scientifically verifiable through biological indicators (B.I.) Spore: Geobacillus stearothermophilus (population:) and chemical indicators (C.I.).



Key words : Hydrogen Peroxide Room Disinfection Technology Principle, Sterility Verification

LS6

동물실험실 Facility Management

Chang Hun Lee

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INTRODUCTION TO WOOJUNGBIO ANIMAL LABORATORY FACILITY MANAGEMENT

The Facility Management Service for animal laboratories has the effect of simplifying animal laboratory management tasks by enabling integrated operation and management in existing separate form of facility management, equipment management, and breeding management.

This service includes final inspection report after visiting on designated periods to perform equipment and facility maintenance services.

WOOJUNGBIO has a certified maintenance team for quick response to unexpected situations and a direct customer HOTLINE for prompt response within 12 hours.

A report is issued after all inspections and maintenance is performed. Through this, maintenance standardization is established by managing the history of facilities and equipment.

This service improves the validity of animal test results through standardization, increases lifespan by at least 20%, and saves maintenance costs through accident prevention and maintenance.

WOOJUNGBIO performs maintenance in animal laboratories for many countries, including several national institutions.

WOOJUNGBIO offers animal laboratory Facility Management and provide solutions for optimal animal laboratory operation.

Key words : Importance of Animal laboratory facility management

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SYMPOSIUM 14 ENG

July 26 (Fri) 14:00–15:50 | Halla Hall A

Immunosuppressive treatment and immune monitoring protocol for the preclinical NHP study of xeno solid organ transplantation

Organizer: **Ik Jin Yun** (Konkuk Univ. Hospital) / Chair : **Ik Jin Yun** (Konkuk Univ. Hospital), **Hyun Il Kim** (OptiPharm)

Immune modulation and monitoring in the nonhuman primate xenotransplantation experiments
Hidetaka Hara (Hainan Medical University)

Immunosuppressive treatment protocol for the xeno solid organ transplantation of NHP preclinical model in Japan
Takashi Yokoo (The Jikei University School of Medicine)

Immunosuppression for solid organ xenotransplantation
Jaeseok Yang (Yonsei Univ.)

Histocompatibility test for xenogenic solid organ transplantation in a preclinical model of NHP in Korea
Eun-Jee Oh (The Catholic Uinv. Seoul St. Mary's Hospital)

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S14-1

Immune modulation and monitoring in the nonhuman primate xenotransplantation experiments

Hidetaka Hara

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The chronic shortage of donor organs has spurred significant interest in xenotransplantation using porcine organs. Advances in genetically engineered pigs and immunosuppressants have markedly improved the engraftment rate and survival time of porcine organs in preclinical studies using nonhuman primates, and human clinical trials are progressing rapidly. However, overcoming xenograft rejection remains a major challenge to achieve stable engraftment.

This presentation will focus on three key objectives:
(i) Understanding the causes of xenograft loss
(ii) Developing genetically engineered pigs and immunosuppressant protocols to modulate both innate and adaptive immunity in primate hosts
(iii) Implementing essential immune monitoring techniques

Antibody-mediated rejection is a primary cause of graft loss. Therefore, removing antigenicity in pigs and inhibiting antibody-mediated complement activity are crucial. Additionally, controlling coagulation dysregulation and inflammatory responses associated with pig xenografts is essential. Complement activation inhibitors and CD40-CD154 pathway blockers are key drugs that contribute to long-term graft survival.

Recent advancements include comprehensive multi-omics profiling, alongside traditional preoperative anti-donor antibody and cytotoxicity tests, and histological evaluations, providing more detailed analyses. Combining comprehensive immunological approaches with advanced genetic engineering of pigs addresses the complex challenges of xenotransplantation and paves the way for successful pig-to-human organ and cell transplantation. This approach offers new hope to patients facing life-threatening organ failure and contributes to resolving the global organ transplant shortage.

Key words : Xenotransplantation, Immunology, Preclinical model, Genetically engineered pig, Immunosuppression

S14-2

Transplantation of a xeno-regenerated Kidney for patients with kidney failure

Takashi Yokoo

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There is no doubt that renal transplantation is a very effective treatment compared to dialysis in terms of patient quality of life and prognosis. However, not all renal failure patients can benefit from kidney transplantation due to the worldwide shortage of donors. In Japan, in particular, there is a chronic shortage of donated kidneys, perhaps due to the country's national character, and kidney transplantation has not progressed very well. In response to this shortage, xenotransplantation using porcine kidneys as a substitute has been considered worldwide. In recent years, the advent of CRISPR-Cas9 has made it possible to edit multiple genes, and the use of organs from genetically modified pigs has dramatically improved the success rate of xenotransplantation. A clinical trial for kidney transplantation has also been filed with the FDA, and a phase I trial is expected to begin soon. However, the complexity of rejection management and the huge upfront investment required for a vast facility to hygienically raise pigs are considerable hurdles to overcome in Japan.

In our previous studies, we have confirmed in primates that fetal kidney transplantation is significantly less immunogenic than mature kidney transplantation and that host urine is produced as host blood vessels wander into the transplanted kidney as it matures in vivo. In addition, fetal kidney transplantation has many advantages over mature kidney transplantation. Therefore, we are challenging to develop a drastic treatment for renal failure by applying this technology using monkey model.

Key words : Monkey, Xenotransplantation, Pig, Kidney

S14-3

Immunosuppression for solid organ xenotransplantation

Jaeseok Yang

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Organ shortage is the most important hurdle in the field of transplantation and xenotransplantation is a promising alternative to solve this problem. Recent remarkable development of gene editing technology has improved generation of multiple genetically-modified pigs for xenotransplantation and subsequent outcomes of xenotransplantation. Thanks to this achievement, solid organ xenotransplantation has been performed in human decendent models and finally in patients as clinical trials. For successful xenotransplantation, establishment of effective and safe systemic immunosuppressive regimens is also important. Depletion of T and B cells are needed as an induction therapy. Costimulatory blockade such as anti-CD40L, anti-CD40, CTLA-4Ig, anti-CD28, and anti-ICAM-1, is an essential component of immuno-suppressive regimens. Inhibitors of pro-inflammatory cytokines, such as TNF-α, IL-1bβ, and IL-6 could be supplemental. Furthermore, complement inhibitors are needed to suppress vigorous activation of complements in xenotransplantation. Oral immunosuppressants, such as prednisolone, tacrolimus, mycophenolate mofetil, and mTOR inhibitors are also needed as a maintenance therapy. Optimal combinations of various categories of immunosuppressants are now under investigation for further application to clinical trials.

Key words : Xenotransplantation, Immunosuppression, Nonhuman primates, Solid organ

S14-4

Histocompatibility test for xenogenic solid organ transplantation in a preclinical model of NHP in Korea

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Xenotransplantation offers a unique opportunity to genetically engineer the pigs to provide organs. For xenotransplantation to be successful, histocompatibility techniques and reagents should be developed to the same level as those used in allogeneic transplantation. In this session, we will review current methods for detecting anti-human (allogeneic) antibodies and methods for detecting anti-pig (xenotransplant) antibodies. Next, we will discuss the limitations of the histocompatibility tests currently used for xenotransplantation and the future direction of histocompatibility testing. The development of appropriate xenotransplant histocompatibility tests will bring significant progress in this field, which will benefit future xenotransplant recipients.

Key words : Xenotransplantation, Histocompatibility, Swine leukocyte antigens

Symposium 15 [KLAT Education 2] KOR

July 26 (Fri) 14:00-15:30 | Halla Hall B

Anatomy and practical Methods for Animal Testing II

Organizer: **Dong-jae Kim** (DGIST), **Yirang Na** (Seoul Natl. Univ. Hospital) / Chair : **Hyunjhung Jhun** (KFRI)

Anatomy and practical methods for laboratory animal eyes	**Won Tae Kim** (Keyprime Research)
Normal anatomy and evaluation methods of bone	**Jin Seok Kang** (Namseoul Univ.)
Mouse models for liver cancer; anatomy, modeling, and histopathology	**Seung-Ho Heo** (Asan Medical Center)

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S15-1

Anatomy and practical methods for laboratory animal eyes

Won Tae Kim

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The eyes have a very complex structure compared to other sensory organs, making it difficult to accurately assess their condition. If problems occur in the eyes, the first signs such as blepharospasm or conjunctival hyperemia can be observed. However, ocular examination with appropriate specialized equipment is necessary for an accurate diagnosis. Ocular examination equipment includes slit lamp biomicroscope, indirect ophthalmoscope, and tonometry. Additional equipment like OCT (Optical Coherence Tonometry) or ERG (Electroretinogram) may also be used.

Key words : Laboratory animal, Eye, Anatomy, Practical method

S15-2

Normal anatomy and evaluation methods of bone

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Bones perform multiple critical functions within the body, including serving as the structural framework that supports and protects organs, facilitating movement, and acting as a reservoir for essential minerals. Selecting the most appropriate disease model for bony tissue requires comprehensive research, with a careful comparison of the biological characteristics of the animal model to the intended therapeutic target molecule. Histopathological examination can assess morphological structures in detail and provide a diagnosis, although it primarily offers qualitative or semi-quantitative information and has limitations in quantifying lesions. To assess arthritis in joint lesions, combining advanced bioimaging techniques with three-dimensional systems and intravital animal models can offer more informative and disease-relevant platforms. Consistent and reliable spatial sampling methods have been developed to evaluate disease-specific regional variables, such as bone volume fraction and joint space. Several bioimaging techniques provide high-resolution anatomical images of animals, detecting and visualizing biological processes at various levels, and allowing *in vivo* examination of arthritic lesions. Quantitative analyses of micro-computed tomography images can assess trabecular bone volume, percent bone volume, bone mineral density and so on. This technique is advantageous for detecting bone changes and quantifying arthritis progression by measuring joint space narrowing and revealing trabecular bone structure and osteophyte formation. For simultaneous analysis of cartilage and bone parameters, fluorescence molecular tomographic imaging and near-infrared absorption spectra are also useful. The animal models of bony tissue offer numerous opportunities for investigating pathophysiology, evaluating drug efficacy, and predicting drug toxicity through the use of conventional histopathological examination and various bioimaging techniques.

Key words : Bone, Efficacy, Toxicity, Histopathology, Bioimaging

S15-3

Mouse models for liver cancer; anatomy, modeling, and histopathology

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The liver is the largest glandular organ in vertebrates and performs essential biological functions such as detoxification, metabolism, and protein synthesis. Mouse liver comprises four main lobes (median, left, right, caudate lobe) which are joined dorsally. Blood is supplied to the liver via the hepatic artery and the hepatic portal vein which open into the sinusoids. The central veins coalesce into hepatic veins, which leave the liver and drain into the inferior vena cava. Liver cancer is the fifth common malignancy worldwide and the liver is an organ prone to metastasis. There are various mouse models to recapitulate liver cancer. To generate a chemically induced hepatocarcinogenesis model, dimethylnitrosamine (DEN), CCL_4, and aflatoxin are typically applied. Representative genetically engineered mouse models include miR-221 transgenic, HBx transgenic, and P53 liver-specific KO. For generating orthotopic or metastasis models, tumor cells can be transplanted into the liver parenchyma, portal vein, and the spleen. Hepatocellular carcinoma can be diagnosed by reading HE-stained slides and immunostaining for alpha-fetoprotein, Hep Par1, etc. Cellular proliferation could be analyzed using immunostaining such as Ki67, proliferating cell nuclear antigen, and bromodeoxyuridine (BrdU).

Key words : Liver, Anatomy, Liver cancer, Mouse models, Histopathology

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SYMPOSIUM 16 KOR

July 26 (Fri) 14:00–15:50 | Samda Hall

Research trends and perspectives of animal models for functional gastrointestinal diseas

Organizer / Chair : **Chang-Woo Song** (KIT)

Animal models for functional dyspepsia (FD) and screening test for drug candidate
Chang-Gue Son (Daejeon Univ.)

Effects of vagotomy on GI motility and evaluation as an animal model
Young-Su Yang (KIT)

Development of gastrointestinal disease model animals using *Helicobacter pylori*
Yung Choon Yoo (Konyang Univ.)

Use of human/animal-derived intestinal stem cells and their differentiated cells to mimic intestinal metabolism and physiology
Kazuya Maeda (Kitasato Univ.)

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S16-1

Animal models for functional dyspepsia (FD) and screening test for drug candidate

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Functional dyspepsia (FD) is a common gastrointestinal disorder characterized by epigastric burning, epigastric pain, postprandial fullness, and/or early satiety in the absence of any underlying organic disease. Its high global prevalence (over 20%), high recurrence rate after cessation of treatment (over 20%), and significant rate of non-responders to current interventions present a clinical challenge. These issues are related to the complex and multifactorial pathophysiological features of FD. Despite this, various animal models of FD have been developed to enhance our understanding of FD's pathophysiology and to explore better treatment options. However, it remains unclear which of these models most closely mimics the human disease. In this presentation, I will provide a comprehensive overview of the currently available animal models of FD in relation to the clinical features of FD. Additionally, I will introduce Damjeok Syndrome, a concept proposed by this symposium, which refers to refractory FD-like symptoms accompanied by a palpable mass-like stiffness in the upper abdomen, as a novel strategy derived from traditional Korean medicine.

Key words : Animal model, Functional dyspepsia, Gastrointestinal disorder, Damjeok Syndrome

S16-2

Effects of vagotomy on GI motility and evaluation as an animal model

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Vagotomy, a surgical procedure involving partial removal of the vagus nerve, disrupts the bidirectional communication between the gut and brain, affecting various gut and brain functions. In clinical practice, vagotomy is utilized for patients with refractory gastric ulcers, while vagus nerve stimulation is emerging as a therapeutic approach for diverse diseases. This study investigates vagotomy techniques in rodent models and present the study results. Rodent vagotomy methods broadly fall into two categories: cervical and subdiaphragmatic. Our study focused on cervical left vagotomy due to its clinical relevance and potential for minimizing adhesions. Following vagotomy, we assessed clinical signs, mortality rates, body weight changes, food consumption, clinical pathology, gastrointestinal (GI) motility, behavioral responses, and histopathological alterations. Cervical vagotomy (VNX) resulted in reduced gastric emptying and intestinal transit without significant GI pathology. Behavioral assessments revealed increased anxiety levels (as observed in the open field test) and decreased short-term memory (Y-maze), while depression (forced swimming test) and motor function (rota-rod) remained unaffected. Further investigations are needed to elucidate underlying mechanisms, which could potentially enhance the management strategies for functional gastrointestinal disorders.

Key words : Vagotomy, Vagus nerve, GI motility, Behavioral assessment, Animal model

S16-3

Development of gastrointestinal disease model animals using *Helicobacter pylori*

Yung Choon Yoo

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A gastrointestinal disease is one that affects the gastrointestinal (GI) tract, the passage that runs from the mouth to the anus. GI disease is an important disease that affects the gastrointestinal tract, including the esophagus, stomach, small intestine, large intestine, and rectum, as well as digestive auxiliary organs such as the liver, gallbladder, and pancreas. However, although there are many GI diseases, there are few experimental models, especially animal models, that are useful for studying these diseases. Functional GI disorders (FGID), such as functional dyspepsia (FD) and irritable bowel syndrome (IBS) are characterized by chronic abdominal symptoms by complex causes that are not easily explained. Their pathophysiology is not yet fully understood, but animal models have been of great value in improving our partial understanding of the complex biological mechanisms of these diseases. Meanwhile, there are almost no animal models for stomach-related diseases such as indigestion, gastritis, or gastric ulcers, so research on these diseases is quite limited. Considering that many GI diseases occur in relation to the stomach, understanding the occurrence and pathological characteristics of stomach-related diseases is very important for the prevention and treatment of GI diseases. *Helicobacter pylori* (*H. pylori*) is a type of bacteria that infects the stomach. It can cause sores and inflammation in the lining of the stomach or the upper part of the small intestine (the duodenum). In some people, infection with this bacterium can lead to stomach cancer. Many GI diseases are accompanied by an inflammatory response during their development, and inflammation is also observed in the stomach or upper small intestine during *H. pylori* infection. Here, we present the usefulness of the *H. pylori* animal infection model in GI disease research, and discuss recent research results related to this bacterial infection.

Key words : GI disease, Functional dyspepsia, Helicobacter pylori infection, Inflammation, Animal model

S16-4

Use of human/animal-derived intestinal stem cells and their differentiated cells to mimic intestinal metabolism and physiology

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In the drug development process, it is essential to quantitively predict intestinal absorption and toxicity of orally-administered drugs. However, due to the difference in the expression/function of causal molecules, in vivo animal studies and in vitro studies with immortalized cells cannot always capture their characteristics. We recently established various experimental systems with the use of crypt-derived intestinal stem cells from human/animal tissue samples. In our approach, the stemness of cells is maintained by conditioned media of L-WRN cells stably expressing Wnt3a/R-spondin 3/Noggin and once these factors are simply removed from the media, the cells are spontaneously differentiated to absorptive epithelial cells. Using these cells, we confirmed the expression/function of various kinds of metabolic enzymes and transporters and succeeded in the accurate prediction of the intestinal availability of CYP3A substrates. Regarding the prediction of drug-induced intestinal toxicity, we found that ATP level of intestinal stem cells after exposure of EGF receptor tyrosine kinase inhibitors (EGFR-TKIs) can rationally explain the rank order of the relative risk of severe diarrhea among different EGFR-TKIs. Moreover, one of the major causes of drug-induced emesis is excessive secretion of serotonin from enterochromaffin (EC) cells, which are only ~1% of the total intestinal cells. Thus, we established EC cell-rich spheroids to sensitively catch the serotonin release. Using that system, we found a nice correlation between the clinical emesis risk induced by various ALK/ROS1-TKIs and drug concentration-dependent serotonin release from those spheroids. Therefore, we suggested that crypt-derived intestinal stem cells and their differentiated cells are very useful for the prediction of intestinal absorption and drug-induced intestinal toxicity.

Key words : Crypt-derived intestinal stem cells, Drug-induced diarrhea, Drug-induced emesis, Intestinal absorption, Tyrosine kinase inhibitors

실험동물연구장학생
POSTER PRESENTATION

July 25 (Thu) 13:20-14:20 I ICC JEJU 3F Lobby

	Chair : **Sun Shin Yi** (Soonchunhyang Univ.)
PS-R-001 (해부병리)	**Hyun-Kyoung Son** Gyeongsang Natl. Univ.
PS-R-002 (독성병리)	**Yeon Su Lee** Eulji Univ.
PS-R-003 (해부병리)	**Tae Ryeol Kim** Pusan Natl. Univ.

KOREAN ASSOCIATION
FOR LABORATORY ANIMAL SCIENCE

실험동물연구장학생 포스터 발표 안내

1. 포스터 발표 안내

발표시간	7월 25일(목) 13:20-14:20
발표장소	제주 국제컨벤션센터 3층 로비
포스터 번호	PS-R-001 (해부병리) PS-R-002 (독성병리) PS-R-003 (해부병리)
	총 3개
부착 시간	7월 25일(목) 09:00-11:00
철거 시간	7월 25일(목) 17:00

※ 철거 시간 이후의 포스터 분실은 책임지지 않습니다.

2. 포스터 발표 및 시상

- 포스터 발표는 좌장의 진행에 따라 포스터당 7분 (5분 발표, 2분 질의응답)으로 진행되며, 발표시간에 포스터 앞에 대기하여 주시기 바랍니다.
- 장학생은 총회에서 진행하는 시상식에 반드시 참석해 주시기 바랍니다. (대리수상불가)
- 포스터 보드에 2회 이상 (개수로 적용) 미부착 시, 교신저자(연구책임자)에게 향후 1년간 포스터 제출 불가의 제재가 주어집니다.

3. 포스터 작성안내

- Poster board의 크기는 **95cm(가로) x 210cm(세로)**이며, 특히 제목이 가로 넓이를 초과하지 않도록 준비하여야 합니다.
- 모든 포스터는 지정된 날짜, 기간 동안에 지정된 board에 부착하여야 합니다.
- 포스터 내용은 abstract, purpose, results (figures and tables), conclusions, references의 순서로 작성합니다.
- 전방 2 m 위치에서 쉽게 읽을 수 있도록 굵고 명확한 글씨체를 이용하여 제작합니다.
- 모든 포스터의 부착 및 철거는 당일 지정된 시간에 발표자가 수행하여 주기 바랍니다. (철거 시간 이후의 포스터 분실은 책임지지 않습니다.)

실험동물연구장학생 Poster

Poster no.	Title	Speaker
PS-R-001	Baicalin ameliorated glutamate toxicity-induced nerve damage in mouse hippocampal neurons	Hyun-Kyoung Son
PS-R-002	The preventive effect of gastrodia elata blume extract on vancomycin-induced acute kidney injury in rats	Yeon Su Lee
PS-R-003	Establishment of platform for the evaluation of deodorizing effects based on the characterization of odor markers associated with aging in animal system	Tae Ryeol Kim

PS-R-001

Baicalin ameliorated glutamate toxicity-induced nerve damage in mouse hippocampal neurons

Hyun-Kyoung Son, Phil-Ok Koh*

Department of Anatomy and Histology, College of Veterinary Medicine, Gyeongsang National University, Jinju, 52828, South Korea

Baicalin, a flavonoid isolated from Scutellaria baicalensis, has anti-inflammatory, antioxidant, and neuroprotective effects. Glutamate is a representative substance that damages nerve cells by inducing excitotoxicity. We investigated the neuroprotective effects of baicalin on glutamate-exposed neurons. Mouse hippocampal neuronal cell line (HT22) were cultured in a general manner, glutamate (5 mM) and/or baicalin were treated on the cells. Baicalin was administered in 10 units from 10 uM to 100 uM 1 hr before glutamate treatment. Cells were collected 24 hr after glutamate, and cell viability was measured using MTT assay. Reactive oxygen species and lipid peroxidation analyses were performed to determine the oxidative stress. Glutamate induced severe neuronal damage including condensation of the cell shape, no dendrite and no axon, and detachment from the culture plate. However, baicalin treatment attenuates these morphological changes, the effect of baicalin was dose dependent. MTT assay results showed that baicalin treatment ameliorates the decrease in cell viability due to glutamate toxicity. Cell viability was dose-dependently increased from 10 uM to 50 uM, maintained at a constant level from 60 uM to 80 uM, and slightly decreased at 90 uM and 100 uM. Thus, we focused on baicalin dose of 10, 30, 50 uM. Cell viability was 0.33 ± 0.02 in only glutamate-treated group and 0.77 ± 0.02 in co-treated group with glutamate and baicalin (50 uM). ROS and LPO analyses showed that baicalin attenuated changes caused by glutamate toxicity. The effect of baicalin on these results was dose-dependent. Baicalin treatment ameliorated the glutamate toxicity-induced increase in caspase-3. Therefore, we confirmed that baicalin performs antioxidant and anti-apoptotic functions against glutamate toxicity in neurons. In conclusion, these findings demonstrate that baicalin exerts neuroprotective effects on damaged neurons. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00248145).

Corresponding author **:** Phil-Ok Koh

Keywords **:** Baicalin, Glutamate, HT22, Neuroprotection

PS-R-002

The preventive effect of gastrodia elata blume extract on vancomycin-induced acute kidney injury in rats

Yeon Su Lee[1], Yu Rim Park[1], Hyo Bin Lee[1], Hye Joon Park[1], Ha Eun Lee[1], Geon A Kim[2], Sang-Hoon Kim[3,4]*, Jae-Ho Shin[1,4]*

[1]*Department of Biomedical Laboratory Science, Graduate School, Eulji University, Gyeonggi-do, South Korea*
[2]*Department of Biomedical Laboratory Science, Eulji University, Uijeongbu, South Korea*
[3]*Department of Internal Medicine, Eulji Hospital, Seoul, South Korea*
[4]*Eulji Medi-Bio Research Institute, Eulji University School of Medicine, Seoul, South Korea*

Gastrodia elata Blume (GEB), a traditional medicinal herb, has demonstrated pharmacological effects including protection against liver, neuronal, and kidney toxicity. This study investigates the protective effects of GEB extract on vancomycin (VAN)-induced nephrotoxicity in rats, focusing on mechanisms of anti-oxidative stress, anti-inflammation, and anti-apoptosis. Five-week-old male Sprague-Dawley rats were randomly divided into the following three groups: control (CON) group, orally administered distilled water (10 mL/kg BW); vancomycin-induced AKI (VAN) group, orally administered distilled water (10 mL/kg BW); and the GEB-treated (GEB) group, orally administered GEB extract (10 mL/kg BW) for 14 days, with VAN (400 mg/kg BW) administered intraperitoneally during the last 3 days. Kidney function was evaluated through serum levels of blood urea nitrogen (BUN) and creatinine (CREA), histological analysis, immunohistochemical analysis, and Western blotting. The GEB group showed significantly lower kidney weight and serum BUN and CREA levels compared to the VAN group. Histological analysis revealed that GEB reduced VAN-induced renal damage, including epithelial detachment and interstitial inflammation. Immunohistochemical analysis showed decreased expression of N-acetyl-D-glucosaminidase (NAG), myeloperoxidase (MPO), and tumor necrosis factor-alpha (TNF-α) in the GEB group compared to the VAN group. The number of TUNEL-positive cells and malondialdehyde levels were lower, while total glutathione levels were higher in the GEB group compared to the VAN group. These findings suggest that GEB extract prevents VAN-induced renal tissue damage through anti-oxidative, anti-inflammatory, and anti-apoptotic mechanisms. GEB could be a potential therapeutic agent for preventing acute kidney injury. This study was carried out with the support of Cooperative Research Program for Agriculture Science & Technology Development funded by the Rural Development Administration, Republic of Korea (RS-2022-RD009980)

Corresponding author **:** Sang-Hoon Kim, Jae-Ho Shin

Keywords **:** Gastrodia elata Blume, Acute kidney injury, Preventive effect, Anti-inflammation, Anti-oxidation

PS-R-003

Establishment of platform for the evaluation of deodorizing effects based on the characterization of odor markers associated with aging in animal system

Ji Eun Kim, Tae Ryeol Kim, Hee Jin Song, Yu jeong Roh, Ayun Seol, Eun Seo Park, Ki Ho Park, Su Ha Wang, Su Jeong Lim, Dae Youn Hwang*

Department of Biomaterials Science (BK21 FOUR Program), College of Natural Resources & Life Science/Life and Industry Convergence Research Institute/Laboratory Animal Resources Center, Pusan National University, Miryang 50463, Korea

Most studies on the identification and characterization of age-related odors are focused only on human body and rarely on experimental animals although they are considered as excellent systems in many biological studies. We wanted to establish the platform for the evaluation of deodorizing effects based on the characterization of odor markers associated with aging in animal system. To achieve this, odor markers associated with aging were characterized from urine of ICR mice with four different ages (2, 6, 8, and 10-months-old), and then alterations on the concentration of these markers were analyzed in ICR mice after treating brown algae for 2 weeks. In GC-MS analysis, the concentrations of 15 odor components such as ethylamine, trimethylamine (TMA), and toluene and total VOCs were enhanced in 8- and 10-months-old ICR mice. Among them, TMA was selected as a candidate for odor biomarker related to aging based on the present results showing that TMA concentration increases with age and it has been reported to have an odor similar to rotten fish. In addition, the increase in TMA concentration was completely reflected in the transcript level of TMA monooxygenase (FMO3) in the liver. Based on these results, we further evaluated the deodorizing effects of two natural products including ethanol extracts of Ecklonia cava (EEC) and Sargassum fulvellum(EES). The concentration of TMA in urine was decreased with dose dependent manner, and similar results were observed in total VOCs including toluene, hexamethyl cyclotrisiloxane, and benzothiazole. Therefore, these results provide scientific evidence that alterations in urinary volatiles associate with age can be regarded as aging-related odor marker in ICR mice. Especially, TMA has potential as a novel diagnostic odor marker for aging. Also, this platform can be used to evaluate deodorization effects of natural products in animal system.

Corresponding author **:** Dae Youn Hwang

Keywords **:** Aging, ICR mice, Trimethylamine, Ecklonia cava, Sargassum fulvellum

포스터 초록
POSTER PRESENTATION

Poster Presentation 1
July 25 (Thu) 13:20~14:20 ICC JEJU Lobby
Chair : **Jae-Hoon Choi** (Hanyang Univ.)
PS-A-001~020 (해부병리)
PS-B-001~030 (독성병리)
PS-C-001~010 (미생물)
PS-D-001~040 (유전자질환모델)
PS-E-001~021 (시설운영 및 기타)

Poster Presentation 2
July 26 (Fri) 13:00-14:00 ICC JEJU Lobby
Chair : **Jun-Won Yun** (Seoul Natl. Univ.)
PS-A-021~048 (해부병리)
PS-B-031~067 (독성병리)
PS-C-011~019 (미생물)
PS-D-041~070 (유전자질환모델)
PS-E-022~041 (시설운영 및 기타)

KOREAN ASSOCIATION
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포스터 초록 (Poster Presentation) 안내

1. 포스터 발표 안내

발표시간	포스터 발표 1	포스터 발표 2
	7월 25일(목) 13:20-14:20	7월 26일(금) 13:00-14:00
발표장소	제주 국제컨벤션센터 3층 로비	
포스터 번호	PS-A-001~020 (해부병리) PS-B-001~030 (독성병리) PS-C-001~010 (미생물) PS-D-001~040 (유전자질환모델) PS-E-001~021 (시설운영 및 기타)	PS-A-021~048 (해부병리) PS-B-031~067 (독성병리) PS-C-011~019 (미생물) PS-D-041~070 (유전자질환모델) PS-E-022~041 (시설운영 및 기타)
	총121개	총124개
부착 시간	7월 25일(목) 09:00-11:00	7월 26일(금) 09:00-11:00
철거 시간	7월 25일(목) 17:00	7월 26일(금) 17:00

※ 철거 시간 이후의 포스터 분실은 책임지지 않습니다.

2. 포스터 심사 및 시상

- **포스터 심사 :** 포스터 발표는 좌장의 진행에 따라 포스터당 4분(3분 발표, 1분 질의응답)으로 진행되며, 과학적 성과와 발표자의 발표력 등을 기준으로 우수포스터를 선정하여 시상하오니 반드시 발표시간에 포스터 앞에 대기해 주시기 바랍니다.
- **미부착 포스터:** 포스터 보드에 2회 이상 (개수로 적용) 미부착 시, 교신저자(연구책임자)에게 향후 1년간 포스터 제출 불가의 제재가 주어집니다.
- **우수포스터상 시상:** 우수포스터상 시상: 7월 26일 (금) 15:50-16:20/폐회식
- 우수포스터의 경우 폐회식에서 선정자를 호명합니다. 호명 시 자리에 없으면 다음 우수자에게 상이 수여되오니, 학술대회 종료일까지 학술대회에 꼭 참석해 주시기 바랍니다. (상장과 상금 15만원 수여, 대리수상불가)

3. 포스터 작성안내

- Poster board의 크기는 **95cm(가로) x 210cm(세로)**이며, 특히 제목이 가로 넓이를 초과하지 않도록 준비하여야 합니다.
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- 포스터 내용은 abstract, purpose, results (figures and tables), conclusions, references의 순서로 작성합니다.
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Anatomy / Physiology

Poster no.	Title	Speaker
PS-A-001	Peroxiredoxin-2 expression is involved the neuroprotective mechanism of retinoic acid on cerebral ischemic tissues and glutamate-exposed neurons	Hyun-Kyoung Son, Phil-Ok Koh
PS-A-002	Retinoic acid alleviates the injury-induced reduction of neuron specific enolase (γ-enolase) expression in ischemic stroke animal model and glutamate-exposed neurons	Hyun-Kyoung Son, Phil-Ok Koh
PS-A-003	The effect of chinese quince and black maca on blood high glucose-induced SD-RAT by Streptozotocin	Junyoung Ahn
PS-A-004	Baicalin ameliorated neurological impairment and cerebral ischemic injury in a stroke rat model	Hyun-Kyoung Son, Phil-Ok Koh
PS-A-005	Sensitivity of cardiomyocytes to oxygen saturation in the cell isolation media varies depending on the original location of each cardiomyocyte in the heart	Ryounghoon Jeon
PS-A-006	Investigating the effects of mixtures of antioxidant and anti-inflammatory natural substances on hippocampal neurogenesis in an MPTP-induced mouse model of Parkinson's disease	Miri Jo
PS-A-007	Evaluation of efficacy through behavioral assessment in a peripheral neuropathy model	Na-Hye Park
PS-A-008	P-selectin-mediated targeted delivery of f-BRDP nanoparticles in MCAO rat models	Suyeon Lee
PS-A-009	Establishment of intratracheal instillation method in neonatal Sprague-Dawley rat	Su-Jin Lim
PS-A-010	Evaluation of anti-obesity and cholesterol level relief for paseolamine in white kidney bean extract	Yoon-seo Choi
PS-A-011	Vascular visualization study for bone regeneration assessment in a calvaria bone defect model in rats	Yoon Beom Lee
PS-A-012	A detailed protocol for isolating and characterizing pulmonary-specific extracellular vesicles from mouse BALF post-acute lung injury	Nayoung Lee
PS-A-013	Efficient miRNA delivery to alveolar macrophages using surfactant protein A-conjugated extracellular vesicles: A novel therapeutic approach for lung inflammation	Do Hyun Kim
PS-A-014	Inhibitory effect of philadelphus schrenkii extract on macrophage inflammation and acute lung injury	Dahyun Ko
PS-A-015	Anti-inflammatory activity of endarachne binghamiae extract and related intracellular mechanisms	Sang Hoon Lee
PS-A-016	Activation of macrophages and NK cells and related mechanism by pine bud	Sung Kyung Yoon
PS-A-017	Endarachine binghamiae ameliorates obesity and oxidative stress in mouse model	Sang Seob Lee
PS-A-018	Platycarya strobilacea leaf extract ingibits NLRP3 inflammasome activation in bone marrow derived macrophage	Ga Young Lee
PS-A-019	CXCL5/CXCL8 promotes inflammatory response in peri-implantitis by activating the PI3K/Akt/NF-κB signaling pathway	Yu Rim Cho
PS-A-020	Discovery of a new long COVID mouse model via systemic histopathological comparison of SARS-CoV-2 intranasal and inhalation infection	Donghun Jeon
PS-A-021	Adult K18-hACE2 mice are suitable model for studying SARS-CoV-2 intranasal infection than direct contact transmission	Jiseon Kim
PS-A-022	Unveiling new therapeutic possibilities through NOX4 deficiency in skeletal development and trabecular bone mass increase	Ka Young Ko
PS-A-023	A comparative study of bone regeneration effects between customized synthetic bone grafts OSTEON-3 collagen and OSTEON-3 block in rat calvaria critical-size defects	Maierdanjiang Wufuer

PS-A-024	Electron electron-producing apparatus protects against folic acid-induced acute kidney injury in rats by inhibiting inflammatory responses	Seukchan Kim
PS-A-025	Evaluation of the biological effects of FLASH radiation on the intestines and testicles	Min-Young Choi
PS-A-026	Giant cell hepatitis in a Burmese python (Python bivittatus)	Gye-Hyeong Woo
PS-A-027	Spirocerca lupi infection in a fennec fox	Gye-Hyeong Woo
PS-A-028	HPRT1 is the most stable reference gene for normalization of mRNA expression in long-term expanded canine skin fibroblast	Miah Rubel
PS-A-029	Role of toll-like receptor 4 in a chronic obstructive pulmonary disease mouse model induced by co-administration of porcine pancreas elastase and lipopolysaccharide	Dong-Hyun Kim
PS-A-030	Tumor-priming CD8+ natural killer T-like cells as an efficient novel cell therapy for gastric cancer peritoneal metastasis	Juheon Lee
PS-A-031	A fine-tuning modulation of mTOR signaling pathway controls the protective antibody responses against influenza A virus	Yejin Lee
PS-A-032	Study on the efficacy of bypass allogeneic acellular nerve graft using supercritical extractor technique in rat sciatic nerve neuroma-in-continuity model	Jinil Choi, Seung hwan Kim
PS-A-033	Apelin mitigates aged-related severity of acute kidney injury in sischemia-reperfusion models	Geum-Lan Hong
PS-A-034	BRCA1 mutation promotes sprouting angiogenesis in inflammatory cancer-associated fibroblast of triple-negative breast cancer	Chae Min Lee
PS-A-035	Therapeutic effect of donepezil on neuroinflammation and cognitive impairment after moderate traumatic brain injury	Ji Hyeon Lee
PS-A-036	Autophagy and mitophagy-related extracellular mitochondrial dysfunction of cerebrospinal fuid cells in patients with hemorrhagic moyamoya disease	Dong Hyuk Youn
PS-A-037	Oxiracetam alleviates anti-inflammatory activity and ameliorates cognitive impairment in the early phase of traumatic brain injury	Dong Hyuk Youn
PS-A-038	Evaluation of the graft uptake and the effacement of melanin pigmentation in giant melanocytic nevus using supercritical fluid extractor (SCFE) decellularization technique: a preliminary study	Celige Li
PS-A-039	Effect of A12, an inverse agonist of estrogen-related receptor gamma (ERRγ), on a sepsis model in vitro and in vivo	Jae-Eon Lee
PS-A-040	Ginseng Berry Juice regulates the inflammation in acute ulcerative mouse models and the major bioactive substances are Ginsenosides Rb3, Rc, Rd, and Re	So-Hyeon Bok
PS-A-041	Saururus chinensis water-extract effectively controls asthma by recovering of Th1/Th2 imbalance and suppressing of NF-kB/COX-2/PGE2-related inflammation	Soon-Young Lee
PS-A-042	Ameliorative effects of Prunella vulgaris on lower urinary tract symptoms induced by benign prostatic hyperplasia in SD rats via nitric oxide and potassium channel	Beno Ramesh Nirujan
PS-A-043	Chronic pelvic ischemic model in rats for assessment of erectile dysfunction and lower urinary tract symptoms	Jeongsook Kim
PS-A-044	Anti-obesity effects of Aceriphyllum rossii extract in high-fat diet induced obese mice	Hye won An
PS-A-045	Altered dynamics of bone development in the MEGF8 mouse model cause Carpenter syndrome-like craniosynostosis	Koeun Hwangbo
PS-A-046	NMUR2 as a therapeutic target in glioblastoma	Yuna Roh
PS-A-047	Antitumor effect of small chemical containing an Indazole group: tumor-associated macrophages repolarization in breast cancer model	Yeon Ju Ryu
PS-A-048	Enhanced therapeutic outcome of primed iMSC-derived extracellular vesicles in acute kidney injury	Ran Kim, Minjae Kim

Toxicology / Pathology

Poster no.	Title	Speaker
PS-B-001	Toxicological assessment of intravenous-infused human adipose-derived mesenchymal stem cells in common marmoset	Ji-Eun Kim
PS-B-002	Pre-clinical safety assessment of a SARS-CoV2 mRNA Vaccine Candidate in Cynomolgus macaque (Macaca fascicularis)	Jae-Hun Ahn
PS-B-003	Protective effect of a natural volatile odorant, β-Caryophyllene, on lipopolysaccharide-induced inflammation in primary human nasal epithelial cells (HNEpC)	Jeong-In Baek
PS-B-004	Restoration of β-amyloid-induced cognitive Impairment by sulforaphane via enhancing neurohormetic stress responses	Chan Lee
PS-B-005	Aggravation of learning and memory functions in C57BL/6 mice by chronic unpredictable mild stress	Chan Lee
PS-B-006	Pulmonary toxicity study of nanoparticles (zinc oxide, carbon black and mixed nanoparticles)	Do-Yeon Seo
PS-B-007	BPA exposure impairs synaptic architecture and function by modulating BDNF signaling via RGS4 in the cerebral cortex	Eui Jun Min
PS-B-008	Granulomatous hepatitis in two Sprague-Dawley rats	Tae-Kyung Kim
PS-B-009	Acute inhalation toxicity of zinc oxide carbon black nanocomposites as tire particles	Jung-Taek Kwon
PS-B-010	Toxicity assessment and mechanism of lung damage induced by substance X	Sangryul Cha
PS-B-011	Advanced organoid models for screening natural products in liver fibrosis therapy	Jiyoung Heo
PS-B-012	Imatinib suppresses oral squamous cell carcinoma by targeting and inhibiting the PI3K/AKT/mTOR signaling pathway	Lei Ma
PS-B-013	Rhein induces apoptosis and ROS in oral cancer cells by inhibiting AKT/mTOR signaling pathway	Zhibin Liu
PS-B-014	Imatinib regulates inflammation and apoptosis on a DSS-induced colitis model mice	Kanghyun Park
PS-B-015	Silibinin activates the JNK/c-Jun pathway leading to ROS generation and cell apoptosis in oral squamous cell carcinoma	Ke Huang
PS-B-016	Compound A promotes alveolar epithelial cell regeneration via RAGE signaling pathway in emphysema	Jimin Jang
PS-B-017	Effects of Erigeron annuus extract on a mouse model of atopic dermatitis-like symptoms	Myeongguk Jeong
PS-B-018	Early diagnosis of chemotherapy-induced peripheral neuropathy through heart rate variability parameters in a mouse model	Yeeun Kim
PS-B-019	Maternal exposure to diesel exhaust particles (DEP) impairs fetal brain development and induces autism-like behaviors in mice	Moon Yi Ko
PS-B-020	The role of the gut microbiome in colitis models using germ-free mouse	Seongyu Choi
PS-B-021	ZL-240317 ameliorate atopic dermatitis(AD) in DNCB-induced AD model using SKH-1 hairless mice	Jeong Hoon Kim
PS-B-022	Novel protein-modified compound C ameliorates bleomycin-induced pulmonary fibrosis in mice	Se Bi Lee
PS-B-023	Acute inhalation toxicity of Cannabidiol (CBD) in ICR mice using vaporization	Joo Hyung Park
PS-B-024	Evaluation of acute inhalation toxicity of vaped THC in ICR mice	Seonghwa Lee
PS-B-025	Beauvericin induces G2/M cell cycle Arrest during mouse oocyte meiosis	Yejin Kim
PS-B-026	Toxicity evaluation of doxorubicin and liposomal doxorubicin in mice	Yeon-Yong Kim, Bori Lee

PS-B-027	The effect of Gastrodia Elata Blume extract on hyperlipidemia in high-fat-diet rat model	Hyeon Jeong Na
PS-B-028	Gastrodia elata Blume extract ameliorates osteoarthritis in a monosodium iodoacetate-induced rat model	Yeon Su Lee
PS-B-029	Anti-inflammatory and anti-allergic effects of Gastrodia elata Blume extract in ovalbumin-induced asthma rat model	Jeong Su Park
PS-B-030	Potential role of macrophage in COVID-19 mRNA vaccine-induced heart injury	Sumin Cho
PS-B-031	Assessment of SARS-CoV-2 mRNA vaccine-induced toxicity in Type 2 diabetic mice	Eunji Lee
PS-B-032	Effects of nanoparticles on innate immunity: study in young, old, and subcutaneous tumor mouse models	Seo-Gyeong Jo
PS-B-033	RNA sequencing data of mouse 4-cell embryo treated with Nanoplastics	Hyeong-ju You
PS-B-034	Effects of nanoplastics exposure on oocyte maturation in mouse and cynomolgus monkey	Hyeong-ju You
PS-B-035	Exposure to PMMA nanoplastics through the mouse respiratory system causes lung abnormalities	Changsic Youn
PS-B-036	Loss of Ninjurin1 alleviates acetaminophen-induced liver injury via enhancing AMPKα-NRF2 pathway	Seung Hyun Oh
PS-B-037	Acute inhalation toxicity test of Dimethyl 1,4-cyclohexanedicarboxylate in SD rats	Dae-Sik Rha
PS-B-038	Loranthus tanakae Franch. and Sav. attenuates respiratory inflammation caused by asian sand dust	Se-Jin Lee
PS-B-039	NLRC4 regulates Th2 differentiation in allergic asthma induced by house dust mite	So-Won Pak
PS-B-040	The effects of Pycnogenol, a pine bark extract on pulmonary inflammation by Asian sand dust in mice	Woong-Il Kim
PS-B-041	TXNIP regulates pulmonary inflammation induced by Asian sand dust	Sin-Hyang Park
PS-B-042	Large-scale profiling of coding and long noncoding transcriptomes in the lungs of mice acutely exposed to vaporized CBD or THC	Jeong-Hyeon Heo
PS-B-043	Acute inhalation toxicity of dipropylene glycol dimethyl ether: a study in Sprague-Dawley rats	Yong Soon KIm
PS-B-044	Effects of AMT-XX05 on pathological mechanisms of Alzheimer's disease in murine neuroblastoma Neuro2a cells	Jeong-Hyeon Heo
PS-B-045	Effects of a salicylic acid derivative, AMT-XX06, on changes of Alzheimer's disease-related factors in murine neuroblastoma Neuro2a cells	Ji Hun Kim
PS-B-046	Evaluation of blood-brain barrier permeability of liposomal AMT-XX05 in C57BL/6 mice	Seok Hwan Chang
PS-B-047	Recombinant human bone morphogenetic protein-2 priming of mesenchymal stem cells ameliorate acute lung injury by inducing regulatory T cells	Jooyeon Lee
PS-B-048	Major pathological lesion and NOAEL analysis of carcinogenicity test on 190 insecticides	Gyu Baek Kim
PS-B-049	Major pathological lesion and NOAEL analysis of repeated dose toxicity test of 190 insecticides	Da Hui Jeong
PS-B-050	Acute inhalation toxicity study of barium carbonate in SD rats	Seong-won Jo
PS-B-051	Maximum tolerated dose (MTD) test of caragana sinica in ICR mice	Min Hee Hwang
PS-B-052	Successful tracheal tissue regeneration using biofabricated analogues in rabbit model	Jae Yeon Lee
PS-B-053	Evaluation of immunotoxicity in ICR mice following oral administration of polypropylene microplastics	Hee Eon Kim

PS-B-054	The toxic effects of environmental risk factors(microplastics) on autism spectrum disorder with autism-like behavioral mouse	Da HEE Son
PS-B-055	Enhancing liver cancer metastasis detection through biomarker analysis in metastatic mouse models	Hee Jung Kwon
PS-B-056	Efficacy of canine stem cell-derived ex vivo vesicles treatment in canine atopic and allergic dermatitis	Ha-Young Shin, Jeong Ho Hwang
PS-B-057	Surface conjugation of microspheres carrying rapamycin on mesenchymal stem cells exerts improved anti-fibrotic effects against pulmonary fibrosis	Hee Jeong Park
PS-B-058	Single oral dose toxicity study of Vaccinium oldhamii in Sprague-Dawley rats	Sang-Myung Han
PS-B-059	Angelica keiskei extract alleviates colitis via attenuating colonic mucosa injury and regulating pro-inflammatory cytokines production	Ui-Jin Bae
PS-B-060	Oral repeated dose range finding study of purple corn husk extract in sprague-dawley rats	Kiyeon Lee
PS-B-061	Protective effects of Sicyos angulatus on binge drinking-induced liver injury through regulation of gut integrity in mice	Min-Chan Kim
PS-B-062	Discovery and identification of tastants in kimchi using bitter taste receptor activation	Junho Lee
PS-B-063	Physiologically-active composition based on Rosa multiflora Thunb and Zizyphus jujuba Miller	Junho Lee
PS-B-064	Biochemical studies of the structure and function of the N-methyl-D-aspartate subtype of glutamate receptors by Ergot	Junho Lee
PS-B-065	Repellent interactions with olfactory receptors and ionotropic receptors analyzed by molecular modeling receptors to find repellents	Junho Lee
PS-B-066	Network pharmacology and molecular docking analyses of mechanisms underlying effects of the kaempferol	Junho Lee
PS-B-067	Discovery and application of Medical Fluorophore 33: a novel theranostic agent for cancer therapy and imaging in mice of colorectal cancer	Kwang Hee Son

Microbiology

Poster no.	Title	Speaker
PS-C-001	Polymicrobial enteric infection and treatment in common marmoset (Callithrix jacchus), especially Enteropathogenic Escherichia coli (EPEC)	Hee Jin Choi
PS-C-002	Comparison of marmoset fecal bacterial monitoring according to origin from Japan and Europe	Hye Mi Kwon
PS-C-003	Heat-killed Limosilactobacillus Reuteri modulates the growth performance and inflammation of weaning pigs via microbiota composition and intestinal stem cell activity management	Jae Han Park
PS-C-004	Changes in gut microbiota after radioactive iodine therapy	Keun-Woo Lee
PS-C-005	Anti-tumor effects of heat-killed Lactobacillus plantarum NCHBL-004 on syngenic melanoma mice model	In Su Seo
PS-C-006	Entamoeba muris infection induces intestinal Inflammation and Gut Microbiota changes	Tae hun Ha
PS-C-007	Generation of Germ-free Lgr5GFP reporter mice to determine microbiome-stem cell interaction in gastrointestinal tract	Kyungrae Cho
PS-C-008	Metagenomic sequencing of the gut microbiome in BALB/c mice administered fermented soybean for 60 days	Hyeokjin Kwon
PS-C-009	Cell penetrating peptide nucleic acid platform for rapid therapeutics development against new emerging pandemic virus	Chiho Yu
PS-C-010	R51-3, a Ricin vaccine, protects rabbits against ricin toxin	Young-Jo Song

PS-C-011	Anti-Viral activity of novel mRNA Antibodies against SARS-CoV-2 delta	Jung-Eun Kim
PS-C-012	Exploring immunological defense mechanisms against Sendai virus infection	Eun-Seon Yoo
PS-C-013	The oral administration of Bacillus velezensis KD1 enhances influenza vaccine efficacy in mice	Jeonghyeon Lee
PS-C-014	Probiotic Lactobacillus sakei regulates intestinal mucosal homeostasis through NOD2 signaling-mediated epithelial proliferation and IL-10 production from stromal cells	Min-Jung Kang
PS-C-015	Exploring novel natural inhibitors against the leptospira interrogans GroEL protein: a structure-based virtual screening and molecular dynamics approach	Guneswar Sethi
PS-C-016	De novo Interleukin-10 production gained by priming with Lactobacillus sakei CVL-001 boosts the immunomodulatory abilities of human mesenchymal stem cells	Jeong Hyun Yu
PS-C-017	Development and analytical evaluation of an indirect ELISA with recombinant nucleocapsid of Sendai virus	Dong Sook Min
PS-C-018	Efficacy evaluation of NK cell therapy in SARS-CoV-2 infected mice	Hyeongseok Yun
PS-C-019	Combination of Lacticaseibacillus paracasei BEPC22 and Lactiplantibacillus plantarum BELP53 attenuates fat accumulation and alters the metabolome and gut microbiota in mice with high-fat diet-induced obesity	Tae-Jun Kwon

Genetic disease model

Poster no.	Title	Speaker
PS-D-001	Regulation of Chi3l1 expression in the mice uterus through estrogen receptor alpha	Byeongseok Kim
PS-D-002	Efficacy study in a rat peripheral neuropathy (L5 spinal nerve ligation) model	Woori Jo
PS-D-003	Genome-wide CRISPR screening to identify host factors for brain infection of SARS-CoV-2	Yu Jin Lee
PS-D-004	Mouse models for dynamics of epithelial cell plasticity during gastric carcinogenesis and metastasis	Hyeok-Won An
PS-D-005	Immunization against SARS-CoV-2 immunologically inhibits metastatic colonization	Jong Wan Kwon
PS-D-006	Establishing rat endometrial organoids and verifying functional mimicry of uterine tissue	Dong-Hyeok Kwon
PS-D-007	Leptin receptor deficiency promotes carbon tetrachloride-induced liver tumor incidence in mice	Seungwoo Lee
PS-D-008	Regulation of anti-inflammatory adipose foamy macrophages by growth differentiation factor 15 and β2-adrenergic receptor in alcohol-related liver disease	Min Jeong Kim
PS-D-009	Lethal SARS-CoV-2 infection reduces tissue-resident macrophages and increases M2 macrophages accompanied by fibrotic reaction in the liver of COVID-19 mouse models	Hyeon Ah Kim
PS-D-010	Humanized mice applying CD47;Prkcd;IL2rg triple KO mice exhibit enhanced human immune cell engraftment and reduced GvHD symptoms	Kang-hyun Kim
PS-D-011	Male infertility phenotype in Ehf knock-out mice	Minjeog Kim
PS-D-012	TXNIP in Kupffer cells regulates liver injury, inflammation and fibrosis	Jun-yeop Song
PS-D-013	Regulation of ERa-induced IL36a in mouse uterus	Joohee Kim
PS-D-014	Simultaneous mutation of Abhd14a and Tmem115 drives gastric tumor while displaying vulnerability to Wnt inhibitors	Sang Hyeok Seok

PS-D-015	Antidiuretic activity and safety of cephalotocin, an oxytocin/vasopressin-related peptide from octopus	Seonmi Jo
PS-D-016	TXNIP regulates the autophagy of liver sinusoidal endothelial cells	Poornima Kumbukgahadeniya
PS-D-017	Hepatitis B virus X protein (HBx) induced an unbalanced metabolism of cholesterol and fibrosis in the high fat, high glucose liver	Gyeonghun Kim
PS-D-018	Adenosylhomocysteinase-like 1 regulates nutrient-induced insulin sensitivity through a calcium-dependent brown adipocyte activation	Soo Kyung Kang
PS-D-019	Generation of mouse models using virus-like particles-packaged CRISPR ribonucleoproteins	Sol Pin Kim
PS-D-020	Establishing a clinically relevant mouse model of acute kidney injury using the Small Animal Radiation Research Platform (SARRP)	Bodokhsuren Tsogbadrakh
PS-D-021	Compositional changes in fecal microbiota in a C57BL/6-Tg(NSE-haSyn) mice as novel Parkinson's disease model	Su Ha Wang
PS-D-022	LRIG1 represents pancreatic acinar cells capable of expansion in homeostasis and regeneration	Chanyang Uhm
PS-D-023	Novel role of ALPI gene associated with constipation caused by complement component 3 deficiency	Hee Jin Song
PS-D-024	Laparoscopic ovum-pick up in common marmoset	Heejong Eom, So-Min Lee, Dohyun Lee
PS-D-025	The medical screening of causative factors for osteoporosis in Macaca fascicularis	Hye-ri Park
PS-D-026	Cannabinoid receptor 1 antagonist (AM251) reduces pancreatic β-cell apoptosis in STZ-induced diabetic female mice	Eun Sun Park
PS-D-027	MRI-based investigation about Focal induction of reactive astrocytes in cortex	Seung ah Oh
PS-D-028	Extracts of Dipterocarpus tuberculatus have a great potential as an effective anti-obesity treatment in Lep knockout mice	Ayun Seol
PS-D-029	DGCR8 is essential for the differentiation of myeloid cells within the bone marrow microenvironment	Jiwon Kim
PS-D-030	Protective effects of green pine cone extract on the HCl/ethanol-induced acute gastritis model	Ki Ho Park
PS-D-031	Therapeutic strategies of FXR signaling and one carbon metabolism for the treatment of colorectal cancer	MINKI KIM
PS-D-032	Estrogen-P2ry2 orchestrates MAPK signaling in mouse uterus and promotes epithelial-mesenchymal transition in endometrial cancer cell	Minju Kang
PS-D-033	3D organotypic culture of human follicle dermal papilla cells and their implantation for enhanced hair follicle regeneration	Eun-Ho Lee
PS-D-034	Characterization of age-dependent phenotypes in a C57BL/6-Tg(NSE-hPS2*N141I)Korl mice as Alzheimer's diseases model	Su Jeong Lim
PS-D-035	Loss of ChREBP heightens susceptibility to osmotic diarrhea and compromises gut barrier function under PEG Treatment	Yeram Lee
PS-D-036	Aortic inflammation and Wnt signaling undergo activation in the context of spondyloarthritis in the HLA-B27 transgenic rat model	Seong-Ryul Kwon
PS-D-037	Inhibition of Kxxx as a potential therapeutic strategy for kidney fibrosis	YoungHoon Seo
PS-D-038	Protective effects of Cxxx overexpression on cardiometabolic syndrom in western diet-induced Ldlr-/- mice	Hye Rang Park
PS-D-039	DGAT2 in adipocytes mitigates MAFLD by suppressing hepatocyte inflammation	Soo Mi Ki
PS-D-040	Anticancer activity of marine peptides derived green sea algae, bryopsis plumose in non-small cell lung cancer	Jeiha Lee

PS-D-041	Study on copper-binding peptides in Wilson's disease and copper metabolism	Seung-Hyun Jung
PS-D-042	Proteasome-associated deubiquitinases regulate both the cell proliferation and the mitochondrial dysfuntion in pancreatic ductal cancer cells	Jae Woong Jeong
PS-D-043	Age-dependent changes in the immuno-environment of uteri of diet-induced obesity mice	Surim Oh
PS-D-044	Effects of high-fat diet on the expression of necroptosis effectors in the mouse ovary	Eunbin Shin
PS-D-045	TXNIP deficiency in liver sinusoidal endothelial cells enhances liver regeneration and modulates inflammation	Sehee Park
PS-D-046	Evaluation of the Xeno pig as a distinct breed: Genetic comparison with MGH, Landrace, and Yorkshire/Landrace Breeds	Won Kil Lee
PS-D-047	ADSSL1-Induced autophagy promotes myogenic fusion for differentiation	Soyeon Won
PS-D-048	Impact of THEMIS deficiency on treg functionality and its role in atopy dermatitis suppression	Gi-Cheon Kim
PS-D-049	Anti-obesity and anti-diabetic effect of fermented fig extracts on high-fat diet fed mice	Hwal Choi
PS-D-050	Anti-NAFLD effects of Fermented gold kiwifruit via activation of AMPK signaling pathway	Jihye Choi
PS-D-051	Cirsium japonicum (CJ) extracts prevent STZ-induced diabetic rats: inhibition of RAGE/AGEs signaling pathway	Jihye Choi
PS-D-052	Common and distinct functions of mouse Dot1l in the regulation of endothelial transcriptome	Hyeonwoo La
PS-D-053	Dynamic change of R-Loop implicates in the regulation of zygotic genome activation in mouse	Ho Soeng Lim
PS-D-054	RNA helicase DEAD-box-5 is involved in R-loop dynamics of preimplantation embryos	Oh Beom Kwon
PS-D-055	Development of a novel humanized knock-in mouse model of retinitis pigmentosa with RP9 and RP1L1 mutations	Hyo Jeong Ki
PS-D-056	Investigating immunomodulatory properties of porcine peripheral blood-derived mesenchymal stem cells: a comparative study with bone marrow-derived MSCs	JI-Woo Shin
PS-D-057	Effect of atherogenic diets on lesion phenotype in LDLR knockout mouse	Shin Hee Park
PS-D-058	Creating promoters for specific expression in porcine vascular endothelial cells using transcriptome analysis	Sang Eun Kim
PS-D-059	Comparative transcriptome analysis of PBMCs in cats diagnosed with and recovered from feline infectious peritonitis virus	Ju Young Lee, Hyeong Ryeol Cho
PS-D-060	The modulation of pro-inflammatory chemokines and cytokines in monocytes and macrophages under the influence of shear stress	Hee-Seon Choi
PS-D-061	Macrophage derived non-canonical WNT promotes pancreatic cancer progression through direct inhibition on T cell proliferation	Na Hyun Kim
PS-D-062	The ablation of NAD(P)H: quinone oxidoreductase 1 alleviates the pathogenesis of primary sclerosing cholangitis in animal models	Dong Woo Kim
PS-D-063	Effects of Humulus japonicus aqueous extract on cognitive function in aging	Kyeong-Seon Min
PS-D-064	Adipocyte specific deficiency of A20 enhances energy homeostasis and lipid metabolism in diet-induced obesity	Sanghun Lee
PS-D-065	Effects of dipeptidyl peptidase-4 inhibitor, sitagliptin, on dyskinesia induced by L-dopa in a Parkinson's disease mouse model	Hye-yeon Park
PS-D-066	Generation of a mouse model expressing Naa10 235 isoform	Myeongbeen Yang
PS-D-067	Generation of Il1rap knock-out mice and phenotype analysis for schizophrenia-related traits	Seunghun Han

PS-D-068	Insight into noncanonical small noncoding RNAs in influenza A virus infection	Eun-A Ko
PS-D-069	Toxicological effects of 6PPD in Caenorhabditis elegans	Moonjung Hyun, Sangjoon Lee
PS-D-070	Progesterone receptor membrane component 1 increases the Smad2-dependent signaling through TGF-β R II expression	Eui-ju Hong

Facility / Management / Others

Poster no.	Title	Speaker
PS-E-001	Improving reproducibility in preclinical research through precision evaluation of clinical chemistry tests	Im Gi Lee
PS-E-002	Evaluation of implantable medical devices for dental and periodontal tissue recovery using animal models	Donghyun Lee
PS-E-003	Barley beta glucan increase osteoblast differentiation via p38/ERK and Smad1/5/9 phosphorylation	Hyeon Oh Kim
PS-E-004	Preliminary investigation into long-term stress by isolated captivity-related changes of reproduction hormones in Cynomolgus monkey	Ji Woon Kim
PS-E-005	Primate resources center (PRC) supports non-human primate infrastructure for biomedical and bioscience research	Seung-Bin Yoon
PS-E-006	Potential food inclination of cynomolgus monkey in laboratory environments: enhancing positive reinforcement training and health optimization	Gwang-Hoon Lee
PS-E-007	The accuracy of estrus prediction in Hanwoo improved by the ruminoreticular biocapsule sensors	Chae Yeon Kim
PS-E-008	LOOK: advanced training program for laboratory animal veterinarians of KCLAM	Young-Shin Joo
PS-E-009	Intrathecal administration and analysis of Lidocaine in CSF of Cynomolgus monkeys	Yang Im Cho
PS-E-010	Confirmation of Bactericidal effect using Hypochlorous acid water in the NHP (Non-human Primate) animal room	Woo-Hyeon Kim
PS-E-011	Derivatives of ferulic acid preserve intestinal barrier tight junctions by suppressing inflammatory responses in a mouse model of dextran sulfate sodium-induced inflammatory bowel disease	Yeon-Yong Kim
PS-E-012	Development of ethical animal experiment education	Hee Yeon Jeon
PS-E-013	Estrogen-related receptor-α (ERRα) modulates the populations of hematopoietic stem and progenitor cells in the bone marrow	Hee Eun Bae
PS-E-014	Rapamycin and ganetespib suppress inflammatory response induced by 27-hydroxycholesterol	Munju Kwon
PS-E-015	Protective role of methanol extract of Microsorum membranaceum (D. Don Ching) against Dex-induced muscle atrophy in C2C12 cells and C57BL/6 mice	Eun Seo Park
PS-E-016	Proposal for the harmonization of health monitoring between common marmoset colonies in South Korea	Seon A Noh
PS-E-017	Discovery of stress-specific biomarkers through correlation analysis of stress and stress-related protein changes in beagle dogs	Kwang Il Park
PS-E-018	Enhancing animal research training: TALK course	Jean Lim
PS-E-019	Flow cytometric xenocrossmatching and clinical outcomes in porcine islet xenotransplanted non-human primates: a comparative analysis	Sang ik Cho
PS-E-020	Effective expansion of primate NK(natural killer) cell by Interleukin-15(IL-15)	Jae-Hwan Hyeon
PS-E-021	SP-8356 attenuates LPS-induced acute lung Injury by Inhibiting inflammatory cytokines and immune cell infiltration	Thai Uy Nguyen

PS-E-022	Neurokinin-2 receptor negatively modulates substance P responses by forming complex with Neurokinin-1 receptor	Lan Phuong Nguyen
PS-E-023	Current status of animal experimentation and committee operations in domestic animal experimentation institutions in 2023	Chae Hong Rhee
PS-E-024	Phlorotannis prevent vocal fld fibrosis via aerosol inhalation in laser-induced firosis model	Tae-Hee Kim
PS-E-025	Introduction of Ajou MBD T2B Center	Kwang min Lee
PS-E-026	Altering SURF4 expression levels enhances tumorigenic MEK-ERK pathway activation in solid cancers	Na ryeong LEE
PS-E-027	Stilbenoid derivatives: Potent inhibitors of HIF-1α-centric metabolism under hypoxia	Tae-Hee Han
PS-E-028	Improved tumor ablation with square waveforms in radiofrequency ablation: a comparative study	Dong-Sung Won
PS-E-029	Enhanced antimicrobial efficacy of Zn/AgNP dual-layer coated catheters in reducing CAUTIs: an in vitro and in vivo study	Dong-Sung Won
PS-E-030	The absence of Sirt1 within the non-hematopoietic bone marrow microenvironment does not impact the functionality of hematopoietic stem cells in adult mice	Hye Jin Lee
PS-E-031	Meta-analysis of the effects of single versus mixed housing for environmental enrichment of Beagle dogs in toxicity studies	Sang-Jin Park
PS-E-032	National primate infrastructure for biomedical and basic science	Sang-Je Park
PS-E-033	Proposal for standardization of GLP equipment validation methods	Jae Chang Song
PS-E-034	Proposal for animal facility validation standards in GLP test facilities	Kyu Hyuk Cho
PS-E-035	AZD7648, a potential DNA-PK inhibitor, acts as a synergistic radiosensitizer in human sarcoma xenograft mice	Yuri Lee
PS-E-036	Calcineurin inactivation by baicalein reduces neuronal apoptosis caused by prion protein	Jeong-Min Hong
PS-E-037	Exploring the functional organization and neural dynamics of the motor cortex using graphene electrodes and wireless recording in rhesus monkeys	Eunha Baeg
PS-E-038	HanDam (Twist) improves wrinkle through activation of TGF-β on UV-B irradiation-Induced skin photoaging in Hairless mice	In Bong Song
PS-E-039	Inhibition of infiltrating monocytes ameliorate neurological and behavioral outcomes of SAH mice model	Dong su Kang
PS-E-040	Assessing brain functional changes in a rat model of lipopolysaccharide-induced sepsis-associated encephalopathy using multi-parametric MRI	Do-Wan Lee
PS-E-041	Therapeutic effects of muscle regeneration at different melittin concentrations in rabbit atrophied muscle	Eun Sang Kwon

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PS-A-001

Peroxiredoxin-2 expression is involved the neuroprotective mechanism of retinoic acid on cerebral ischemic tissues and glutamate-exposed neurons

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Retinoic acid is known as a representative metabolite of vitamin A that exerts the effects of anti-oxidant and anti-apoptosis. It also has neuroprotective effects against neurodegenerative disorders. Peroxiredoxin-2 is one of peroxiredoxin family protein of antioxidant enzymes. We purpose that retinoic acid exerts the neuroprotective effect through the regulation of peroxiredoxine-2. The aim of this study is to elucidate whether retinoic acid regulates peroxiredoxine-2 expression in focal cerebral ischemia and glutamate-exposed condition. Focal cerebral ischemia was induced via middle cerebral artery occlusion (MCAO) surgery in male adult rats. Agents including phosphate buffer saline or retinoic acid (5 mg/kg) was administrated intraperitoneally for four days before MCAO damage. Twenty four hours after MCAO surgery, neurobehavioral score tests were carried out and measured DCF and MDA levels to examine oxidative stress in cerebral cortex. Reverse transcription-PCR and Western blot analysis was performed to elucidate the change of peroxiredoxin-2 expression. In vitro study, glutamate (5 mM) and/or retinoic acid (1, 3, 5, 10 mM) was treated in cultured neurons. Cell viability and oxidative stress were measured, Western blot analysis of peroxiredoxin-2 was performed. Retinoic acid alleviates MCAO damage-induced neurobehavioral disorder and oxidative stress. MCAO damage induced a decrease in peroxiredoxin-2, retinoic acid attenuates this decrease. Furthermore, retinoic acid alleviates glutamate-induced a decrease in cell viability, the effect of retinoic acid is dose-dependent manner. Retinoic acid also prevents glutamate-induced a decrease in peroxiredoxin-2 expressions. These results have shown that retinoic acid protects neurons from MCAO damage and glutamate toxicity, also exerts antioxidant effect in damaged condition, and regulates the peroxiredoxin-2 expressions. Thus, these findings suggest that peroxiredoxin-2 expression is contributed on neuroprotective mechanism of retinoic acid in ischemic brain tissue and glutamate-exposed neurons. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00248145).

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***Keywords :** Cerebral ischemia, Glutamate, Neuroprotection, Peroxiredoxin-2, Retinoic acid

PS-A-002

Retinoic acid alleviates the injury-induced reduction of neuron specific enolase (γ-enolase) expression in ischemic stroke animal model and glutamate-exposed neurons

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Retinoic acid is a metabolite of vitamin A, exerts a neuroprotective effect against cerebral ischemia through its anti-inflammation and anti-oxidant function. γ-enolase is a glycolytic enzyme that abundantly exist in neuron, regulates nerve differentiation, growth, and survival. This study was performed to investigate whether retinoic acid regulates γ-enolase expression in cerebral ischemia and glutamate-exposed neurons. Middle cerebral artery occlusion (MCAO) was carried out to induce focal cerebral ischemia in adult male rats. Retinoic acid (5 mg/kg) or phosphate buffer saline was injected intraperitoneally for four days before MCAO operation, neurological behavioral tests were performed 24 h MCAO damage, and cerebral cortex was collected. The change of γ-enolase expression by retinoic acid treatment was detected various technique including proteomic approach, reverse transcription-PCR, Western blot analysis, and immunofluorescence staining. In cultured neurons, glutamate and/or retinoic acid was treated, γ-enolase expression levels was measured by Western blot analysis. We have clearly confirmed mitigation of neurological functional impairment by administration of retinoic acid in MCAO animals. We also identified decrease in γ -enolase expression in MCAO animals, retinoic acid treatment prevents this decrease. Moreover, glutamate toxicity reduced cell viability and γ-enolase expression. However, retinoic acid treatment alleviates glutamate toxicity-induced reduction of cell viability and γ-enolase expression. Since γ-enolase contribute to neuronal cell growth and survival, decrease in γ-enolase induces neuronal cell death and affects cell fate. Thus, maintenance of γ-enolase is important to preserve neuron from neuronal damage. Retinoic acid exerts a neuroprotective effect and prevents decrease in γ-enolase expression in cerebral ischemia and glutamate-exposed neurons. Thus, our findings can demonstrate that the regulation of γ-enolase by retinoic acid in neuronal cell damage is involved to neuroprotective mechanism of retinoic acid. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00248145).

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***Keywords :** Cerebral ischemia, γ-enolase, Glutamate, Neuroprotection

PS-A-003

The effect of chinese quince and black maca on blood high glucose-induced SD-RAT by Streptozotocin

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This study aimed to investigate the hypoglycemic effects of quince and black maca powder in STZ-induced hyperglycemic SD-RAT. Four-week-old male SD-RAT (105-115g) were divided into five groups (control, toxic, black maca, quince, quince + black maca) and the experiment was conducted over five weeks. The quince and black maca groups were administered quince and black maca powder (100%) at a single concentration, while the quince + black maca group received a mixture of 50% concentration of each. To induce hyperglycemia, STZ was intraperitoneally injected at a dose of 40 mg/kg twice at one-week intervals. Hyperglycemia induction (200 mg/dl) was confirmed using a blood glucose meter (Accu-check Performa). Subsequently, hyperglycemic SD-RAT were orally administered quince powder, black maca powder, and quince powder + black maca powder. Biochemical analysis revealed that GLU levels were significantly reduced in the quince, black maca, and quince + black maca groups compared to the toxic group. Furthermore, the quince group exhibited lower GLU levels than the control group. These findings suggest that quince and maca have potential for development as hypoglycemic foods and pharmaceuticals.

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***Keywords :** Chinese quince, Black maca, Streptozotocin

PS-A-004

Baicalin ameliorated neurological impairment and cerebral ischemic injury in a stroke rat model

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Ischemic stroke causes neuronal cell death due to lack of oxygen and glucose in the ischemic region of the brain. Baicalin is a flavonoid which has antioxidant and anti-inflammatory properties. The aim of this study was to investigate the neuroprotective effects of baicalin in animal models of stroke. Male Sprague Dawley rats were used for this study and middle cerebral artery occlusion (MCAO) surgery was performed to induce cerebral ischemia. Baicalin (100 mg/kg) or vehicle was injected into the abdominal cavity immediately after MCAO surgery. Neurological behavioral tests were performed 24 hr after MCAO surgery and brain tissue was isolated to evaluate edema, infarct volume, histological changes, and apoptosis. Severe neurological deficits have been found in MCAO animals, but baicalin treatment has alleviated these disorders. MCAO damage led to brain edema and infarction, these changes were attenuated by baicalin treatment. In addition, we found histopathological changes and an increase in the number of TUNEL-positive cells in the cerebral cortex of MCAO animals. However, baicalin treatment alleviated these morphological changes. Baicalin also alleviated the increase in caspase-3 expression caused by MCAO damage. Changes in caspase-3 expression in each experimental group were confirmed by immunohistochemical staining and Western blot analysis. Caspase-3 is a representative protein of the apoptosis process and is used as a marker for apoptosis. These results clearly showed that baicalin has a neuroprotective effect by an anti-apoptotic mechanism. In conclusion, we can suggest that baicalin acts as a potent neuroprotective agent by regulating the apoptotic signaling pathway. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00248145).

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***Keywords :** Baicalin, Cerebral ischemia, Neuroprotection, Stroke

PS-A-005

Sensitivity of cardiomyocytes to oxygen saturation in the cell isolation media varies depending on the original location of each cardiomyocyte in the heart

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Cardiomyocytes are exposed to different oxygen environments depending on their anatomical location, so the oxygen saturation level appropriate for the study of primary cardiomyocytes is still controversial. In this study, the survival rate and morphological characteristics of cardiomyocytes isolated from the left ventricle, left atrium, right ventricle, and right atrium were compared between the oxygen saturated (OS) and oxygen non-saturated (ON) media groups. The cells were exposed to room temperature (20 ± 2℃) and atmospheric environment to provide an environment similar to general in vitro experiments condition. Based on cell condition immediately after isolation from the heart, The survival rate of left ventricle and left atrium derived cardiomyocytes in the ON group decreased significantly ($p<0.05$) within 2 hours, whereas it was maintained for more than 5 hours in the OS group. On the other hand, the survival rate of right ventricular and right atrium derived cardiomyocytes was maintained for more than 8 hours regardless of the oxygen saturation level of the isolation media. The microscopic morphology of cells showed a bubble shape on the live cell membrane in the ON group isolated from the left ventricle and left atrium. No bubble shape was found in the right ventricle and right atrium-derived live cells of the ON group and in all live cells of the OS group. In conclusion, this study revealed that the oxygen saturation level of the isolation media was related to the cell membrane integrity of left ventricle and left atrium derived cardiomyocytes, which is also expected to affect cell survival rate. Additional studies, including analysis of intracellular structure and energy metabolism, will be necessary to elucidate the mechanism of decreased survival rate.

***Corresponding author :** Ryounghoon Jeon, SangHyun An

***Keywords :** Cardiomyocytes, Cell membrane, Isolation media, Oxygen saturation level, Survival rate

PS-A-006

Investigating the effects of mixtures of antioxidant and anti-inflammatory natural substances on hippocampal neurogenesis in an MPTP-induced mouse model of Parkinson's disease

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Parkinson's disease(PD) is a neurodegenerative disorder marked by motor dysfunction due to the loss of dopaminergic neurons, with mitochondrial dysfunction and NADPH oxidase 4(NOX4) induced oxidative stress playing pivotal roles. Consequently, the neuroprotective effects of natural substances are receiving attention. Resveratrol(RES) enhances neuronal survival via Sirtuin1 activation, while crocin and crocetin from Saffron(SFN) reduce ROS and inflammation. Passiflora incarnata(PI) also protects neurons through GABA system regulation, antioxidant, and anti-inflammatory actions. This study aims to histologically observe hippocampal neurogenesis after repeated oral administration of natural substances with antioxidant and anti-inflammatory properties RES, SFN, PI alone or in mixture(RES+SFN+PI) in a mouse model of PD (C57BL/6J) induced by MPTP. For a total of 4-weeks, MPTP(30mg/kg) was administered intra-peritoneally, and natural substances(50mg/kg) were administered orally either alone or in a mixture. Behavioral assessments to evaluate motor dysfunction, conducted before and after the 4-week treatment, revealed that groups treated with natural substances showed improved motor function compared to the MPTP group. Oxidative stress levels were assessed by measuring NOX4 expression using IF, revealing decreased NOX4 expression in the hippocampus of mice treated with natural substances, indicating reduced oxidative stress and neuronal protection. Proliferating cells were labeled with BrdU for three days starting from the treatment. The natural substance groups showed increased BrdU and NeuN co-labeling in the dentate gyrus granule cell layer compared to the MPTP group, indicating that the proliferating cells had differentiated into mature neurons. IHC results also showed higher expression levels of proliferation and differentiation markers Ki67 and Doublecortin(DCX) in the natural substances groups. The natural substances RES, SFN, and PI have been shown to promote the differentiation of new cells into neurons and reduce NOX4 levels in astrocytes, a new pathological mechanism in PD. Notably, the mixture of these three substances appears promising. To more accurately confirm these findings, additional quantitative measurements of specific biomarkers in hippocampal tissues and functional assessments of mitochondria are required.

***Corresponding author :** Sun Shin Yi

***Keywords :** Parkinson's disease, Hippocampal Neurogenesis, Resveratrol, Saffron, Passiflora incarnata

PS-A-007

Evaluation of efficacy through behavioral assessment in a peripheral neuropathy model

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In this study, we developed a pain model and a streptozotocin (STZ)-induced diabetic peripheral neuropathy (DPN) model in rats to investigate peripheral neuropathy. We proposed an assessment method for peripheral neuropathy based on symptoms. The evaluation of peripheral neuropathy was primarily conducted by assessing mechanical allodynia using Von Frey filaments, with additional evaluations of thermal allodynia, hyperalgesia, and Nerve Conduction Velocity (NCV) tests. The first model studied was the plantar incision model, which induces acute pain by incising the skin and plantar muscle. This model is used for research on pain due to surgery and trauma. The second model was the DPN model induced by STZ administration. After the preparation of the rat models, Paw Withdrawal Threshold (PWT) was assessed using the up-down method for the ipsilateral hind paws. Additionally, thermal allodynia and hyperalgesia were evaluated using the Hargreaves test and Hot/Cold plate tests. This non-invasive efficacy evaluation method allows for the assessment of drug efficacy without sacrificing the animals. Furthermore, the sciatic nerve was stimulated percutaneously using bipolar needle electrodes placed at the level of the gastrocnemius and soleus muscles. The aim of this study was to establish an efficacy evaluation method for peripheral neuropathy in rats through clinically relevant NCV assessment. As a result, a significant decrease in PWT was observed in all animals, and the results of thermal allodynia and hyperalgesia showed a significant decrease only in the plantar incision model. Additionally, the Von Frey test was suitable for evaluating pain in both the pain incision model and the DPN model, while the tests for thermal allodynia and hyperalgesia were applicable to the pain incision model within 4 days post-surgery. The NCV results demonstrated significant differences between the DPN model and the normal control group.

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***Keywords :** Peripheral neuropathy, Pain model, Diabetic peripheral neuropathy model, Von Frey test, Nerve Conduction Velocity test

PS-A-008

P-selectin-mediated targeted delivery of f-BRDP nanoparticles in MCAO rat models

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Background: Drug delivery in Stoke has some limitations such as passing the blood-brain barrier (BBB), difficulty maintaining concentration, and non-specificity of the drug. To overcome these drug delivery systems, target-oriented drug delivery research is important and is being studied. P-selectin plays an important role in the occurrence and progression of stroke through thrombus formation and migration of inflammatory cells into damaged blood vessels. Therefore, P-selectin can be a target for drug delivery and therapeutic effects can be achieved by lowering P-selectin.
Aim: This study aimed to establish an MCAO model and confirm the targeting efficacy of P-selectin-Mediated f-BRDP nanoparticles within the infarction lesion of MCAO Rat Models.
Methods: MCAO was induced by inserting a filament through the right common carotid artery to occlude the middle cerebral artery for 60 minutes, followed by reperfusion. Model validation included TTC and H&E staining, alongside MRI. Post-reperfusion, fluorescent BRDP or f-BRDP nanoparticles were intravenously administered, followed by brain harvesting after 24 hours for ex vivo fluorescence imaging.
Results: TC staining, H&E, and DWI image of brain MRI confirmed ischemic infarction of the white and gray matter of the MCA distribution. Immunofluorescence staining demonstrated higher P-selectin expression in the ischemic lesion area of the MCAO group compared to controls. Furthermore, fluorescence imaging confirmed precise targeting and localization of f-BRDP nanoparticles within the lesion areas of the MCAO group, whereas BRDP particles showed negligible accumulation. Evaluation of therapeutic effect is ongoing.
Conclusion: This study successfully established and validated a reliable MCAO model through histological and MRI analyses. P-selectin overexpression facilitated precise targeting of f-BRDP nanoparticles to ischemic lesion areas, highlighting its critical biomarker role and potential to enhance therapeutic delivery in ischemic stroke treatments. The demonstrated efficacy of this targeted system, confirmed via fluorescence imaging, suggests significant advancements in stroke therapies by enabling precise drug delivery across the BBB to damaged brain areas.

***Corresponding author :** Gi-Wook Kim

***Keywords :** Ischemic Stroke, Middle Cerebral Artery, P-Selectin, Drug Delivery Systems, Nanoparticles

PS-A-009

Establishment of intratracheal instillation method in neonatal Sprague-Dawley rat

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Premature infants are born with the saccular stage of lung development. The stage corresponds to postnatal day (PND) 1 through PND 7 in rats. Administering drugs directly into the lungs is known to be important method for drug development study in premature infant model. In this study, we investigated to establish intratracheal instillation method in neonatal Sprague-Dawley rat. Rats were assigned based on PND into 4 experimental groups (each of fifteen male and fifteen female): (1) PND 4, (2) PND 5, (3) PND 6, (4) PND 7. Because neonatal rats have underdeveloped respiratory function, we measured an anesthesia time to intratracheal instillation (5% isoflurane in 50% oxygen and 50% nitrous oxide). Ten males and ten females in each group were administered 0.4% trypan blue by intratracheal instillation to verify the administration success rate. Histopathological examination of the lungs was performed on the other rats in each group to confirm the premature infant model. Histopathological studies showed that less alveolarization and thin smooth muscle thickness. These characteristics were considered typical features of the saccular stage. In the case of anesthesia time, PND 4 group was 32.1 ± 3.7 seconds, PND 5 group was 47.7 ± 4.4 seconds, PND 6 group was 65.0 ± 5.1 seconds, PND 7 group was 60.8 ± 10.9 seconds. The success rates were 70% for both male and female on PND 4 group, 90% for males and 100% for females on PND 5 group, and 100% for both male and female on PND 6 group, 7 group. According to these results, the appropriate anesthesia time to intratracheal instillation was approximately PND × 10 seconds, and the appropriate day for intratracheal instillation was considered to be PND 6 - PND 7. This establishment of intratracheal instillation method will be useful to respiratory disease research of premature infants using neonatal rat models.

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***Keywords :** Premature infant, Neonatal rat, Intratracheal instillation, Anesthesia time, Administration success rate

PS-A-010

Evaluation of anti-obesity and cholesterol level relief for paseolamine in white kidney bean extract

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The effect of white kidney bean extract paseolamine on anti-obesity prevention in SD-Rats was investigated. SD rats fed a 60% high-fat chow diet were orally administered white kidney bean extract phaseolamine at low, medium, and high concentrations for 21 days; the positive group was fed a 60% high-fat chow diet and the negative group was fed a normal chow diet, which was discontinued 1 day before the end of the experiment. At the end of the experiment, blood was collected and analyzed for T-P, T-G, GLU, and HDL concentrations, and livers were harvested and examined histopathologically. Inhibitory effects of white kidney bean extract paseolamine on GLU and T-G levels in an obese SD-RAT model induced by 60% high fat diet feeding. Increasing effect on HDL levels. Improvement of liver function by white kidney bean extract paseolamine administration. Improvement of liver function by WSB extract administration. Histological analysis of 3T3-L1 in a 60% high fat diet-induced obesity model. In conclusion, WSB is effective in reducing the TG and GLU levels, inhibiting the differentiation of 3T3-L1 cells, and reducing the accumulation of fatty liver and body fat by reducing the Lipid droplet of liver tissue. Therefore, WSB can be used as a preventive and therapeutic agent for fatty liver in the future.

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***Keywords :** White kidney bean, Paseolamine, Anti-obesity, Obesity

PS-A-011

Vascular visualization study for bone regeneration assessment in a calvaria bone defect model in rats

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In this study, blood vessels were visualized using MICROFIL in experimental rats. The subjects were 10-week-old male Sprague-Dawley (SD) rats, anesthetized by intraperitoneal injection of Zoletil and Rompun. The chest cavity was incised, the left ventricle was opened, and a cannula was inserted into the aorta, followed by perfusion with 1 unit of heparinized saline. After perfusion, MICROFIL was injected using an infusion pump. MICROFIL products are radiopaque rubber injection compounds that fill and opacify microvascular and other spaces in non-surviving animals and post-mortem tissue under physiological injection pressure. The continuous, closed vascular system allows for flow-through injection or perfusion techniques. After injection, MICROFIL compounds cure to form a three-dimensional cast of the vasculature. The rats injected with MICROFIL were refrigerated for one day to allow hardening. Subsequently, the liver, kidneys, stomach, testes, eyes, and skin were extracted and subjected to MicroCT imaging. The imaging confirmed that MICROFIL had filled and visualized the capillaries of the organs. Following this, MICROFIL was applied to the calvarial bone defect model rats to observe the formation of new blood vessels over time. The study confirmed the correlation between vascular formation and bone regeneration. This research demonstrated the vascular structures of various organs and applied these findings to the calvarial bone defect model in rats, showing that MICROFIL can be used to evaluate bone regeneration through neovascularization. Therefore, this research is expected to aid in the development of new drugs and medical devices by contributing to angiogenesis studies.

***Corresponding author :** Yoon Beom Lee, Woori Jo

***Keywords :** Blood vessel visualization, Angiogenesis, Calvarial bone defect, Bone Regeneration

PS-A-012

A detailed protocol for isolating and characterizing pulmonary-specific extracellular vesicles from mouse BALF post-acute lung injury

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Extracellular vesicles (EVs) are membrane-bound nanoparticles categorized by dimensions and surface markers unique to different cell types. This study presents a detailed protocol for isolating pulmonary-specific EVs from mice, particularly from bronchoalveolar lavage fluid (BALF) of C57BL/6 mice post-acute lung injury. The protocol includes steps for differential centrifugation, density gradient centrifugation, and PEG-based precipitation, utilizing pulmonary-specific EV-bound chemicals and antibodies. These steps ensure the efficient isolation of EVs with minimal contamination. Following isolation, comprehensive characterization of these EVs is performed using nanoparticle tracking analysis, flow cytometry, scanning electron microscopy, and transmission electron microscopy. Each characterization method provides critical information on the size, concentration, and morphology of the EVs, confirming their pulmonary origin and purity. The protocol is optimized for pulmonary-specific EVs from BALF, although modifications may be necessary when adapting the protocol for BALF from different sources. All procedures are conducted in a Class II biosafety cabinet using sterile techniques to ensure contamination-free results. In summary, this protocol provides a robust and reproducible method for isolating and characterizing pulmonary-specific EVs from BALF in mice. It facilitates further research into their role in pulmonary diseases and potential therapeutic applications. This study serves as a valuable tool in pulmonary disease research and contributes to exploring the therapeutic potential of EVs, advancing the understanding of their biological functions and clinical relevance.

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***Keywords :** Pulmonary-specific EVs, Bronchoalveolar lavage fluid (BALF), Acute lung injury, Differential centrifugation, Characterization

PS-A-013

Efficient miRNA delivery to alveolar macrophages using surfactant protein A-conjugated extracellular vesicles: A novel therapeutic approach for lung inflammation

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Alveolar macrophages (AMs) are the first line of defense against pathogens that initiate an inflammatory response in the lungs and exhibit a strong affinity for surfactant protein A (SP-A). In this study, we explored the potential of SP-A-associated extracellular vesicles (SPA-EVs) as drug delivery systems to combat lung inflammation. To achieve this, we first confirmed that lung-derived EVs express SP-A receptor (SP-R210). The purified EVs were then incubated with SP-A to generate SPA-EVs, which were investigated for their ability to be internalized by AMs. Our results indicate that AMs effectively internalized SPA-EVs *in vitro* and *in vivo*. Moreover, by transfecting anti-inflammatory microRNA (*let-7b*) into the SPA-EVs, we successfully attenuated AM activation and LPS-induced lung inflammation. Our findings suggest that SP-A-coated EVs can serve as effective drug delivery systems for lung-specific therapeutics by exploiting the high affinity of AMs for SP-A.

This work was supported by the National Research Foundation of Korea (NRF) grant, funded by the Ministry of Science and ICT (MSIT) (Grant No. NRF-2022R1C1C1007541). Additional support was provided by the Korea Basic Science Institute and the Regional Innovation Strategy, funded by the Ministry of Education (Grant Nos. 2023R1A6C101B022, 2021RIS-003).

***Corresponding author :** Hee Doo Lee

***Keywords :** Surfactant protein A, Extracellular vesicle, Alveolar macrophage, MicroRNA, Lung disease

PS-A-014

Inhibitory effect of philadelphus schrenkii extract on macrophage inflammation and acute lung injury

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We investigated anti-inflammatory activity of DJ-001, the hot-water extract of *Philadelphus schrenkii,* (DJ-001) and its intracellular mechanisms associated with the anti-inflammatory response in murine macrophages. DJ-001 treatment reduced the production of nitric oxide (NO), tumor necrosis factor (TNF-α) and interlukin-6 (IL-6) in LPS-stimulated RAW 264.7 cells. DJ-001 decreased level of mRNAs of the pro-inflammatory cytokines. Furthermore, DJ-001 suppressed the phosphorylation of mitogen-activated protein kinases (MAPKs) including ERK, JNK and p38, down-regulated the pathway of mammalian target of rapamycin (mTOR) related factors, and inhibited the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). In addition, DJ-001 treatment decreased interleukin-1 beta (IL-1β) and the level of NOD-like receptor pyrin domain-containing protein 3 (NLRP3), apoptosis-associated speck-like protein containing caspase recruitment domain (ASC) and caspase-1, responsible for NLPR3 inflammasome activation in BMDM stimulated by LPS and ATP. Finally, we confirmed that DJ-001 inhibited the oligomerization of NLPR3, ASC and caspase-1 using the confocal microscope. LPS-induced acute lung injury (ALI) models have been extensively used in studies with a focus on damage to both alveolar epithelium. Therefore, we administered DJ-001 orally for 3 days to 7-week-old male Balb/c mice, followed by an intranasal injection of LPS (50μg/head) to induce ALI. We then extracted bronchoalveolar lavage fluid (BALF) and measured body temperature, and lung wet/dry ratio. In mice administered with DJ-001, the lung wet/dry ratio was reduced compared to the LPS group, and body temperature was lower. Additionally, DJ-001 demonstrated anti-inflammatory effects, as evidenced by decreased levels of TNF-α and IL-6 in BALF. These results suggest that DJ-001 has strong anti-inflammatory activity and it can be a promising candidate for development of anti-inflammatory reagent. This research was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT).

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***Keywords :** Philadelphus schrenkii, Inflammation, MAPK, NLRP3 inflammasome, ALI

PS-A-015

Anti-inflammatory activity of endarachne binghamiae extract and related intracellular mechanisms

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In this study, we investigated the anti-inflammatory activity of Endarachne binghamiae hot water extract (EB-WE) in LPS-stimulated RAW 264.7 macrophages and bone marrow-derived macrophage (BMDM). Treatment of EB-WE signeficantly inhibited the production of inflammatory mediators like NO, and pro-inflammatory cytokines such as TNF-a and IL-6 in LPS-stimulated RAW264,7 cells. This anti-inflammatory effect of EB-WE was confirmed in the analysis for mRNA expression such as iNOS, COX-2, TNF-a, and IL-6. EB-WE also effectively suppressed the phosphorylation of MAPK anf IkB in the early period of LPS stimulation in RAW 264.7 cells. This fact indicates that EB-WE inhibited inflammation via dowen-regulation of signal pathways of MAPK anf NF-kB. Further analysis of signal pathway associated with anti-inflammatory effect of EB-WE clearly demonstrated that it also suppressed PI3K/AKT/mTOR pathway during LPS-induced inflammation. In addition, EB-WE was shown to inhibit NLRP3 inflammasome activation in BMDM. Collectively, EB-WE has high activity to inhibit inflammation in LPS-stimulated macrophages, and its anti-inflammatory activity is due to down-regulation of MAPK and NF-kB activation. This research was funded by Korea Ministry of Oceans and Fisheries, grant number G22202106562301 (Bio Healthcare Demonstration Support Project).

***Corresponding author :** Yung Choon Yoo

***Keywords :** Ndarachne binghamiae, Inflammation, NF-kB, MAPK, mTOR

PS-A-016

Activation of macrophages AND nk cells and related mechanism by pine bud

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Pine bud extract (PDE) is an extract obtained through hot water extraction of pine bud parts. Unlike the well-known physiological and immune activities of pine needles, little is known about the immune effects of PDE. Therefore, in this study, we investigated the immune enhancing effect of PDE on immune cells. As a result, we confirmed dose -dependent induction of NO and cytokines such as TNF-a and IL-6 in PDE-treated RAW 264.7 cells. In addition, PDE effectively induced the secretion of CXC-type and CC-type chemokines in RAW 264.7 macrophages. Moreover, PDE up-regulated the phosphorylation of MAPKs such as ERK, JNK, p38, and IkB during the macrophage activation pathway. These results indicate that PDE activates macrophages through MAPK and NF-kB pathways to secrete immunomodulatory cytokines and chemokines. In an experiment in which bone marrow-derived macrophages (BMDM) of TLR2- or TLR4-knock out mice were stimulated with PDE, and cytokines produced from BMDM were detected, we found that PDE activated macrophages dominently through TLR4-mediated pathway. In addition, FACS analysis revealed that treatment of PDE up-regulated the expression both of MHC-I and MHC-II molecules on the surface of macrophages. To determine whether PDE can enhance NK cell activity, NK cell activity against Yac-1 NK-sensitive cell was determined using splenocytes of mice that had been administered with PDE. As a result, PDE also significantly enhanced NK cell activity. These results suggest that PDE has immunimodulating activity to activate macrophages and NK cells. This study was carried out with the support of ´R&D Program for Forest Science Technology (Project No. 2023471B31-2325-EE01)' provided by Korea Forest Service (Korea Forestry Promotion Institute).

***Corresponding author :** Yung Choon Yoo

***Keywords :** Pine bud, Immune modulation, Macrophage, NK cell, Signal pathway

PS-A-017

Endarachine binghamiae ameliorates obesity and oxidative stress in mouse model

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In this study, we investigated the effect of Endarachine binghamiae hot water extract (EB-WE) in the NAFLD mouse model induced by 12 weeks of high-fat diet (HFD) intake, the 3T3-L1 cell obesity model induced by MDI treatment, and the HepG2 cell fatty liver model induced by free fatty acid treatment. Administration of EB-WE for 12 weeks showed significant anti-obesity effects in body weight and lipid-related serological indicators. As a result of examining mRNA expression in liver and skeletal muscle tissue, EB-WE was analyzed to have an effect of improving metabolic function through the regulation of expression of several metabolic genes including AMPK, PPAR-gamma, and SREBP-1c, and as a result of Western blot analysis, the process of increasing brown fat production through the AMPK/PGC-1 alpha/UCP-1 pathway was analyzed as a key mechanism. In addition, in this study, EB-WE extract significantly improved antioxidant- related indicators, which was analyzed to be due to the regulation of the KEAP-1/ NRF-2/HO-1 pathway. In our other study, EB-WE was investigated to have immunomodulatory and anti-tumor activity, which has much to do with metabolic and antioxidant regulation. In this regard, HPLC component analysis revealed several strong candidates related to the physiologically active effect of seaweed extract, and further studies on these single substances are currently being completed. Consequently, this study, EB-WE significantly improved NAFLD through multidisciplinary regulation related to metabolism, oxidation-reduction reactions. This research was funded by Korea Ministry of Oceans and Fisheries, grant number G22202106562301 (Bio Healthcare Demonstration Support Project).

***Corresponding author :** Yung Choon Yoo

***Keywords :** Endarachine binghamiae, Inflammation, Obesity, Oxidative stress, NAFLD

PS-A-018

Platycarya strobilacea leaf extract ingibits NLRP3 inflammasome activation in bone marrow derived macrophage

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We examined anti-inflammatory activity of *Platycarya strobilacea* (PS) and investigated the intracellular mechanisms related to its activity in murine macrophages. Treatment with PS significantly inhibited the production of inflammatory mediators such as NO and PGE-2, and pro-inflammatory cytokines like TNF-a and IL-6 in LPS-stimulated RAW 264.7 macrophages in dose-dependent manner. Moreover, treatment of PS showed the decreased level of the expression of iNOS, COX-2, TNF-a and IL-6 mRNA. Analysis for signal pathways associated with PS's anti-inflammatory effect showed that it markedly suppressed activation of MAPKs including ERK, JNK and p38 in RAW 264.7 cells. PS also effectively blocked the phosphorylation of IkB molecules, indicating its inhibition of NF-kB activation during inflammation pathway. Interestingly, treatment of PS significantly inhibited IL-1b and IL-18 secretion from bone marrow-derived macrophages (BMDM) stimulated by LPS and ATP. Western blot assays revealed that PS apparently inhibited the oligomerization of NLRP3, ASC and caspase-1 molecules in LPS/ATP-stimulated BMDM. Inhibitory effect of PS on NLRP3 activation was confirmed in confocal microscopic analysis. Collectively, PS definitely inhibited the production of inflammation-related mediators through down-regulation of signal pathway, mRNA expression, and NLRP3 inflammasome activation. Our finding strongly suggests that PS suppresses inflammation-related intracellular signalings to inhibit the secretion of inflammatory mediators from macrophages under inflammation stage, and PS can be applicable to prevention and cure of inflammatory diseases. This study was carried out with the support of ´R&D Program for Forest Science Technology (Project No. 2023471B31-2325-EE01)' provided by Korea Forest Service(Korea Forestry Promotion Institute).

***Corresponding author :** Yung Choon Yoo

***Keywords :** Platycarya strobilaceaInflammation, Macrophage, NLRP3 inflammasome, NF-kB

PS-A-019

CXCL5/CXCL8 promotes inflammatory response in peri-implantitis by activating the PI3K/Akt/NF-κB signaling pathway

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This study aimed to investigate the roles of CXCL5 and CXCL8 in neutrophil-mediated inflammation associated with peri-implantitis, as well as to elucidate their underlying mechanisms in disease pathogenesis. The study involved 40 patients categorized into two groups: 20 with healthy implants (HI group) and 20 with peri-implantitis (PI group) from Kyungpook University Dental Hospital. Biopsy specimens from peri-implantitis and healthy tissues were collected and analyzed using RNA sequencing. Gene expression profiles were further validated by RT-qPCR, and histological analyses were conducted using hematoxylin and eosin staining. Immunohistochemistry (IHC) analysis was performed to visually assess expression levels and analyze tissue histology. Heatmap analysis revealed significantly elevated levels of CXCL5 and CXCL8 in the PI group compared to the HI group ($p < 0.045$) and they are known to be associated with inflammatory responses. Conversely, interleukin 36 receptor antagonist (IL36RN) mRNA level was significantly lower in PI tissues ($p < 0.008$).The enhanced expression of CXCL5/CXCL8 proteins in PI tissues was confirmed by immunohistochemistry. In peri-implant tissues, elevated levels of CXCL5/CXCL8 stimulate inflammation, cell proliferation, migration, and invasion. These effects are mediated through the activation of the PI3K/Akt/NF-κB signaling pathway. This study shows that CXCL5 and CXCL8 increase in peri-implantitis tissue, indicating that they might make the treatment strategy and diagnosis more accurate. Such knowledge may aid in the precision of peri-implantitis care techniques.

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***Keywords :** Cytokines, Dental implants, Inflammation, Peri-implantitis

PS-A-020

Discovery of a new long COVID mouse model via systemic histopathological comparison of SARS-CoV-2 intranasal and inhalation infection

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Intranasal infection is a common technique for establishing a SARS-CoV-2 mouse model, favored for its non-invasive nature and minimal operational effects compared to intratracheal infection, which targets the lower respiratory tract. However, a significant limitation of the intranasal method is the high mortality rate in mice, restricting its use for studying therapeutic strategies and non-fatal COVID-19 outcomes. To address these issues, aerosolized viral administration has been proposed, though comparative pathological analyses between these methods are limited. In our study, we evaluated inhalation and intranasal SARS-CoV-2 infection models in K18-hACE2 mice, revealing distinct pathological features in the respiratory and central nervous systems attributable to the infection route. The inhalation model showed milder pathological parameters, with weight loss recovery and an increased adaptive immune response beginning at 7 days post-infection. At 14 days post-infection, focal and peripheral lung lesions with fibrotic scarring were observed in the inhalation model, closely resembling common chest CT findings in COVID-19 patients. Both models demonstrated trigeminal nerve infection and neuro-invasion of the olfactory epithelium to the olfactory bulb. However, the inhalation model exhibited delayed olfactory bulb infection, with viral clearance by day 14. These results indicate that the inhalation-infection model more accurately mimics the pathological features of non-fatal COVID-19, making it a valuable tool for studying long-term effects and potential treatments for COVID-19. This model's ability to replicate non-fatal COVID-19 symptoms suggests it may be advantageous for research into long COVID sequelae and therapeutic interventions.

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***Keywords :** Infection route, Neuro-invasion, Histopathology

PS-A-021

Adult K18-hACE2 mice are suitable model for studying SARS-CoV-2 intranasal infection than direct contact transmission

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The rapid global spread of the highly contagious SARS-CoV-2 virus since its emergence in 2019 has highlighted the critical need to comprehend its primary transmission routes, which are predominantly through airborne dissemination and direct contact. Contact transmission, in which the virus passes from person to person through direct or indirect contact, plays a crucial role in disease epidemiology. Therefore, investigating contact transmission in animal models is instrumental for understanding SARS-CoV-2 behaviour and devising effective preventive measures. Although ferrets, cats, and hamsters have been established as models for studying contact transmission, the susceptibility of mice, the most commonly used experimental animal model, to SARS-CoV-2 contact infection remains uncertain. In this study, contact transmission was examined by co-housing K18-hACE2 mice intranasally infected with the SARS-CoV-2 S type, isolated from Koreans, with uninfected adult K18-hACE2 mice. The results showed that mice subjected to contact infection exhibited no changes in clinical signs, as compared to animals infected intranasally. Furthermore, a thorough examination of the respiratory and non-respiratory organs revealed no histopathological changes, and SARS-CoV-2 was not detected in any of the tested samples. Collectively, these results suggest that adult K18-hACE2 mice are not susceptible to SARS-CoV-2 contact infection. This study underscores the importance of utilising appropriate animal models to accurately elucidate transmission dynamics.

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***Keywords :** SARS-CoV-2, Contact transmission, HCoV-19/Korea/KCDC03/2020_WA-1, K18-hACE2 mice model, Histopathological change

PS-A-022

Unveiling new therapeutic possibilities through NOX4 deficiency in skeletal development and trabecular bone mass increase

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Recent research on endochondral ossification, essential for skeletal development, suggests that elevated intracellular reactive oxygen species (ROS) can lead to skeletal abnormalities. This study investigates the role of NADPH oxidase 4 (NOX4) in bone functionality, particularly in osteoblast formation and osteogenic signaling. Utilizing NOX4-deficient ($NOX4^{-/-}$) and ovariectomized (OVX) mice, the research explores NOX4's impact on bone maturation. The bone structure was evaluated using staining methods like Hematoxylin & Eosin (HE), Masson's trichrome, Safranin O, and Toluidine Blue, alongside a protein proteome array to identify cytokines linked to NOX4 in bone marrow-derived mesenchymal stem cells (MSC). The findings show distinct variations in bone mass and structure among the $NOX4^{-/-}$, control, and OVX mice, with $NOX4^{-/-}$ mice exhibiting the most trabecular bone volume. Proteomic analysis revealed higher levels of MPO and OPN in the MSC of $NOX4^{-/-}$ mice. Immunohistochemical analysis confirmed elevated MPO, OPN, and collagen II (COL II) around the epiphyseal plates. Further analyses supported enhanced bone development in $NOX4^{-/-}$ mice through increased collagen production and chondrogenesis. The study concludes that NOX4 is critical in shaping bone morphology, influencing MSC proteomics, and modifying collagen production and chondrogenesis. A deficiency in NOX4 appears to promote bone development and endochondral ossification by upregulating MPO, OPN, and COL II. These insights could offer new therapeutic approaches for skeletal disorders.

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***Keywords :** Endochondral ossification, Myeloperoxidase, NADPH oxidase 4, Osteopontin, Ovariectomy

PS-A-023

A comparative study of bone regeneration effects between customized synthetic bone grafts OSTEON-3 collagen and OSTEON-3 block in rat calvaria critical-size defects

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Bone regeneration remains a critical challenge in biomedical research and clinical applications. This study compares the bone regeneration effects of two customized synthetic bone grafts, OSTEON-3 Collagen and OSTEON-3 Block, in combination with polydeoxyribonucleotide (PDRN) solution in rat calvaria critical-size defects. Using a well-established rat model, critical-size defects were created and treated with different combinations of the synthetic grafts and PDRN. Bone regeneration was evaluated at 4 and 8 weeks post-implantation using micro-computed tomography (μ-CT) and histological analysis. The results demonstrated that the OSTEON-3 Collagen combined with PDRN significantly enhanced bone formation compared to other groups, showing the highest bone volume/total volume (BV/TV) percentage and most substantial new bone formation. This study suggests that OSTEON-3 Collagen combined with PDRN could be a promising candidate for clinical applications in bone regeneration, offering a potential alternative to autogenous bone grafts without the associated donor site complications. Further research and clinical trials are recommended to confirm these findings and explore the underlying mechanisms of enhanced bone regeneration.

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***Keywords :** Bone regeneration, OSTEON-3 Collagen , OSTEON-3 Block, Polydeoxyribonucleotide (PDRN)

PS-A-024

Electron electron-producing apparatus protects against folic acid-induced acute kidney injury in rats by inhibiting inflammatory responses

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Acute kidney injury is a common clinical problem with no specific treatment; therefore, understanding the molecular mechanisms of acute kidney injury is crucial for developing novel therapies. This study sought to examine the efficacy of utilizing electrons delivered via an electron-producing apparatus (EPA) in mitigating folic acid (FA)-induced acute renal injury (AKI). To achieve this, rats were intraperitoneally injected with folic acid (250 mg/kg) to induce acute kidney injury, followed by treatment with EPA (0.4mV) five times for 48 hours. Renal tissue was investigated using histological evaluation and ionized calcium-binding protein-1 (Iba-1) immunoreactivity including inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) was evaluated by immunohistochemistry and Western blot analysis, respectively. EPA treatment mitigated the pathological alterations, ameliorated inflammatory cell infiltration, and improved kidney dysfunction in rats with FA-induced AKI. Treatment with EPA significantly attenuated FA-induced increases in serum creatinine and BUN levels, and the infiltration of inflammatory cells. In addition, EPA significantly reduced the expression of inflammatory mediators, including iNOS and COX-2, compared with the vehicle-treated group. Overall, EPA's protective role was closely related to inhibiting inflammatory mechanisms. These findings provide strong evidence that using EPA before folic acid insult may offer a potential treatment for AKI. (Funding Source: This work was supported by the National Research Foundation of Korea: Grant number NRF-2021M3H9A1097596)

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***Keywords :** Electron-producing apparatus, Folic acid, Inflammation, INOS, COX-2

PS-A-025

Evaluation of the biological effects of FLASH radiation on the intestines and testicles

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Purpose: FLASH radiation (average dose rate: > 40 Gy/s) delivers ultra high doses of radiation, which are several times higher than the clinically used conventional radiation doses (average dose rate: > 5 Gy/s). This study aimed to identify the protective effect against intestinal and testicular damage through biological safety evaluation and verification of FLASH radiotherapy compared to conventional radiation.
Materials and Methods: C57BL/6 mice were divided into three groups: control (0 Gy), FLASH (40 Gy/s), and conventional (0.067 Gy/s). Irradiated mice were euthanized at 2, 4, 7, 14, and 28 days after total body irradiation (TBI) at 3 Gy.
Results: The testicular size of mice irradiated with FLASH radiation and conventional radiation tended to decrease rapidly after 4 weeks of irradiation, and the decrease was less in FLASH radiation than in conventional radiation. In addition, the length of intestinal cilia was shown to be impaired by irradiation, and there was less radiation-induced damage in FLASH radiation.
Conclusion: Our results suggest that FLASH radiation therapy may reduce the adverse effects of conventional radiation in the testicles and intestines. These findings suggest the possibility of therapeutic devices that can shorten the duration of treatment by improving cancer treatment outcomes and reducing radiation side effects, and will serve as a fundamental study in radiological biology studies.

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***Keywords :** FLASH radiation, Mice, Radiotherapy, Radiation-induced toxicity, Total body irradiation

PS-A-026

Giant cell hepatitis in a Burmese python (Python bivittatus)

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In humans, liver disease in which multinucleated giant hepatocytes form is frequently reported in newborns and infants, and is called postinfantile giant cell hepatitis (PGCH) or syncytial giant cell hepatitis. The cause of PGCH is thought to be related to viral infection, drug toxicity, and autoimmunity. However in some cases, the cause is not yet clearly known. On the other hand, in animals, it has been reported in cats and tilapia, and the cause of its occurrence is considered to be related to viral infection in tilapia, but in cats it is still undetermined. It has not been reported in snakes to date. Therefore, we report here focusing on morphological characteristics. A Burmese python died suddnly, and an necropsy was submitted for diagnostic investigation. Other than being somewhat thin, no specific clinical signs were observed in te submitted snake. After necropsy, all tissues and organs were collected and fixed, and tissue sections were made through general tissue processing. Tissue sections were stained with H&E and histopathological examination was performed. Gram staining was also performed on intestinal tissues. Grossly, the liver showed scattered yellow-white spots of various sizes. In the intestines, a white or reddish-yellow substance was attached to the mucous membrane. The kidneys were entirely red and somewhat enlarged. Other than that, other organs were normal. Histopathologically, numerous multinucleated giant cells with severe necrosis were observed in the liver. Necrosis of the intestinal epithelium was observed in the small and large intestines, bleeding was also present in the mucous membrane, and bacterial colonies were also observed. Edema and bleeding were observed in the kidneys. Bacteria observed in the intestinal mucosa were confirmed to be gram positive. Based on the above results, the submitted animal was diagnosed with giant cell hepatitis with necrotisizing hemorrhagic enteritis. Although the cause related to giant cell hepatitis has not been identified, additional experments will be conducted to confirm the relationship with known causes in humans. To our knowledge, this case is believed to be the first giant cell hepatitis reported in a snake.

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***Keywords :** Giant cell hepatitis, Burmese python, Python bivittatus

PS-A-027

Spirocerca lupi infection in a fennec fox

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Spirocercosis is a disease infected with the mematode *Spirocerca lupi* which has a various clinical signs and is found worldwide especially in tropical and subtropical areas. This nematode has been extensively reported in the dog and also demonstrated in the cat, coyote, fo, jackal, jaguar, lynx, snow leopard and wolf. Clinical signs vary widely depending on the movement and persistence of the larvae or adult worms within the host and secondary bacterial infections. The main clinical signs are known to be reflux or vomiting, weight loss, and dysphagia due to nodules on the esophageal wall. Additionally, clinical symptoms may vary depending on the movement or aberrant migration of parasites. A severely emaciated and pale fennec fox was submitted for diagnostic investigation. The requested animal was imported from Egypt three weeks ago, and was treated for inflammation due to inuries to the hindquarters and buttocks due to stress during transportation. 2-3 days before death, the animal's appetite suddenly decreased, blisters formed on the extremities of the limbs, and weight loss was severe. After necropsy, all tissues and organs were collected and fixed, and tissue sections were made throught general tissue processing. Tissue sections were stained with H&E and histopathological examination was performed. Fecal testing was also performed. Grossly, there was a moderate amount of clear light yellow fluid accumulated in the thoracic and abdominal cavities. The skin, abdominal organs, and gastrointestinal mucosa were pale, and the blood was thin. A 3mm round nodule was observed protruding into the lumen on the vessel wall at the origin of the aorta. A nematode was observed in the nodule section. Numerous nematodes were observed in the lumen of the heart. Histopathologically, granulomatous inflammation was observed in the aortic wall, and nematode was observed in granuloma. Focal lymphocytic hepatitis was present in the liver. No histopathological findings were observed in ther tissues or organs. In the fecal examination, many coccidia eggs were observed. Based on the above results, the submitted animal was diagnosed with heartworm infection and Spirocerca infection. To our knowledge, this case is believed to be the first spirocercosis confirmed in the fennec fox.

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***Keywords :** Spirocerca lupi, Fennec fox

PS-A-028

HPRT1 is the most stable reference gene for normalization of mRNA expression in long-term expanded canine skin fibroblast

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The fibroblast is a type of cell embedded within fibrous or loose connective tissues of most mammalian organs. These cells are widely used in molecular biological experiments, such as cell culture models, gene expression studies, and disease models. In research, fibroblasts are occasionally subjected to long -term culture under defined conditions, during which their properties can change. In molecular biology, qRT-PCR is the most reliable and widely utilized method for quantifying specific gene expression. To accurately compare the expression levels of the gene of interest (GOI) across multiple experiments using qRT-PCR. it is crucial to normalize the data using an appropriate reference gene. Therefore, the most stable reference genes for long -term expanded canine fibroblasts were evaluated. Fibroblasts were successfully isolated from canine skin tissue. Compared with early passage (E-skin fibroblasts), the late passage (L -skin fibroblasts) showed significantly longer doubling times and elevated β -galactosidase activity. Both the geNorm and Normfinder algorithms suggested that HPRT1 is the most stable reference gene, regardless of whether the cells are at early or late passage. In contrast, the traditional reference gene GAPDH was found to be less stable. In the normalization of Vimentin, the use of stable and unstable reference genes showed statistical differences. Therefore, our study indicates that using HPRT1 for normalization is recommended to obtain accurate and reliable gene expression levels in early and late passage fibroblasts. These findings offer essential insights into internal controls for gene expression studies and can be applied to analyze gene expression patterns in molecular biology.

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***Keywords :** Dog, Fibroblasts, Reference gene, QRT-PCR

PS-A-029

Role of toll-like receptor 4 in a chronic obstructive pulmonary disease mouse model induced by co-administration of porcine pancreas elastase and lipopolysaccharide

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Chronic obstructive pulmonary disease (COPD) is a respiratory disorder characterized by pulmonary emphysema and inflammation of the airways. In our previous study we established a new method for COPD mouse model induced by co-administration of porcine pancreas elastase (PPE) and lipopolysaccharide (LPS) by intubation-mediated intratracheal instillation technique. Toll-like receptor (TLR) 4 belongs to the TLR family, and when being stimulated by LPS from gram-negative bacteria causes inflammation, but there are a few studies conducted in vivo role of LPS. In this study, we conducted to see the role of TLR4 in COPD model by using $TLR4^{-/-}$ mice. The mice were divided into two groups: C57BL/6J wild-type mice and $TLR4^{-/-}$ mice. Both groups were administered PPE twice at 3-day intervals, followed by LPS four times at 3-day intervals. After the last LPS administration, the mice underwent a 7-day recovery period before being sacrificed for examination. Four lung lobes (left, right middle, right caudal, accessory) were histopathologically evaluated. We measured Air/Tissue (A/T) ratio to evaluate the degree of emphysema caused by PPE and number of inflammatory sites caused by LPS at each lobe. The histopathological evaluation results showed no difference in the A/T ratio between the two groups, but there was a significant decrease in the number of inflammatory sites in the $TLR4^{-/-}$ group across all four lobes. This study confirmed the relationship between TLR4 and LPS in vivo by applying a new COPD model using TLR4 knockout mice.

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***Keywords :** COPD, TLR, PPE, LPS, Intubation-mediated intratracheal instillation

PS-A-030

Tumor-priming CD8+ natural killer T-like cells as an efficient novel cell therapy for gastric cancer peritoneal metastasis

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Gastric cancer is a disease that causes a significant health burden worldwide, accounting for a significant number of cancer cases and deaths worldwide. Despite advances in diagnostic techniques and treatment modalities, the prognosis for patients with advanced gastric cancer remains poor, particularly for those who have developed peritoneal metastases and ascites. Current therapeutic approaches, including surgery, chemotherapy, and targeted therapy, are staples of the treatment paradigm, but their limited efficacy necessitates the exploration of alternative strategies. In this study, we present substantial evidence that priming cord blood cells with ascites cells from gastric cancer patients induces a functional conversion to tumor-priming $CD8^+$ natural killer T (NKT)-like cells (TPNCs). This conversion increases tumor-specific cytotoxicity and enhances perforin and granzyme synthesis. Notably, TPNCs exhibit rapid cytotoxicity compared to NKT-like cells obtained from cytokine-induced killer cells, form strong immune synapses, and induce efficient target cell lysis. The granules showed a much faster polarization time, shorter killing time and higher frequency of interaction with target cells. TPNCs effectively inhibited the growth of gastric cancer tumors *in vivo*, and no significant toxicity was observed in treated mice. In addition, TPNCs produced using ascites from patients with other solid cancers also exhibited tumor-specific cytotoxicity, highlighting the versatility of this therapy. Overall, these results suggest that TPNCs are a promising cell therapy for gastric cancer, as well as a variety of solid cancers, with the potential to change the paradigm of cancer treatment.

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***Keywords :** Gastric cancer, Peritoneal metastasis, Tumor-priming CD8+ natural killer T (NKT)-like cells

PS-A-031

A fine-tuning modulation of mTOR signaling pathway controls the protective antibody responses against influenza A virus

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Host defense against pathogenic microbes requires an appropriate humoral immune response produced by B cells. Although mTOR signaling is essential for survival and clonal expansion of B cells, dynamic modulation in this signaling pathway during germinal center (GC) reactions and generation of plasma cells remains unclear. In this study, we have investigated how mTOR pathway integrates immune signals in GC microenvironments using an *in vitro* cocultivation system mimicking the GC reactions and *in vivo* immunization models. While hyperactivated mTOR signaling elicited by PTEN loss impaired GC reactions, inactivation of mTORC2 but not by that of mTORC1 in the PTEN-deficient B cells upregulated isotype switching such as IgG1 in both *in vitro* GC B cell cultures and *in vivo* immunization experiments. We also observed a substantial reduction of IgG1 antibodies against influenza A virus in mice depleted PTEN specifically in GC B cells, which was restored by inactivating mTORC2. In a passive immunization model, transferring sera of mice pre-immunized with influenza A virus protected mice from lethal challenge with the viral infection as shown by an ability of viral clearance and improved lung pathology. Of note, passive immunization with sera of mice lacking PTEN in GC B cells was not sufficient to provide a protective humoral immune response to the lethal viral infection, which was rescued by suppressing mTORC2. Mechanistically, we found that attenuation in Akt downstream from PTEN-mTORC2 axis was important for IgG1 class switching via promoting an induction of AID. Taken together, our data highlight a fine-tuning modulation in PTEN-mTORC2-Akt signaling pathway to generate an optimal humoral immune response against viral infection.

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***Keywords :** Antibody isotype switching, PTEN, MTORC2, Influenza A virus, Akt

PS-A-032

Study on the efficacy of bypass allogeneic acellular nerve graft using supercritical extractor technique in rat sciatic nerve neuroma-in-continuity model

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Introduction: Recently, allogenic nerve graft has gained its popularity to prevent donor site morbidity from autologous nerve graft. However, destruction of extracellular matrix (ECM) during detergent based de-cellularizing procedure causes inferior postoperative results compared with autologous graft. In this study, we used supercritical de-cellularization technique (SC group) to preserve ECM structure. Nerve regeneration was evaluated among SC, detergent, and autologous graft groups in neuroma-in continuity model in rats.
Methods: Neuroma-in-continuity formation : After exposing the Lewis rat sciatic nerve, perform nerve compression for 3 seconds after clamping with a micromosquito at a length of 3 mm, centered on the proximal 10 mm from the branch point (step 1). After that, cut the center point, harvest the fascia of the rat, insert it between both never ending, and perform a neve repair using 10-0 nylon thread. Plan a bypass experiment 3 weeks later after pure tagging in the area. Nerve graft harvest: Harvest both sciatic nerves by 20mm from eight SD rats, Through Dope Co. Ltd. eight go through a supercritical decellular process, and eight make a detegent based acellular nerve graft. Bypass nerve graft: After creating a 1.5 mm nerve window in the proximal 4 mm and distal 4 mm area from the center of the neuroma-in-continuity, For each experimental group bypass transplantation is performed using isograft, supercritical extractor technology acellular nerve graft, and detergent-based acellular nerve transplantation 10 mm.
Results: The degree of nerve recovery can be evaluated by calculating the sciatic nerve function index through the mouse walking track analysis. As a result, all groups tend to recover sciatic never from two weeks later, of which Isograft (-64.18 ± 0.62) has the highest resilience, followed by SC (-67.07 ± 2.00), Detergent (-73.59 ± 0.81), and control (-80.34 ± 1.42). In the results, the SC group we are expecting has similar results to ISO, and it is expected to be a study that can replace Isograft. The SONO ratio results showed no significant difference regardless of the experimental group except for control. (Control : 0.669 ± 0.054, Detergent : 0.764 ± 0.017, Supercritical : 0.786 ± 0.038, Isograft : 0.742 ± 0.041) After 8 weeks, rat was sacrified and the tibialis anterior and gastrocnemius muscle mass and ratio values of Control and Experimental were measured. Gastrocnemius (Control : 0.467 ± 0.050, Detergent : 0.557 ± 0.038, Supercritical : 0.620 ± 0.032, Isograft : 0.500 ± 0.034) Tibialis anterior (Control : 0.611 ± 0.065, Detergent : 0.615 ± 0.025, Supercritical : 0.666 ± 0.064, Isograft : 0.529 ± 0.031) Comparing the tibialis anterior and gastrocnemius muscle mass ratio values after autopsy, the ratio value was the highest in the SC group, and the high SC value is expected to be able to use supercritical decellular cells to produce results equivalent to autologous nerve transplantation and to replace autologous nerves.
Conclusion: SC group showed superior postoperative results in neuroma in continuity model compared with conventional detergent-based group. Future human study should be followed.

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***Keywords :** Supercritical de-cellularization technique

PS-A-033

Apelin mitigates aged-related severity of acute kidney injury in sischemia-reperfusion models

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Age-related changes in kidney function increase susceptibility to aging and might exacerbate the severity of acute kidney injury (AKI). However, the precise risk and etiology of AKI in older age remain unclear. In this study, we investigated the severity of AKI in aged mice and explored the underlying causes. Aged (18 months) and young (8 weeks) C57BL/6 mice were subjected to unilateral ischemia-reperfusion (I/R) injury. Three days post-surgery, kidney function and differentially expressed proteins were evaluated. Blood creatinine and blood urea nitrogen levels were significantly higher in aged mice compared to young mice. Additionally, glomerular and proximal tubular damage were more pronounced in the aged mice. Mass spectrometry analysis revealed a significant decrease in apelin levels in aging mice subjected to I/R-induced AKI, which contributed to aggravated renal fibrosis. This was accompanied by increased expression of Smad 2/3 and α-smooth muscle actin. Notably, apelin treatment in aged mice reduced kidney damage and decreased renal fibrosis by lowering the expression of Smad 2/3 and α-smooth muscle actin. These findings provide strong evidence that apelin plays a critical role in the progression of AKI in aged mice.

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***Corresponding author :** Geum-Lan Hong

***Keywords :** Acute Kidney injury, Aging, Apelin, Renal firosis

PS-A-034

BRCA1 mutation promotes sprouting angiogenesis in Inflammatory Cancer-Associated Fibroblast of Triple-Negative Breast Cancer

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Triple-negative breast cancer(TNBC) is an aggressive subtype of breast cancer that lacks targeted therapies. Given that 48-66% patients with breast cancer those who possess *BRCA1* mutation carriers develop into TNBC. We further identified possible involvement of *BRCA1* mutation in tumorigenicity of TNBC. When we randomly identified gene set enrichment analysis between *BRCA1* mutant and wildtype of TNBC, immune-related pathways were enriched in *BRCA1* mutation patients. Since cancer-associated fibroblasts(CAFs) are major component of breast cancer for tumorigenicity in tumor microenvironment and involved in inflammatory response, we focused on fibroblast to identify whether *BRCA1* mutation is associated with CAFs in single-cell RNA sequencing. We confirmed inflammatory CAFs(iCAFs) were preferentially represented in *BRCA1* mutation compared to wildtype. Besides, *BRCA1* mutation also exhibited signals towards endothelial cell, which contributes to angiogenesis in TNBC. Our findings provide suppressing iCAFs activity can be latent therapeutic targets by reducing angiogenesis in TNBC patients with *BRCA1* mutation.

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***Keywords :** Triple Negative Breast Cancer, BRCA1, ICAF, Single cell RNA sequencing

PS-A-035

Therapeutic effect of donepezil on neuroinflammation and cognitive impairment after moderate traumatic brain injury

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Background: Cognitive impairment following moderate traumatic brain injury (TBI) presents a significant clinical challenge, and currently, there is no effective treatment available. This study explored the effects of Donepezil, an acetylcholinesterase (AChE) inhibitor, on cognitive deficits observed in the acute phase post-injury, with a focus on neuroinflammation and markers associated with autophagy and mitophagy.
Methods: The research aimed to examine the potential neuroprotective effects of Donepezil on TBI-induced cells in vitro, and its therapeutic impact on cognitive impairment in vivo during the acute post-injury phase by analyzing neuroinflammation and markers related to autophagy and mitophagy. The in vitro model involved damaging SH-SY5Y cells using a cell injury controller and then treating them with Donepezil at 80 μM concentration. For the in vivo model, male C57BL/6J mice were subjected to TBI using a stereotaxic impactor. After administering Donepezil (1 mg/kg/day) within 4 hours post-TBI, immunohistochemical markers and cognitive functions were evaluated over 7 days. The mice were divided into four groups: sham operation with saline, sham operation with Donepezil, TBI with saline, and TBI with Donepezil (18 mice per group).
Results: In vitro results indicated that Donepezil treatment enhanced cell viability and JC-1 levels, while reducing reactive oxygen species (ROS), lactate dehydrogenase (LDH), DCFH-DA-positive cells, and TUNEL-positive cells. Donepezil also reduced the mRNA and protein levels of neuroinflammation markers (COX-2, NLRP3, Caspase-1, IL-1β) and autophagy- and mitophagy-related markers (DAPK1, PINK1, BNIP3L, BECN1, BAX, LC3B, and p62). In vivo findings showed that Donepezil treatment mitigated cortical tissue loss and brain swelling in TBI-affected mice compared to those untreated. The treatment also led to decreased expressions of all markers, especially COX-2 and BNIP3L. Additionally, cognitive performance in TBI mice improved, as evidenced by decreased escape latency, increased alteration rate, and a higher preference index following Donepezil treatment.
Conclusions: Donepezil may offer benefits in improving early cognitive impairment following moderate TBI by reducing neuroinflammation and modulating autophagy and mitophagy processes.

***Corresponding author :** Jin Pyeong Jeon

***Keywords :** Donepezil, Traumatic brain injury, Cognition, Neuroinflammation, Mitochondria

PS-A-036

Autophagy and mitophagy related extracellular mitochondrial dysfunction of cerebrospinal fuid cells in patients with hemorrhagic moyamoya disease

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We aimed to investigate whether mitochondrial dysfunction in extracellular cerebrospinal fuid (CSF),which is associated with autophagy and mitophagy, might be involved in neurological outcomes in adult patients with hemorrhagic moyamoya disease (MMD) whose pathogenesis related to poor outcomes is not well-known. CSF samples were collected from 43 adult MMD patients and analyzed according to outcomes at 3 months. Fluorescence-activated cell sorter analysis (FACS) and the JC-1 red/green ratio were used to assess mitochondrial cells and intact mitochondrial membrane potential (MMP). We performed quantitative real-time polymerase chain reaction and Western blotting analyses of autophagy and mitophagy-related markers, including HIF1α, ATG5, pBECN1, BECN1, BAX, BNIP3L, DAPK1, and PINK1. Finally, FACS analysis with specifc fuorescence-conjugated antibodies was performed to evaluate the potential cellular origin of CSF mitochondrial cells. Twentyseven females (62.8%) with a mean age of 47.4 ± 9.7 years were included in the study. Among 43 patients with hemorrhagic MMD, 23 (53.5%) had poor outcomes. The diference in MMP was evident between the two groups (2.4 ± 0.2 in patients with poor outcome vs. 3.5 ± 0.4 in patients with good outcome; p= 0.02). A signifcantly higher expression ($2^{-\Delta Ct}$) of HIF1α, ATG5, DAPK1 followed by BAX and BNIP3L mRNA and protein was also observed in poor-outcome patients compared to those with good outcomes. Higher percentage of vWF-positive mitochondria, suggesting endothelial cell origins, was observed in patients with good outcome compared with those with poor outcome (25.0± 1.4% in patients with good outcome vs. 17.5 ± 1.5% in those with poor outcome; p< 0.01). We observed the association between increased mitochondrial dysfunction concomitant with autophagy and mitophagy in CSF cells and neurological outcomes in adult patients with hemorrhagic MMD. Further prospective multicenter studies are needed to determine whether it has a diagnostic value for risk prediction.

***Corresponding author :** Jin Pyeong Jeon

***Keywords :** Moyamoya disease (MMD), Autophagy, Mitophagy, Mitochondrial dysfunction

PS-A-037

Oxiracetam alleviates anti inflammatory activity and ameliorates cognitive impairment in the early phase of traumatic brain injury

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Background: We aimed to investigate the effects of oxiracetam on cognitive impairment in the early phase of traumatic brain injury (TBI), for which no specific treatment is currently available.
Methods: The in vitro study used a cell injury controller to damage SH-SY5Y cells and evaluate the effect of oxiracetam at a dosage of 100 nM. The in vivo study used a stereotaxic impactor to induce a TBI model in C57BL/6 J mice and analyzed immunohistochemical changes and cognitive function after an intraperitoneal injection of oxiracetam (30 mg/kg/day) for 5 days. The number of mice used in this study was 60. They were divided into three groups (sham, TBI, and TBI with oxiracetam treatment) (20 mice in each group).
Results: The in vitro study showed that oxiracetam treatment resulted in increased superoxide dismutase (SOD)1 and SOD2 mRNA expression. The mRNA and protein expression of COX-2, NLRP3, caspase-1, and interleukin (IL)-1 β were decreased after oxiracetam treatment, along with decreases in intracellular reactive oxygen species production and apoptotic effects. TBI mice treated with oxiracetam exhibited the loss of fewer cortical damaged lesions, less brain edema, and fewer FluoroJade B (FJB)-positive and terminal deoxynucleotidyl transferase dUTP nick end-labeling (TUNEL)-positive cells compared to those without oxiracetam treatment. The mRNA and protein expression of COX-2, NLRP3, caspase-1, and IL-1β were decreased significantly after oxiracetam treatment. These inflammation-related markers, which colocalized with Iba-1-positive or GFAP-positive cells after TBI, were also decreased after oxiracetam treatment. TBI mice treated with oxiracetam had a smaller decrease in preference and more latency time than those not treated with oxiracetam, suggesting the amelioration of impaired cognitive impairment.
Conclusions: Oxiracetam may be helpful in restoring cognitive impairment by ameliorating neuroinflammation in the early phase of TBI.

***Corresponding author :** Jin Pyeong Jeon

***Keywords :** Oxiracetam, Traumatic brain injury, Cognition, Neuroinflammation

PS-A-038

Evaluation of the graft uptake and the effacement of melanin pigmentation in giant melanocytic nevus using supercritical fluid extractor (SCFE) decellularization technique: a preliminary study

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Current methods for treating giant congenital melanocytic nevus (GCMN), including skin grafting and culturing techniques, have several drawbacks. Skin grafting often results in significant donor site morbidity and requires multiple operations, leading to prolonged recovery periods and increased patient discomfort. Culturing techniques, while innovative, can be complex and costly, with variable success rates. The use of tissue expanders, though effective in providing additional skin for grafting, also comes with its challenges, such as donor site morbidity and the necessity for serial operations, which require repeated hospital visits for saline injections, further inconveniencing patients.To address these shortcomings, we need a novel surgical approach. In this preliminary study, we evaluated the effectiveness of the Supercritical Fluid Extractor (SCFE) decellularization technique. We categorized GCMN specimens into three groups: those sterilized with gamma rays (control group, n=2), those decellularized with the epidermis intact (wEp/SC group, n=2), and those decellularized after epidermis removal (woEp/SC group, n=2). These specimens were grafted onto the backs of Sprague-Dawley (SD) rats. After two weeks, we assessed the degree of skin contraction, melanin content, and collagen volume fraction through visual inspection and histological analysis.The results showed no significant differences in skin contraction and melanin content among the three groups. However, the collagen volume fraction was significantly higher in the woEp/SC group compared to the other two groups. This suggests that removing the epidermis and applying the SCFE decellularization technique enhances graft integration by increasing collagen content. The increased collagen fibers promote better structural integrity and support in the grafts, potentially reducing complications and improving aesthetic outcomes. Therefore, this method could be a promising alternative for GCMN treatment. Moreover, due to the limited sample size, the current results regarding skin contraction and melanin levels are inconclusive. Further research with larger sample sizes and extended observation periods is required to validate and refine these findings.

***Corresponding author :** Byung jun Kim

***Keywords :** Giant congenital melanocytic nevus, Supercritical Fluid Extractor, Skin grafting

PS-A-039

Effect of A12, an inverse agonist of estrogen-related receptor gamma (ERRγ), on a sepsis model in vitro and in vivo

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Purpose: Estrogen-related receptor gamma (ERRγ) has been identified as a promising therapeutic target for metabolic disorders, including diabetes, inflammation, and cancer. In this study, we aimed to examine the effects of A12, a novel modulator of the ERRγ receptor, on sepsis induced by cecal ligation and puncture (CLP).
Methods: The effects of A12 on the viability of Raw264.7 macrophages were determined using the CCK8 assay. The influence of A12 on proinflammatory cytokines, COX-2, iNOS, NF-κB, and MAPK-related molecules was assessed via real-time PCR and western blot analysis. For the in vivo efficacy study, C57BL/6 mice were divided into four distinct groups: the control group, the CLP-induced group, the CLP+10 mg/kg A12 group, and the CLP+20 mg/kg A12 group. Various parameters, including survival rate, changes in body weight, levels of inflammatory cytokines, and histological analyses, were evaluated.
Results: The results of the CCK8 assay revealed that A12 did not reduce the viability of Raw264.7 cells. Moreover, A12 decreased the mRNA expression of proinflammatory cytokines (IL-1α, IL-6, and TNF-α) and inhibited NO production. Western blot analysis showed that A12 downregulated iNOS, COX-2, phosphorylated p38, and phosphorylated IKKα/β. Following CLP surgery, mice treated with A12 had a higher survival rate and better body weight maintenance compared to mice treated with the vehicle. Consistently, A12 significantly lowered serum levels of proinflammatory cytokines, such as IL-6 and TNF-α. Histological examinations demonstrated that A12 effectively mitigated CLP-induced pulmonary damage.
Conclusion: We have successfully demonstrated that A12 effectively suppresses inflammation and offers protective effects against sepsis induced by CLP. These findings strongly indicate the potential of A12 as a promising therapeutic agent for addressing sepsis and other inflammatory diseases.

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***Keywords :** Estrogen-realted receptor, ERR inverse agonist, Sepsis, Inflammation

PS-A-040

Ginseng Berry Juice regulates the inflammation in acute ulcerative mouse models and the major bioactive substances are Ginsenosides Rb3, Rc, Rd, and Re

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Panax ginseng fruit is known to have various biological effects owing to its large amount of saponins such as ginsenosides. In the present study, ginseng berry juice was confirmed to be effective against acute inflammation. Ginseng berry juice was used for analysis of active constituents, antioxidant efficacy, and in vivo inflammation. A high-performance liquid chromatography method was used for analysis of ginsenosides. In an HCl/ethanol-induced acute gastric injury model, microscopic, immunofluorescent, and immunohistochemical techniques were used for analysis of inhibition of gastric injury and mechanism study. In a mouse model of acute gastritis induced with HCl/ethanol, ginseng berry juice (GBJ, 250 mg/kg) showed similar gastric injury inhibitory effects as cabbage water extract (CB, 500 mg/kg, P.O). GBJ dose-dependently modulated the pro-inflammatory cytokines such as Tumor Necrosis Factor-α (TNF-α), Interleukin-6 (IL-6), and Interleukin-13 (IL-13). GBJ inhibited the activation of Nuclear Factor kappa bB (NF-κB) and suppressed the expressions of cyclooxigenase-2 (COX-2) and prostaglandin 2 (PGE2).The anti-inflammatory effect of GBJ is attributed to ginsenosides which have anti-inflammatory effects. Productivity as an effective food source for acute gastritis was analyzed and showed that GBJ was superior to CB. In addition, as a functional food for suppressing acute ulcerative symptoms, it was thought that the efficacy of gastric protection products would be higher if GBJ were produced in the form of juice rather than through various extraction methods.

***Corresponding author :** Dae-Hun Park, Seung-Sik Cho

***Keywords :** Ginseng berry juice, Ginsenosides, Acute gastric injury model, Inflammation

PS-A-041

Saururus chinensis water-extract effectively controls asthma by recovering of Th1/Th2 imbalance and suppressing of NF-kB/COX-2/PGE2-related inflammation

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Asthma is an incurable chronic inflammatory pulmonary hyperresponsiveness. The prevalence of asthma in the young and elderly is higher than that in others, and in 2019, the number of patients with asthma was estimated to be 262 million, and caused 461,000 deaths worldwide. As current medications have many adverse effects, the development of new effective and safe drugs is required. To define the anti-asthmatic and anti-inflammatory effects of Saururus chinensis, ovalbumin-induced asthma animal model and LPS-induced inflammation RAW 264.7 cell model were used. Histopathological evaluation such as H&E staining and PAS staining; inflammatory cell analysis, such as cell count using equipment and Diff-Quick staining; serum IgE measurement; and asthma / inflammation-related specific proteins evaluation via real time-PCR, immunofluorescence, enzyme-linked immunosorbent assay (ELISA), immuno-histochemistry, and western blotting were conducted. In animal study, S. chinensis prevented asthmatic pulmonary changes, such as epithelial cells hyperplasia, inflammatory cells increment, and mucous hypersecretion; controlled Th2 cell-related cytokines (IL-4 and IL-5) including GATA-3 and blocked inflammation occurrence via NF-κB/COX-2/PGE2 pathway. The anti-inflammatory effects and pathways of S. chinensis were confirmed in a cell-based study. Asthma is caused by both Th1/Th2 imbalance and inflammation and as S. chinensis effectively prevents the occurrence of asthma, it should be considered an anti-asthmatic candidate.

***Corresponding author :** Dae-Hun Park

***Keywords :** Saururus chinensis, Animal study, Th1/Th2 imbalance, Inflammation

PS-A-042

Ameliorative effects of Prunella vulgaris on lower urinary tract symptoms induced by benign prostatic hyperplasia in SD rats via nitric oxide and potassium channel

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Urinary tract symptoms (LUTS) due to prostate hyperplasia are the most frequent urological symptoms in aged men, and their prevalence is increasing significantly worldwide. Various cellular and physiological changes, such as aging and inflammation, cause prostate proliferation, obstruct the urinary tract due to its anatomical location, and interfere with voiding, resulting in LUTS such as frequency, nocturia, and urge urinary retention. Current pharmacological treatments include finasteride, a 5-α reductase inhibitor, and alpha1-receptor blockers like Tamsulosin, which are widely used clinically. However, due to the adverse effects of these drugs, there is still a demand for alternative drugs or supplements that are easily accessible daily. Although Prunella vulgaris Linne(PVE) has a long history of use in treating various diseases in both the East and the West, research on its effects on the prostate and urinary tract is lacking. This study aimed to determine the relaxant activity of a PVE on rat prostate smooth muscle ex vivo and to evaluate its potential to improve voiding dysfunction using intravesical cystometry in vivo. The results showed that the PVE has relaxant effects on prostatic smooth muscle in a concentration-dependent manner, mediated by nitric oxide and potassium channels without antagonizing adrenergic receptors. Additionally, intravesical cystometry in SD rats treated with the PVE extract for 4 weeks revealed an improvement in voiding abnormalities induced by prostatic hyperplasia. These findings suggest the potential of Prunella vulgaris and its compounds as a therapeutic strategy to improve LUTS in benign prostatic hyperplasia (BPH).

***Corresponding author :** Kyu Pil Lee

***Keywords :** Benign prostatic hyperplasia, Prunella vulgaris, Lower urinary tract symptoms, Relaxant, Nitric oxide

PS-A-043

Chronic pelvic ischemic model in rats for assessment of erectile dysfunction and lower urinary tract symptoms

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Erectile dysfunction (ED) and benign prostatic hyperplasia induced lower urinary tract symptoms (LUTS/BPH) have a high prevalence in older men. ED and LUTS/BPH share common etiologies, and especially chronic ischemia of the pelvic organs caused by age-related atherosclerotic occlusion is the critical risk factor. However, the relationship between these diseases has only recently been investigated, and there is a need to develop effective drugs with fewer cardiovascular side effects. LDD175 is a potent activator of BKCa channels, known as large conductance calcium-activated potassium channels, which cause smooth muscle relaxation through hyperpolarization of membrane potential. BKCa channels are ubiquitously expressed in the body. But compared to other potassium channels, they are relatively less expressed in cardiovascular system and are reported to have fewer hemodynamic side effects. Furthermore, LDD175 exhibits effective smooth muscle relaxant activity in the bladder and prostate and has also been shown to act on corpus cavernosum. This study was designed to concurrent evaluate atherosclerosis-induced ED and LUTS/BPH in the same rat model. We induced chronic pelvic ischemia (CPI) by balloon de-endothelialization of the iliac artery with high cholesterol diet. We then measured intracavernosal pressure and intraurethral pressure to assess erectile and urinary function. In addition, we evaluated in vivo integrated therapeutic effects of LDD175 on CPI models. This study provides a preclinical basis for the approach to the integrated evaluation and treatment of ED and LUTS/BPH and suggests the possibility of new drugs for use in both diseases.

***Corresponding author :** Kyu Pil Lee

***Keywords :** Pelvic ischemia, Erectile dysfunction, Lower urinary tract symptoms, Animal model, LDD175

PS-A-044

Anti-obesity effects of Aceriphyllum rossii extract in high-fat diet induced obese mice

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According to a report by the World Health Organization (WHO), many studies have focused on functional food materials exhibiting anti-obesity activity, as the obese population is rapidly increasing worldwide and obesity is known to be the basis for various diseases such as diabetes, hyperlipidemia, hypertension, and arteriosclerotic diseases. This study aimed to utilize the potential for the development and industrialization of excellent materials in agricultural resources in Gangwon Province, South Korea, and was conducted to study the anti-obesity effects of Aceriphyllum rossii extracts in high-fat diet-induced obese mice (C57BL/6J). Mice were divided into four groups: ND (normal fatty diet), HFD (high-fat diet), HFDAR100 (high-fat diet administered with Aceriphyllum rossii extract 100 mg/kg), and HFDAR200 (high-fat diet administered with Aceriphyllum rossii extract 200 mg/kg). The experiment was conducted over a total of 8 weeks. The high-fat diet induction period lasted for 4 weeks, after which Aceriphyllum rossii extract was administered for an additional 4 weeks while continuing the high-fat diet. The final mouse weight gain in the HFDAR100 and HFDAR200 groups was lower than that in the HFD group, and for HFDAR200, both weight gain and dietary efficiency showed similar values to ND. It was found that epididymal adipose tissue weight was significantly reduced in both the Aceriphyllum rossii extract groups compared to the HFD group. Analysis of the fat distribution using bone density measuring equipment also showed a significant decrease compared to HFD in all groups administered with the Aceriphyllum rossii extract. These results indicate that the orally administered Aceriphyllum rossii extract has the effect of reducing body weight and total fat weight. Based on the results of the experiment, which demonstrated the anti-obesity effects of Aceriphyllum rossii extract, it can be concluded that Aceriphyllum rossii extract is an effective material for anti-obesity.

***Corresponding author :** Jae hee Lee

***Keywords :** Aceriphyllum rossii, Anti-obesity, High-fat diet, Materials

PS-A-045

Altered dynamics of bone development in the MEGF8 mouse model cause Carpenter syndrome-like craniosynostosis

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Carpenter syndrome, a rare congenital disorder characterized by the premature fusion of cranial bones and associated with other variable developmental abnormalities in facial features, heart, and limbs, has been linked to mutations in the RAB23 and *MEGF8* genes, known as negative regulators of Hedgehog (Hh) signaling. Recent studies unveiled the molecular basis of Megf8 in Hh signaling, its involvement in controlling Smo ubiquitination and degradation in the ciliary membrane. Elevated Hh signaling due to Megf8 mutation can give rise to several Carpenter syndrome symptoms such as congenital heart disease and preaxial polydactyly. However, the precise mechanism by which *MEGF8* contributes to craniosynostosis in human, a birth defect characterized by the premature fusion of skull bones, remains unclear. Here, we demonstrate that mouse embryos with the removal of Megf8 gene exhibit Carpenter syndrome-like phenotypes and altered craniofacial morphology. The mutant mouse embryos showed enhanced development of chondrocranium and premature fusion of cranial suture. These changes appear to be related to osteogenesis, and we confirmed that Megf8 negatively regulates the osteogenesis using cultured cells. Megf8 knockdown cells exhibited more advanced osteogenesis progression than the control cells. We also observed that the deletion of *Megf8* upregulates the expression of osteogenic markers in bone primordia. Our results suggest that Megf8 plays a significant role in craniofacial bone development by regulating osteogenesis. These findings provide a new perspective on how MEGF8 is involved in developing craniosynostosis in Carpenter syndrome.

***Corresponding author :** Hyuk Wan Ko

***Keywords :** Carpenter syndrome, Craniosynostosis, Megf8, Osteogenesis

PS-A-046

NMUR2 as a therapeutic target in glioblastoma

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Glioblastoma (GBM) is a highly malignant brain tumor with a poor prognosis and the standard treatment for GBM is temozolomide. However, this treatment has significant limitations due to the high rate of recurrence caused by the development of drug resistance in GBM patients. Therefore, discovering novel targets and drugs is needed to improve survival rate for GBM patients. This study aims to investigate the functions of NMUR2 as a novel target for GBM and to identify NMUR2-specific regulatory drugs. We found that NMUR2 is highly expressed in the Glioma CpG island methylator phenotype (G-CIMP) high molecular subtype of GBM. Overexpression of NMUR2 in GBM cells increased cell proliferation and migration, whereas NMUR2 knockdown suppressed these oncogenic properties. RNA sequencing analysis of NMUR2 knockdown cells revealed downregulation of cell cycle-related genes. To discover an NMUR2-specific antagonist, we performed cell-based drug screening with 6,331 repurposing drugs and identified compound X. In vitro and in vivo experiments showed that compound X reduced GBM cell viability and increased apoptosis by binding to NMUR2, which decreased cell cycle progression through its downstream signaling pathway. Additionally, we observed a synergistic effect between compound X and temozolomide in GBM cells. In conclusion, this study suggests that NMUR2 is a promising novel target, and its antagonist, compound X, combined with temozolomide, might offer a promising strategy to improve GBM treatment.

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***Keywords :** Glioblastoma, NMUR2, Drug screening system, Compound X

PS-A-047

Antitumor effect of small chemical containing an Indazole group: Tumor-Associated Macrophages repolarization in breast cancer model

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This study investigates the pharmacokinetic properties and antitumor efficacy of a novel small molecule containing an indazole group. Following oral administration, the compound exhibited higher systemic concentrations and prolonged presence compared to intravenous administration, with no observed toxicity. In a breast cancer model, the indazole-containing compound significantly reduced tumor volume. Flow cytometry (FACS) analysis revealed a repolarization of tumor-associated macrophages from the pro-tumorigenic M2 phenotype to the anti-tumorigenic M1 phenotype, indicating a potent anti-tumorigenic effect. These findings suggest that the small molecule with an indazole group holds significant promise as a new therapeutic agent for cancer treatment. The compound effectively inhibits tumor growth and promotes tumor regression while maintaining a favorable safety profile. The observed pharmacokinetic and pharmacodynamic properties support its potential for clinical application. The higher bioavailability and prolonged presence after oral administration highlight the compound's therapeutic advantage. Moreover, the absence of observed toxicity underscores its potential for safe long-term use. Further research is warranted to explore the full therapeutic potential of this compound in various tumor models. Additional studies should aim to elucidate the mechanisms underlying the observed macrophage repolarization and assess the compound's efficacy in different cancer types. The promising results from this study provide a strong foundation for the development of the indazole-containing small molecule as an effective cancer treatment. In conclusion, this study demonstrates that the small molecule containing an indazole group is a promising candidate for cancer therapy. Its ability to significantly reduce tumor volume, repolarize tumor-associated macrophages, and maintain a non-toxic profile suggests considerable potential for clinical use. The favorable pharmacokinetic and pharmacodynamic profiles warrant further investigation and development. This research lays the groundwork for future studies and potential clinical trials, aiming to establish this indazole-containing compound as a viable and effective option for cancer treatment.

***Corresponding author :** Sang Kyoon Kim

***Keywords :** Small chemical containing an Indazole group, Breast cancer, Antitumor effect, Tumor-associated macrophages, Macrophages repolarization

PS-A-048

Enhanced therapeutic outcome of primed iMSC-derived extracellular vesicles in acute kidney injury

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Induced mesenchymal stem cells (iMSC) are unique cell source for therapeutic purposes due to their homogeneity and the potential for low immune rejection. Extracellular vesicles (EVs) derived from iMSCs have tremendous advantages for tissue regeneration and immune diseases. Herein, we investigated the possibility of augmenting the therapeutic efficacy of EVs against acute kidney injury (AKI) by stimulating iMSCs with a pan-peroxisome proliferator-activated receptor (PPAR) agonist. After iMSCs were cultured for 24 hours in the presence of absence of a PPAR agonist, EVs were extracted. Using cryo-transmission electron microscopy imaging, immunoblot detection of EV markers, tracking analysis of nanoparticles, and localization in AKI kidneys, the fundamental properties of EVs were assessed. The ability of the EVs to inhibit M1-polarized THP-1 inflammation and to support the proliferation and survival of HK-2 cells following cisplatin-induced apoptosis was compared in vitro. Then, cisplatin was used to produce AKI in BALB/c mice. Intravascular injections of iMSC-EVs or pan-PPAR-iMSC-EVs were administered following cisplatin treatment. Serum biochemistry, histology, and immunohistochemistry were used to examine the renoprotective effects of iMSC-EVs or pan-PPAR-iMSC-EVs in suppressing inflammation at 96 hours after cisplatin administration. Both EV forms displayed characteristic EV morphology and expressed EV markers. their location in the renal tissue was verified. HK-2 cell survival and proliferation were greater in pan-PPAR-iMSC-EVs than in iMSC-EVs. The reduction in inflammatory cytokine mRNA expression in M1-polarized THP-1 cells was greater in pan-PPAR-iMSC-EVs than in iMSC-EVs. Compared to iMSC-EVs, pan-PPAR-iMSC-EVs significantly increased renoprotective effects in the mouse model of cisplatin-induced AKI. Pan-PPAR-iMSC-EVs specifically decreased tissue inflammation. This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (2021R1A2C2093867).

***Corresponding author :** Tae Min Kim

***Keywords :** IMSC (induced mesenchymal stem cells), EV (extracellular visicles), AKI (Aucte kidney injury)

PS-B-001

Toxicological assessment of intravenous-infused human adipose-derived mesenchymal stem cells in common marmoset

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Human adipose-derived mesenchymal stem cells (hADMSCs) possess self-renewal and multi-lineage differentiation capabilities. Compared to other MSC sources, hADMSCs are accessible, abundant, and less ethically controversial, making them promising for regenerative medicine. Intravenously injected hADMSCs trapped in mouse lungs due to small size blood vessels, potentially causing pulmonary embolism. To mitigate this, we considered that more adequate animal models are needed for human trial. Common Marmosets (*Callithrix jacchus*) are nonhuman primates phylogenetically closer to humans than mice, sharing similar anatomical characteristics and easy to handle. Marmosets were injected hADMSCs intravenously with 5.0 (high) × 10^8 cells/kg and compared with NOG mice injected intravenously hADMSCs at 1.25 (low), 2.5 (medium), and 5.0 (high) × 10^8 cells/kg. IVIS analysis demonstrated that hADMSCs were predominantly localized in the lungs and liver of common marmoset. Marmosets showed no significant changes in mortality, body weight, clinical signs, coagulation and urinalysis parameters, while medium-dose and high-dose mice showed mortality. However, a marmoset in high-dose group showed focal red spots with histopathological abnormalities. Some hematological and serum biochemical parameters showed significant differences within the normal ranges for marmosets. Through this study, we considered that marmoset is a better model for the safety assessment of intravenous cell therapy compared to mice.

Corresponding author **:** Byeong-Cheol Kang

Keywords **:** Human adipose-derived mesenchymal stem cells (hADMSCs), Pulmonary embolism, Common Marmoset, NOG mice

PS-B-002

Pre-clinical safety assessment of a SARS-CoV2 mRNA Vaccine Candidate in Cynomolgus macaque (Macaca fascicularis)

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SARS-CoV2 mRNA vaccine-induced side effects have been extensively reported in the clinical field. However, the potential toxicity of mRNA vaccines has not been fully identified. We aimed to clarify mRNA vaccine-induced toxicity in cynomolgus macaque. Four~five years-old male and female cynomolgus macaques were used. A SARS-CoV2 S protein coding nucleoside-modified mRNA vaccine candidate, was injected intramuscularly (IM) 4 times with 2-week intervals (800 ug/head). Blood was collected before every injection and 2 days post every injection. Animals were sacrificed at 2 days post final injection. IM injection of the mRNA vaccine did not induce significant clinical signs including body weight change. Of note, blood coagulation time (PT and aPTT) was slightly delayed and circulating platelet level was decreased at 2 days post every injection. Furthermore, a decrease of serum LDL-C level and increase of serum C-reactive protein was observed at 2 days post every injection. However, these hematological and serological changes were fully recovered at 7 days post every injection. At the endpoint, histopathological analysis revealed that the mRNA vaccine induces remarkable inflammation at the injection site (Brachialis muscle). Furthermore, a decrease of lymphocyte cellularity at the follicular marginal zone of the spleen was confirmed. Any pathological changes were not found in other major organs. In this study, we identified that mRNA vaccine can affect on blood coagulation system, inflammation at the injection site, and immune response at the spleen. We hope that our results contribute to clarifying the potential side effects of the mRNA vaccine.

Corresponding author **:** Byeong-Cheol Kang

Keywords **:** SARS-CoV2 mRNA vaccine, Toxicity, Cynomolgus macaque, Coagulation, Inflammation

PS-B-003

Protective effect of a natural volatile odorant, β-Caryophyllene, on lipopolysaccharide-induced inflammation in primary human nasal epithelial cells (HNEpC)

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Allergic rhinitis (AR), a type of inflammatory disease of the nasal mucosa caused by exposure to allergens, is prevalent worldwide and is closely associated with asthma and nasal sinusitis. Previous studies on the pathogenesis of RA have focused on inflammatory cells and responses in nasal mucosal tissue, while nasal epithelial cells, the first line of defense against allergen infiltration. In this study, we have investigated anti-inflammatory effect of several volatil odorants contained in natural essential oils from herbal plants in HNEpC cells, a human nasal epithelial cell line. Preventive effect of Limonene, 3-Carene, β-Caryophyllene against LPS-induced inflammation was examined by anlayzing expression and/or activation of major inflammatory cytokines in HNEpC cell, by RNAseq, RT-PCR, western blot analysis, and ELISA. The cytotoxicities of the odorants were tested by measuring cel viability using CCK-8 assay, and no cytotoxic effect was observed up to a concentration of 1000 μM. Major inflammatory cytokines, IL-1β, IL-6, iNOS, and TNF-α were all significantly increased by pre-treatment of each odorant (Limonene, 3-Carene, and β-Caryophyllene), suggesting anti-inflammatory effect of the odorants. The levels of intracellular ROS were measured to examine if administration of the odorants protect the cells from oxidative stress caused by activation of inflammatory signaling pathway, and the result showed that Limonene, 3-Carene, β-Caryophyllene all prevent accessive accumulation of ROS. It suggests the applicability of the odorant molecules as the functional materials for health supplements or even further as medicines to prevent AR.

Corresponding author **:** Jeong-In Baek

Keywords **:** Allergic rhinitis, Inflammation, Odorant, Nasal epithelial cell

PS-B-004

Restoration of β-amyloid-induced cognitive Impairment by sulforaphane via enhancing neurohormetic stress responses

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The β-Amyloid peptide (Aβ), a major component of senile plaques, plays a significant role in the neuropathology of Alzheimer's disease (AD). A range of in vitro and in vivo data indicates that Aβ-induced neuronal cell death and damage are mediated by oxidative stress. In this study, we aimed to investigate the neuroprotective effect and underlying molecular mechanism of sulforaphane (SUL) on Aβ-induced cognitive impairment in C57BL/6 mice. Neuronal cell death induced by $A\beta_{25\text{-}35}$, involving apoptosis markers such as the activation of c-Jun N-terminal kinase (JNK) and altered expression of Bcl-2 family proteins, was effectively attenuated by intraperitoneal administration of SUL (0.5 and 2 mg/kg, i.p.). The anti-apoptotic activity of SUL appeared to be mediated by the inhibition of oxidative damages to critical cellular macromolecules such as lipids and proteins. SUL up-regulated the expression of antioxidant enzymes, including γ-glutamylcysteine ligase (GCL), NAD(P)H oxidoreductase-1 (NQO-1), manganese superoxide dismutase (MnSOD), copper/zinc superoxide dismutase (CuZnSOD), and heme oxygenase-1 (HO-1) via activation of NF-E2-related factor 2 (Nrf2). In another experiment, treatment of C57BL/6 mice with SUL increased the expression of repressor element 1-silencing transcription factor (REST), which regulates a network of genes mediating stress resistance, and elevated levels of brain-derived neurotrophic factor (BDNF). Taken together, these findings suggest that pharmacologic activation of neurohormetic stress responses by SUL could be a practical preventative and/or protective strategy for the management of AD.

Corresponding author **:** Jung-Hee Jang

Keywords **:** Beta-amyloid, Cognitive impairment, Oxidative stress, NF-E2-related factor 2, Sulforaphane

PS-B-005

Aggravation of learning and memory functions in C57BL/6 mice by chronic unpredictable mild stress

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Stress influences both physical and mental health, leading to a variety of physiological and psychological ailments that can impair learning and memory. In this study, we examined the impact of chronic unpredictable mild stress (CUMS) on learning and memory function. C57BL/6 mice were subjected to CUMS for 4 weeks, and behavioral tests including the open field test (OFT) and fear conditioning test (FCT) were conducted to assess stress levels and memory functions. Compared to the control group, CUMS significantly increased stress levels and resulted in learning and memory impairment. To explore the underlying molecular mechanisms, we analyzed molecules associated with oxidative stress and neuroinflammation. The CUMS group showed elevated oxidative stress, indicated by increased lipid peroxidation and deteriorated antioxidant defense system. Additionally, levels of inflammation-related proteins such as IL-1β, IL-6, and TNF-α were significantly upregulated in CUMS-exposed mice. These findings suggest that CUMS may contribute to cognitive impairment through the induction of oxidative stress and inflammation in C57BL/6 mice.

***Corresponding author :** Jung-Hee Jang

***Keywords :** Chronic unpredictable mild stress, Learning and memory, Oxidative stress, Inflammation

PS-B-006

Pulmonary toxicity study of nanoparticles (zinc oxide, carbon black and mixed nanoparticles)

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This study investigated the pulmonary toxicity of tire wear particles (TWPs) aiming at nano-particles of zinc oxide (ZnO) and carbon black (CB) that are used as additives in tires, which can be released in the air. In the animal pulmonary toxicity study, intratracheal instillation for the respiratory tract toxicity in mice (C57BL/6, 8 weeks) was studied during 2 weeks. Intratracheal instillation to mice with ZnO nano-particles (6 μg), CB nano-particles (162 μg), and ZnO-CB (6+162 μg,168 μg) mixed nano-particles, respectively showed increased total cell counts and polymorphonuclear leukocytes (PMNs) in bronchoalveolar lavage fluid across all exposure conditions. Interestingly, we observed that the concentrations of total protein, tumor necrosis factor-alpha, and interleukin-6 were higher in the exposure of ZnO nano-particles comparing to the exposure of CB nano-particle and ZnO-CB mixed nano-particles. The lowest toxicity was observed in the exposure of CB nano-particles. Based on the toxicity study result of ZnO-CB mixed nano-particles, it may imply on the hindering effects of CB nano-particles that reduced the pulmonary toxicity from ZnO nano-particles by eliminating its direct interface chances. From our post-exposure autopsy at 2 weeks, we observed that the black pigment is widely distributed in the lymph nodes of lung tissue due to the macrophages.

***Corresponding author :** Jaewoong LEE

***Keywords :** Pulmonary Toxicity, Acute Inflammation, Nanoparticles

PS-B-007

BPA exposure impairs synaptic architecture and function by modulating BDNF signaling via RGS4 in the cerebral cortex

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Bisphenol-A (BPA), a widely recognized chemical compound known for its potential to disrupt the endocrine system, is commonly found in a multitude of products across different industries such as plastics, medical devices, and receipts. consequently, most individuals encounter BPA through skin contact, ingestion , or inhalation in their daily lives. Additionally, BPA can cross the blood-brain barrier and is associated with various neurological issues observed in neurodegenerative and neuropsychological conditions. However, the mechanisms underlying BPA-associated neurological dysfunctions remain poorly understood. Here, we report that BPA exposure alters brain functions by dysregulating synapse morphology and function in mice. We found that BPA exposure resulted in reduced size and numbers of dendrites and spines in the cerebral cortex. In addition to our findings on BPA exposure reducing the density of excitatory synapses in the cerebral cortex, we also observed that inhibitory synapses were not affected by exposure to BPA. Additionally, we observed that exposure to BPA impacts synaptic activity and cognitive behavior. Intriguingly, we found that BPA-mediated effects on synaptic architecture and function involved RGS4 and its downstream BDNF/NTRK2 pathway signaling. The results of our research provide a better understanding of the molecular mechanisms involved in the anatomical and physiological neurotoxic effects caused by endocrine disruptor.

***Corresponding author :** Minhan Ka, Sung-Ae Hyun

***Keywords :** Bisphenol-A, Dendritic spine, Synaptic transmission

PS-B-008

Granulomatous hepatitis in two Sprague-Dawley rats

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Microgranuloma naturally develops rats in the liver to as the rat gets older. increases in size, becomes more widely distributed, and, in severe cases, tends to manifest as granulomatous inflammation. Therefore, when determining the cause of a lesion, it is essential to consider the morphological similarity of whether it is a naturally occurring granulomatous lesion or an induced granulomatous lesion. The cause of these local inflammatory changes is unclear, but intestinal substances, such as bacteria and endotoxins, and certain chemicals, such as carbon tetrachloride, are suspected to be involved via the portal bloodstream. Some bacteria, especially those that can cause granulomatous lesions in the liver of laboratory animals, such as murine tuberculosis caused by infection with Mycobacterium species, can cause serious health problems not only in laboratory animals but also in researchers conducting preclinical studies. Two cases of granulomatous hepatitis were found in the livers of male 10-week-old rats, the control animals of a repeated-dose toxicity study. Grossly, 3-4 yellow or white discrete foci were scattered on the surface of the caudate lobes of the livers of the two rats. Microscopically, the multi-focal lesions showed characteristic granulomatous inflammations with histopathological features, including central necrosis, calcification, the infiltrations of mononuclear cells and multinucleated giant cells, and surrounding fibrosis in hepatic lobules. As a result of acid-fast staining to identify the causative bacteria, no acid-fast bacteria were observed in the lesion area. These rare cases of granulomatous inflammation in rat liver should be further elucidated for the etiology of the lesions.

***Corresponding author :** Byeongwoo Ahn

***Keywords :** Rat granulomatous inflammations, Dystrophic calcification, Bridging necrosis

PS-B-009

Acute inhalation toxicity of zinc oxide carbon black nanocomposites as tire particles

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The inhalation toxicity of tire-wear particles (TWPs) as microplastics (MPs) is insufficient because difficult for obtaining test materials for inhalation exposure. Therefore, the purpose of this study is to investigate the potential inhalation toxicity of TWPs using ZnO-carbon black nanocomposites (ZnO-CB NCs), which are the main components of tires. Acute inhalation toxicity of ZnO-CB NCs in male C57BL/6 mice were evaluated using a nose-only exposure chamber (NOEC) system. The mean total patricides number concentration in the NOEC were maintained at 1.3×10^{6}#/CC (44.2 nm) in nano size range and 4.5×10^{3}#/CC (397.1 nm) in micro size range, respectively. The bronchoalveolar lavage fluid (BALF) analysis showed that ZnO-CB NCs exposed groups revealed dose-dependent increases in total cells counts and lymphocytes. In addition, inflammatory cytokines, including tumor necrosis factor-alpha and interleukin-6 were increased in the ZnO-CB NCs exposed groups. In summary, single inhalation of ZnO-CB NCs can caused mild pulmonary toxicity in the lung, so additional investigation on repeated inhalation toxicity is necessary.

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***Keywords :** Acute, Inhalation Toxicity, Mice

PS-B-010

Toxicity assessment and mechanism of lung damage induced by substance X

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Substance X is widely used in industry as a corrosion inhibitor and wood preservative. Substance X is a known human respiratory carcinogen and can cause lung damage. Respiratory diseases such as pulmonary fibrosis, adenocarcinoma, and cell carcinoma frequently occur due to long-term exposure at construction sites. The aim of this study is to investigate the damage and mechanisms caused by substance X. To determine the damage in the lungs, C57BL/6 mice were treated with substance X by airway. Body weight was reduced by substance X in a concentration-dependent manner over a 7-day period, with a half reduction in survival at 25 mg/kg. To determine the effects at the cellular level, we investigated the mechanisms of inflammation and damage following substance X exposure in alveolar type II cells (ATII cells). Cell proliferation was significantly reduced, and apoptosis increased in response to substance X treatment. In addition, pro-inflammatory cytokines TNF-α and IL-6 were upregulated, and the NFκB and MAPK pathways were activated by substance A. Increased ROS was confirmed by an increase in DCF-DA intensity and a significant decrease in GSH levels. Blockade of the activated NFκB and MAPK pathways by treatment with NFκB and MAPK inhibitors, respectively, confirmed a significant recovery of cell viability and reduction of oxidative stress. Our data demonstrate that substance X induces damage in vivo, induces inflammation and damage in ATII cells, and induces cell death through ROS-mediated NFκB and MAPK mechanisms. This study provides information on the mechanisms of airway injury affected by substance X and the potential for therapeutic intervention through inhibition of NFκB and MAPK mechanisms.

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***Keywords :** Pulmonary fibrosis, Apoptosis, NFκB pathway, MAPK pathway, Oxidative stress

PS-B-011

Advanced organoid models for screening natural products in liver fibrosis therapy

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Liver fibrosis research frequently utilizes hepatic stellate cells (HSCs) for drug screening, but traditional two-dimensional (2D) cultures often fail to mimic *in vivo* conditions, affecting the accuracy of drug responses. To overcome these limitations, our study focused on developing and comparing three distinct fibrosis models: Hepatic stellate cell line (LX-2), mouse liver organoids, and direct *in vivo* analyses. We began by testing 80 natural products on TGF-β1-induced activated LX-2 selecting three candidates with significant anti-fibrotic properties, evidenced by reduced expression of pro-fibrotic markers (Col1a1, α -Sma, Mmp2) and increased levels of the anti-fibrotic marker Timp1. We then advanced to differentiating mouse liver organoids into mature hepatocyte organoids, which better represent liver conditions compared to 2D cultures, as confirmed through hepatocyte marker expression (Alb, Hnf4a, Cyp3a11). These organoids allowed for more sophisticated validation of the natural product candidates, focusing on both anti-fibrotic and hepatocyte functionality. Our findings demonstrate that while all models provide valuable insights, the organoids most closely resemble *in vivo* liver conditions. This establishes our mouse liver fibrosis organoid model as a promising tool for deeper investigation into the pathology of liver fibrosis, highlighting natural product A as a potential therapeutic agent.

***Corresponding author :** Kyung-Rok Yu

***Keywords :** Liver Fibrosis, Hepatic Stellate Cell, Liver Organoid, Drug Screening

PS-B-012

Imatinib suppresses oral squamous cell carcinoma by targeting and inhibiting the PI3K/AKT/mTOR signaling pathway

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Background: Oral squamous cell carcinoma (OSCC) is a common and lethal form of oral and maxillofacial cancer, characterized by its aggressive invasion and frequent metastasis to cervical lymph nodes. While imatinib has shown significant anticancer properties and clinical efficacy across various cancer types, its specific effects on OSCC remain underexplored.
Purpose: This study aimed to assess the anticancer potential of imatinib on OSCC cells and elucidate its underlying mechanisms.
Results: Cell viability was measured using the Cell Counting Kit-8 (CCK-8) assay. Morphological analyses were conducted to observe changes in OSCC cell proliferation due to imatinib treatment. Cell migration was assessed through wound-healing assays, and colony formation was evaluated using soft agar assays. Apoptosis induction by imatinib was confirmed via flow cytometry, and the inhibition mechanisms were further examined through Western blot analysis. Our findings indicate that imatinib effectively inhibits OSCC cell proliferation and reduces cell viability in a dose- and time-dependent manner. Additionally, imatinib suppressed OSCC cell migration and colony formation, while promoting apoptosis. This apoptotic effect was associated with increased expression of p53, Bax, and PARP, and decreased expression of Bcl-2.
Conclusions: Furthermore, imatinib inhibited the PI3K/AKT/mTOR signaling pathway, underscoring its potential as a therapeutic agent for oral cancer.

***Corresponding author :** Myoung Ok Kim

***Keywords :** Imatinib, Oral squamous cell carcinoma, PI3K/AKT/mTOR signaling pathway, Proliferation

PS-B-013

Rhein induces apoptosis and ROS in oral cancer cells by inhibiting AKT/mTOR signaling pathway

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Oral cancer continues to be a major cause of mortality worldwide. Rhein, a natural compound derived from the traditional Chinese herbal medicine rhubarb, has shown therapeutic potential in various types of cancer. Nonetheless, its specific impact on oral cancer remains poorly understood. This study sought to explore the potential anticancer properties and mechanisms of Rhein in oral cancer cells. The effects of Rhein on cell growth were evaluated using assays for cell proliferation, soft agar colony formation, migration, and invasion. Apoptosis and cell cycle phases were analyzed using flow cytometry. The underlying mechanisms were further investigated through immunoblotting. In vivo anticancer activity was assessed using oral cancer xenograft models. The findings revealed that Rhein markedly inhibited the growth of oral cancer cells by inducing apoptosis and causing cell cycle arrest in the S phase. Rhein also reduced cell migration and invasion by modulating proteins related to epithelial-mesenchymal transition. Furthermore, Rhein induced the accumulation of reactive oxygen species (ROS) in oral cancer cells, leading to the suppression of the AKT/mTOR signaling pathway. Both in vitro and in vivo studies demonstrated that Rhein exerts its anticancer effects by inducing apoptosis and ROS production through the inhibition of the AKT/mTOR pathway. These results suggest that Rhein could be a promising therapeutic agent for the treatment of oral cancer.

***Corresponding author :** Myoung Ok Kim

***Keywords :** Apoptosis, Autophagy, MTOR, Oral cancer, Rhein

PS-B-014

Imatinib regulates inflammation and apoptosis on a DSS-induced colitis model mice

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Background: Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, is characterized by a multifactorial etiology and dysregulation of immune responses caused by genetic and environmental factors. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly treated for the treatment of IBD patients. However, using NSAIDs long-term has side effects including fatigue, abdominal pain, and diarrhea. Imatinib has been developed for the treatment of immune-related diseases with anti-inflammatory and anti-microbial immunity. While the potential effects of imatinib against IBD remain underexplored.
Purpose: We aimed to investigate the therapeutic effects of imatinib in a dextran sulfate sodium (DSS)-induced IBD mice model.
Results: A DSS was used to establish a colitis model to mimic IBD in mice. Imatinib was simultaneously administered orally to mice with DSS treatment. In the DSS-induced colitis model, treatment with imatinib exhibited protective effects by ameliorating weight loss, recovering colon length, reducing spleen weight, and restoring the DAI score and histological injuries. In addition, imatinib decreased the expression level of proinflammatory cytokines, including IL-1β, IL-6, and TNF-α. Moreover, treatment with imatinib recovered tight-junction integrity and reduced the expression of apoptosis marker proteins.
Conclusions: In conclusion, treatment with imatinib significantly ameliorated the symptoms of DSS-induced colitis model by attenuating the expression of proinflammatory cytokines, injury of tight-junction proteins, and apoptosis in mice. These findings indicate imatinib as a potential therapeutic candidate agent for IBD.

***Corresponding author :** Myoung Ok Kim

***Keywords :** Apoptosis, Imatinib, Inflammatory bowel disease, Large intestine, Tight junction

PS-B-015

Silibinin activates the JNK/c-Jun pathway leading to ROS generation and cell apoptosis in oral squamous cell carcinoma

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Background: Oral cancer is one of the most common malignant tumors worldwide. Silibinin has been shown to have therapeutic effects in several cancer models. However, the mechanism of Silibinin in oral cancer remains unknown.
Purpose: The goal of our research was to investigate the molecular mechanisms that underlie the effects of silibinin on oral cancer both *in vivo* and *in vitro*, along with any prospective anticancer effects.
Results: YD10B and Ca9-22 oral cancer cells were used in cell proliferation and anchorage-independent colony formation experiments to examine the impact of silibinin on the growth of the above cells. Transwell assays were employed to assess the impact of silibinin on the migration and invasion of oral cancer cells. Reactive oxygen species (ROS) accumulation, cell cycle dispersion, and apoptosis were all investigated using flow cytometry. Using immunoblotting, the molecular mechanism behind silibinin's anticancer actions was investigated. Using a Ca9-22 xenograft mouse model, the effects of silibinin were assessed *in vivo*.Silibinin efficiently and dose-dependently inhibited the growth and colony formation of YD10B and Ca9-22 cells. In addition, it caused apoptosis, ROS production, and cell cycle arrest in the G0/G1 phase in these cells. Furthermore, silibinin regulated the production of proteins involved in the epithelial-mesenchymal transition, which prevented YD10B and Ca9-22 cells from migrating and invasion. In oral cancer cells, silibinin activated the JNK/c-Jun pathway and downregulated SOD1 and SOD2, according to Western blotting. Silibinin has no obvious toxicity and significantly decreased the growth of xenograft tumors in nude mice.
Conclusions: Our findings indicate that silibinin may be a promising option for the prevention or treatment of oral cancer.

***Corresponding author :** Myoung Ok Kim

***Keywords :** Silibinin, ROS, JNK, Oral cancer, Xenograft

PS-B-016

Compound A promotes alveolar epithelial cell regeneration via RAGE signaling pathway in emphysema

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Chronic obstructive pulmonary disease (COPD) is characterized by lung injury and a sustained inflammatory response through the DAMP-RAGE signaling pathway. Although alternative approaches are being explored, the specific role of RAGE in alveolar epithelial cells in the pathogenesis of COPD remains unclear. Therefore, in this study, we aimed to induce antagonistic inhibition of RAGE using Compound A (CA) to determine its protective effect against emphysema. We used GEO data to investigate the expression of RAGE ligands and RAGE-binding signaling in COPD patients. We made a PPE-induced emphysema mouse model and CA-treated in AGER-/- mice. The association between RAGE and emphysema development was investigated by H&E staining and Western blot analysis of mouse lung tissue and BALF. Next, we analyzed the damage and regeneration caused by oxidative stress and inflammation in human alveolar epithelial cell line A549 by treatment with cigarette smoke extract (CSE) and CA. The results showed that inhibiting RAGE alleviated emphysema independent of macrophage infiltration by regulating inflammation and MMP2 by inhibiting MAPKs. Furthermore, CA was found to ameliorate CSE-induced oxidative stress, inflammation, and cell cycle arrest in human alveolar epithelial cells and promote proliferation. These findings demonstrate that inhibiting RAGE in alveolar epithelial cells suppresses oxidative stress-induced inflammation and MMP2 and promotes alveolar epithelial cell proliferation, thereby inhibiting lung injury and emphysema. Therefore, blocking DAMP-RAGE interaction through CA may be a promising therapeutic approach to alleviate emphysema.

***Corresponding author :** Se-Ran Yang

***Keywords :** RAGE, Chronic obstructive pulmonary disease, Emphysema, Matrixmetalloproteinase, Alveolar epithelial cell

PS-B-017

Effects of Erigeron annuus extract on a mouse model of atopic dermatitis-like symptoms

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Atopic dermatitis (AD) is a persistent inflammatory skin condition resulting from an intricate interplay among genetic, immunological, and environmental factors. *Erigeron annuus* (EA), an annual winter plant belonging to the family Asteraceae, possesses anti-inflammatory, cytoprotective, and antioxidant activities. In this study, we hypothesized that *Erigeron annuus* extract (EAE) could be an effective agent for ameliorating AD-like symptoms. To confirm this hypothesis in vitro, we used H_2O_2-stimulated human keratinocytes (HaCaT cells) to demonstrate that pre-treatment with EAE protected against oxidative stress. HaCaT cells pretreated with EAE and stimulated with H_2O_2 showed decreased intracellular malondialdehyde content, increased superoxide dismutase activity, and reduced intracellular reactive oxygen species accumulation. To verify the *in vivo* hypothesis based on the intracellular results, an AD disease mouse model was induced with 1-chloro-2,4-dinitrobenzene (DNCB), and EAE was orally administered at a non-toxic concentration according to the toxicity evaluation results. The results showed that AD disease models in BALB/c mice exhibited reduced ear epidermal thickness, scratching behavior, and mast cell infiltration. In conclusion, our results indicate that EAE has the potential to improve AD by upregulating the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) signaling pathway.

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***Keywords :** Erigeron annuus, Atopic dermatitis, Antioxidant, Nrf2/HO-1

PS-B-018

Early diagnosis of chemotherapy-induced peripheral neuropathy through heart rate variability parameters in a mouse model

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Paclitaxel is one of the most commonly used cancer chemotherapy drugs and it is used to treat patients with breast, lung, and ovarian cancer. However, paclitaxel and other chemotherapy drugs cause chemotherapy-induced peripheral neuropathy (CIPN) in many cancer patients, which is a dose-dependent adverse event. Symptoms of neuropathy include pain, numbness, tingling, or cold hypersensitivity in the hands and feet, as well as motor weakening or disorders of the autonomous nerve system. These side effects can lead to discontinuation of cancer treatment and in severe cases can persist after the end of treatment, affecting the patient's quality of life, so early diagnosis of neuropathy is very important. The electrocardiogram (ECG) is a non-invasive test and it can measure heart rate variability (HRV), which is an indicator of the activity of the autonomic nervous system. In our study, both 2mg/kg and 10mg/kg paclitaxel-treated mice showed thermal hyperesthesia and decreased serum epinephrine, norepinephrine and nerve growth factor (NGF) expression levels. Electrocardiographic results showed a dose-dependent decrease in HRV, HF, LF and an increase in LF/HF ratio in a mouse model of peripheral neuropathy. The results of this study confirmed autonomic nervous system imbalance through HRV in chemotherapy-induced peripheral neuropathy in animals and identified a correlation between peripheral neuropathy and HRV. Therefore, we suggest the possibility of early diagnosis through HRV parameters in the pathogenesis of peripheral neuropathy.

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***Corresponding author :** Go-Eun Choi

***Keywords :** Chemotherapy-induced peripheral neuropathy (CIPN), Paclitaxel, Heart rate variability (HRV)

PS-B-019

Maternal exposure to diesel exhaust particles (DEP) impairs fetal brain development and induces autism-like behaviors in mice

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Diesel exhaust particles (DEP) are nanoparticles composed of a mixture of substances, including carbon, organic compounds, metals, and other elements. Recent scientific research has shown that there are connections between exposure to DEP and its effects on brain function, neurodegenerative conditions, and disorders related to development, even though the specific reason for developmental issues in the brain is not fully understood. To investigate the impact of maternal exposure on fetal brain development, we administered 10μg/10μl/day of DEP to pregnant mice through intranasal injection. Our results demonstrate that maternal DEP exposure affects fetal neuronal development, altering brain size at embryonic day 14.5. Additionally, our findings indicated that there were irregularities in both synaptic and spine formation within the cerebral cortex as a result of exposure to DEP. To further explore the effects of DEP on neuronal activity, we treated primary cortical neurons with 0.1-100 μg/ml of DEP, finding that DEP inhibits neuronal activity. Finally, maternal DEP exposure led to hypoactivity and reduced anxiety behaviors in offspring. This research suggests that maternal exposure to DEP can lead to atypical brain development in the fetus, impair neuronal function, and induce behavioral changes, potentially playing a role in the development of neuro-developmental disorders such as autism.

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***Keywords :** Diesel exhaust particles, Neural activity, Neurodevelopmental disorder, Hazardous chemicals

PS-B-020

The role of the gut microbiome in colitis models using germ-free mouse

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The gut microbiome is related to maintaining immune homeostasis and intestinal barrier function. However, the disruption of such homeostasis and intestinal inflammation are encountered in inflammatory bowel disease (IBD). Dextran sodium sulfate (DSS), oxazolone, and trinitrobenzene sulphonic acid (TNBS) are well-known as IBD animal models. However, studies on the microbiome in these models have not yet been well studied. Therefore, we compared SPF mice and GF mice in three models to compare the differences in the degree of lesions developed in each model. DSS causes epithelial cell death, impairing barrier function and causing subsequent inflammation. DSS-treated GF mice showed rectal bleeding as early as 5 days, and the rectal bleeding score was higher than SPF. When comparing body weight change, GF was reduced more than SPF, and comparing survival rates, it was shown that GF was lower than SPF. The histopathological score was more severe in GF than in SPF. For lamina propria cellularity, SPF is more severe than GF, but for architectural damage and epithelial abnormalities, GF is more severe than SPF. In the DSS-induced colitis model, the microbiome has a protective effect. Colitis induced by oxazolone and TNBS, known as hapten reagents results in T-cell-mediated inflammation. Only TNBS-treated SPF mice were observed hemoccult. When comparing the body weight change of oxazolone-treated mice, SPF was reduced more than GF and there was no difference in body weight change of TNBS-treated mice. When comparing the survival rate of oxazolone-treated mice, GF was lower than SPF, and TNBS-treated mice were lower in SPF than in GF. The inflammation occurred both in GF and SPF, but SPF mice showed a more severe inflammatory signature. Our findings reveal that the degree of lesions varies depending on the presence or absence of the microbiome in each colitis model.

***Corresponding author :** Ki Taek Nam

***Keywords :** Germ-free (GF), Microbiome, DSS, Oxazolone, TNBS

PS-B-021

ZL-240317 ameliorate atopic dermatitis(AD) in DNCB-induced AD model using SKH-1 hairless mice

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In the course of developing an atopic dermatitis (AD) model, we replaced the commonly used BALB/c mice with SKH-1 hairless mice due to issues encountered during the BALB/c mouse experiments, such as skin irritation caused by clippers or depilatory cream application. Utilizing SKH-1 hairless mice eliminated the need for hair removal, streamlining the experimental process. This study investigates the anti-atopic efficacy of ZL-240317, a natural product provided by NutraCore, using the SKH-1 hairless mouse model predisposed to dermatitis-like symptoms. Method for inducing AD involved application of 1% DNCB to trigger immune response, followed by 2-days application of 0.5% DNCB for 6-weeks to exacerbate and remain AD symptoms. Mice were treated topically with ZL-240317 for 6-weeks daily. Various parameters, including body weight, transepidermal water loss (TEWL), erythema index, IgE levels, organ weight, visual evaluation, and behavioral assessment and histopathologic assessment were measured to evaluate the effects. Results indicated significant improvements in skin barrier function, reduced pro-inflammatory cytokines, and decreased scratching behavior without adverse systemic effects, suggesting the potential of ZL-240317 as a therapeutic agent for atopic dermatitis. Also, we founded interesting side results. When utilizing SKH-1 hairless mice, severe AD symptoms were induced by applying 0.5% DNCB following initial immune induction with 1% DNCB. However, cessation of DNCB treatment resulted in rapid skin recovery within 3 to 4 days, resembling normal control conditions. Based on these findings, co-administration of test substances and DNCB treatment duration adjustments hold promise for reducing experimental duration. This approach not only contributes to ethical considerations in animal experimentation but also enhances experimental conditions for future research.

***Corresponding author :** Sang Woo Kim

***Keywords :** Atopic dermatitis, Natural product, Hairless mouse

PS-B-022

Novel protein-modified compound C ameliorates bleomycin-induced pulmonary fibrosis in mice

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Idiopathic pulmonary fibrosis (IPF) is a chronic and irreversible lung disease characterized by progressive fibrosis of the lung parenchyma and has a high mortality rate and poor prognosis. IPF is influenced by several factors, including genetic predisposition, environmental exposures, immunological responses, and aging. Additionally, clinical reports suggest that COVID-19 may cause pulmonary fibrosis. Collagen accumulation and epithelial injury in alveoli are major pathological features in pulmonary fibrosis. Recently, it has been reported that a specific compound C is closely involved in the etiology of pulmonary fibrosis and the recovery from alveolar epithelial cell damage. However, the use of this growth factor is hindered by many obstacles, including its hydrophilic nature, substantial molecular weight, and short duration of effectiveness. To address these issues, we used a modified version of this factor conjugated with a novel protein delivery system, developed to enhance the delivery of therapeutic proteins. To investigate the therapeutic effects of this modified growth factor on cell damage and myofibroblast differentiation in pulmonary fibrosis mice, the results were confirmed by treating the modified factor intraperitoneally in a bleomycin (BLM)-induced fibrosis model. The obtained results showed that the modified growth factor significantly inhibited BLM-induced epithelial cell injury and collagen deposition. Treatment with the modified growth factor could protect cells from various forms of damage such as apoptosis and cell cycle arrest. Also, it regulated gene expression related to Fibroblast-to-Myofibroblast Transition (FMT) and collagen that were upregulated by TGF-β1. Taken together, the results of the study showed the significance of this novel protein delivery system through the advanced effect of the modified growth factor on BLM-induced fibrosis in animal models.

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***Keywords :** IPF, Pulmonary Fibrosis, PTD-FGF2, BLM

PS-B-023

Acute inhalation toxicity of Cannabidiol (CBD) in ICR mice using vaporization

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Cannabidiol (CBD) is the second most prevalent active ingredient in cannabis and has been extensively studied for its pharmacological and toxicological properties. Despite the wealth of research, the effects of inhalation exposure to CBD are not well-documented. In this study, we aimed to evaluate the acute inhalation toxicity of CBD using vaporization, a method known for its reliability and reproducibility, which is particularly advantageous for comparative medical research. Oil was employed as a vehicle to enhance the bioavailability of CBD. Thirty 8-week-old male ICR mice were exposed to a single 50 mg dose of CBD via a vaporizer. Necropsies were performed on days 1, 3, and 14 post-exposure. A control group of twelve mice were exposed to the base oil only and necropsied on day 1. Data collected included body weight, organ weights, complete blood count (CBC), and histopathological examination of the liver and lungs. The study provides comprehensive data on the acute inhalation toxicity of CBD in ICR mice. Key findings included variations in body weight, organ weights, CBC parameters, and histopathological changes in the liver and lungs. This research underscores the importance of exploring the inhalation toxicity of CBD to better understand its safety profile when administered via vaporization. The study was conducted in accordance with ethical guidelines and received the necessary institutional approval.

***Corresponding author :** Yeung Bae Jin

***Keywords :** Δ9-tetrahydrocannabinol, Vaping, Acute inhalation toxicity

PS-B-024

Evaluation of acute inhalation toxicity of vaped THC in ICR mice

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Cannabis is one of the most widely abused psychoactive drugs globally. Δ9-Tetrahydrocannabinol (THC), the primary psychoactive cannabinoid, elicits a multitude of effects through the systemically expressed endocannabinoid system. Inhalation is the most common method of cannabis consumption. Furthermore, the prevalence of inhaling aerosolized cannabis, referred to as vaping, has increased significantly. Despite the perception that vaping is a safer method of cannabis consumption, clinical reports have documented adverse effects associated with vaping. The findings of studies on vaping highlight the need for further research into the underlying mechanisms involved. Nevertheless, in preclinical research, cannabinoids were frequently administered via the intraperitoneal or oral routes, which exhibit distinct pharmacodynamics and drug distribution characteristics compared to inhalation. To represent human cannabis consumption behavior, we employed a whole-body inhalation method to expose THC to 8-week-old male ICR mice. The objective of the present study was to investigate the acute toxicological effects of vaped THC on the lungs and liver. The inhalation system consisted of an air pump, vaporizer, and vaping chamber. THC dissolved in ethanol was incorporated into commonly used vaping base oils. Mice were exposed to either 50 or 100 mg of THC and sacrificed at 1, 3 and 14 days post-exposure. Histopathological evaluations of the lungs and liver were performed using hematoxylin and eosin (H&E) staining. Additionally, clinical pathology diagnostic techniques were employed to further assess the toxicological effects on these organs.

***Corresponding author :** Yeung Bae Jin

***Keywords :** Δ9-tetrahydrocannabinol, Vaping, Acute inhalation toxicity

PS-B-025

Beauvericin induces G2/M cell cycle arrest during mouse oocyte meiosis

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Beauvericin(BEA) is a naturally occurring mycotoxin produced by *Fusarium* species. Many papers already showed a contaminated of food such as cereals, fruits, corn, rice, and wheat etc by BEA. Mycotoxin contamination samples were confirmed through Multi-mycotoxin analysis the BEA contamination rate reached 98%. Also, reported maximum BEA levels up to 520 mg/kg in maize from Italy. These BEA has a wide range of toxicological effects, including porcine and juvenile sheep reproductive toxicity. However, the effects of BEA on reproductive toxicity their underlying mechanisms remain unclear. Therefore, based on previously reported papers that BEA induces cell cycle arrest, we hypothesized that mycotoxin of BEA induced to mouse oocyte can damage maturation through PI3K/AKT dependent mechanism. The treated BEA concentration (0, 2.5, 5 and 10 μm) significant concentration-dependent reduced during mouse oocyte *in vitro* maturation. In particular, a germinal vesicle (GV) stage arrest occurred at 10 μm, and the meiotic resumption rate significant decreased. Oocyte meiotic resumption process regulated by various pathways, which act in concert to activate the major regulator maturation promotion factor (MPF), which is composed of cyclin-dependent kinase 1 (CDK1) and its co-activator cyclin B1. The Phosphoinositide 3-kinase/ Protein Kinase B (PI3K/AKT) pathway is known to be involved in Cyclin B1 expression and CDK1 activation, pathway also involved in meiotic resumption. In addition, DNA damage checkpoints are responsible for delaying or preventing the cell cycle progression in response to DNA damage. Therefore, their protein level was confirmed through Western blot. As a result, p-AKT was significantly reduced. DNA damage was confirmed through DNA damage checkpoint protein p-H2A histone family member X(p-H2AX). We found that the rate of γ-H2AX-positive oocytes was significantly reduced in the BEA-treated group compared to the control. Thus, this study highlights that BEA affect cell cycle arrest through DNA damage response to PI3K/AKT pathway in mouse oocytes.

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***Keywords :** Mycotoxin, Beauvericin, Oocyte, Cell cycle, Reproduction

PS-B-026

Toxicity evaluation of doxorubicin and liposomal doxorubicin in mice

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Doxorubicin (Dox), a chemotherapy drug widely used in cancer treatment, is known to cause a variety of side effects. Recently, numerous nano-drugs, such as liposomal doxorubicin (Doxil), have been developed to enhance the efficacy and safety of Dox. In this study, we performed single-dose toxicity assessments in mice to provide fundamental data for supporting the development of anti-cancer nano-drugs. The mice were administered Dox intravenously at 1-30 mg/kg doses, and body weight, food intake, and water intake were measured daily for 14 days. The Dox-treated group showed significant and dose-dependent weight loss beginning at 15 mg/kg. Importantly, the weights of lymphoid organs including the thymus, spleen, and lymph nodes were decreased significantly in a dose-dependent manner. Moreover, significant changes in blood cells such as myeloid and lymphocyte counts and organ function biomarkers were observed. To compare the toxicity of Dox and Doxil, we administered mice intravenously with 5, 10, and 15 mg/kg dose of Doxil. The Doxil-treated group showed body and thymus weight loss, change of blood cell populations and organ function biomarker levels in a dose-dependent manner. However, signs of toxicity induced by Doxil were milder compared to those observed with equivalent doses of Dox. Histological analysis revealed that Doxil caused liver and spleen atrophy and cell infiltration, as well as thymus atrophy and kidney tubular dilation, although these effects were less severe than those induced by Dox at the same dose. Additionally, flowcytometry analysis demonstrated that Doxil had a lower impact on regulatory T cell populations in the lymphoid organs compared to Dox at the equivalent dose. Our study demonstrated the relative safety of Doxil compared to Dox, suggesting that liposomal formulation may mitigate *in vivo* toxicity of the drug. These findings suggest the potential for developing safer and more effective nano-drug treatments for cancer.

***Corresponding author :** Soyoung Lee

***Keywords :** Doxorubicin, Doxil, Single dose toxicity, Liposomal nano-drugs, Anti-cancer

PS-B-027

The effect of Gastrodia Elata Blume extract on hyperlipidemia in high-fat-diet rat model

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Excessive intake of high-fat-diet (HFD) can easily cause cholesterol to deposit in the blood vessels. Persistent high blood lipid levels can increase the risk of cardiovascular disease. *Gastrodia elata* Blume (GEB) is known to have beneficial effects on obesity and blood improvement. In this study, we investigated the improvement effects of GEB extract in hyperlipidemia model induced by HFD in rats. Wistar rats (five-week-old) were divided into 3 groups (n=7-10) : Control (CON) group, high-fat-diet induced (HF) group, and GEB treated (GEB) group. The CON group was fed normal diet and the other two groups were fed a HFD containing 60% kcal from fat for 12 weeks. GEB (4 g/kg BW) was treated orally for the last 4 weeks of experimental period. To investigate the effects of GEB on rats fed a HFD, organ weight, biochemical parameters, and histological analysis were determined. The treatment of GEB reduced body weight gain, visceral fat, and epididymal fat weights. We examined serum triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), alkaline phosphatase (ALP), and alanine aminotransferase (ALT) levels. Levels of serum TC, LDL, ALP, and ALT were significantly reduced in GEB group than in the HF group. Histological analysis in liver showed that the GEB group alleviates of lipid accumulation in hepatocyte compared to the HF group in hematoxylin & eosin staining. Atherogenic index (AI) was calculated using the following formula: (TC-HDL)/HDL. The AI was significantly lowered in GEB group compared to HF group. Furthermore, the thickness of carotid artery wall was reduced in the GEB group compared to the HF group. Although more systematic studies will be needed, these results indicated that GEB extract improves hyperlipidemia by attenuating blood lipid levels.

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***Corresponding author :** Jae-Ho Shin

***Keywords :** Hyperlipidemia, Gastrodia elata Blume, High-fat diet, Anti-obesity

PS-B-028

Gastrodia elata Blume extract ameliorates osteoarthritis in a monosodium iodoacetate-induced rat model

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Osteoarthritis, a degenerative joint disease characterized by the breakdown of joint cartilage and bone, often results in pain and reduced mobility. This study investigated the therapeutic effects of *Gastrodia elata* Blume (GEB) on arthritis induced by monosodium iodoacetate (MIA) in rats. Five-week-old male Sprague-Dawley rats were randomly divided into the following three groups: i) Control (CON) group, ii) Osteoarthritis (OA) group, and iii) GEB-treated (GEB) group. The CON and OA groups were orally administered distilled water, while the GEB group received GEB extract (7.5 g/kg BW). All treatments were administered for a total of five weeks. OA was induced only in the OA and GEB groups by a single intra-articular injection of MIA into the left knee joint on the 21st day of administration. Histological analysis using Hematoxylin & Eosin (H&E) staining revealed that the OA group exhibited damages such as roughening of the cartilage surface, progressive thinning and loss of cartilage, fibrotic changes in damaged areas, and the formation of fissures within the cartilage, while these damages were less observed in the GEB group. Using Safranin O and Alcian Blue staining to identify proteoglycans, we observed a significant reduction in proteoglycans in the cartilage matrix of the OA group, while proteoglycans were preserved in the GEB group. In the cartilage of knee joints, the mRNA expression of matrix metalloproteinase (MMP)-9, -13, and tissue inhibitor of metalloproteinases (TIMP)-1 increased in the OA group, but decreased in the GEB group. Additionally, the mRNA expression of IL-6, a pro-inflammatory cytokine, also increased in the OA group and decreased in the GEB group, a trend that was also observed in the results of IL-6 immunohistochemical staining. These results suggest that GEB extract exhibits anti-inflammatory and anti-osteoarthritic properties in an MIA-induced model of OA. (This project was supported by the Rural Development Administration business (RS-2022-RD009980.)

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***Keywords :** Gastrodia elata Blume, Osteoarthritis, MIA, Anti-inflammation, Anti-osteoarthritic

PS-B-029

Anti-inflammatory and anti-allergic effects of Gastrodia elata Blume extract in ovalbumin-induced asthma rat model

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Asthma is a chronic inflammatory disease in which bronchial inflammation causes narrowing of the bronchi when exposed to allergens, wheezing, and difficulty breathing. In this study, we investigated the anti-allergic effects of the *Gastrodia elata* Blume (GEB) extract in asthma. Animals were randomly divided into 3 groups with 8 rats per group: i) Control (CON) group, ii) Ovalbumin-induced asthma (OVA) group, and iii) GEB-treated (GEB) group. On days 1, 2, 3, and 11, the OVA and GEB groups were sensitized by dissolving 200 μg OVA into 1 ml saline containing 10 mg alum as an adjuvant, and CON group was received 10 mg alum without OVA into saline. On days 20, 21, and 22, 100 μL of 1% ovalbumin in saline was intranasally inoculated in the OVA and GEB groups, while the CON group received the same amount of saline intranasally. GEB extract (7 g/kg BW) was administered orally once daily from days 11 to 23. At 24 h after the last instillation, all rats were sacrificed. The serum total IgE level was decreased in the GEB group compared to the OVA group. Additionally, the levels of IL-4, IL-5, and IL-13 in the lung were significantly decreased in the GEB group compared to the OVA group. Histological analysis of lung tissue using hematoxylin & eosin and periodic acid Schiff staining revealed that the tracheal and alveolar walls of the OVA group were thickened, and there was increased infiltration of inflammatory cells in the bronchi, perivascular and alveolar spaces. Lung damage caused by ovalbumin was ameliorated by GEB treatment. Immunohistochemical analysis showed that the expression levels of IL-4, IL-5, and CD206 were reduced in the GEB group compared to the OVA group. In conclusion, GEB extract has anti-allergic effects and ameliorates asthma in rats. (This project was supported by the Rural Development Administration business (RS-2022-RD009980.)

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***Keywords :** Gastrodia elata Blume, Asthma, Anti-inflammation, Anti-allergic, Rat

PS-B-030

Potential role of macrophage in COVID-19 mRNA vaccine-induced heart injury

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The mRNA vaccine is an advanced vaccine introduced to end the pandemic caused by COVID-19, which has resulted in numerous confirmed cases and deaths. Following the extensive vaccination program with the mRNA vaccine, a range of target populations for vaccination included the elderly, children/adolescents, pregnant women, breastfeeding women, and immunocompromised individuals. Among these groups, despite the potential for immunocompromised patients may become more severely ill when infected with COVID-19 compared to healthy individuals, it has been reported that mRNA vaccination does not induce a normal immune response. To analyze the immune response induced by mRNA vaccination under immunodeficient conditions, we adopted a nude mouse model. Both WT and nude mice were administered CUK3/LNP128. a novel SARS-CoV-2 mRNA vaccine recently developed, twice at two-week intervals. Following mRNA vaccination, the expression of T cells and the subsequent immune responses were not observed in nude mice, which is consistent with their characteristic lack of a thymus. However, when measuring the levels related to anaphylaxis (IgE) and myocardial injury (cTn-I), which are known adverse effects of mRNA vaccines, we found that while there was little change in IgE levels in nude mice, troponin-I levels increased in both WT and nude mice. Additionally, the results of RT-qPCR and IHC staining showed an increase in pan-macrophages, which coincided with an elevation in inflammatory M1 macrophages. The increase of M1 macrophages is considered to be associated with myocardial damage in nude mice, and it is known that pro-inflammatory cytokines released by M1 macrophages play a significant role in heart damage. We aim to investigate the influence of macrophages on heart injury in the immune response induced by mRNA vaccination.

***Corresponding author :** Jun-Won Yun

***Keywords :** Immunodeficiency model, MRNA vaccine, Nude mouse, Myocardial damage, Macrophage

PS-B-031

Assessment of SARS-CoV-2 mRNA vaccine-induced toxicity in Type 2 diabetic mice

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The global spread of SARS-CoV-2 has necessitated the swift development of vaccines. Due to the capability of mRNA vaccines to be developed rapidly, they are widely used as a preventive tool against SARS-CoV-2 among other platforms. This study aims to evaluate the effects and toxicological profiles associated with CUK3/LNP128, that is a new SARS-CoV-2 mRNA vaccine introduced in recent studies. The mRNA vaccine was delivered intramuscularly two times, with intervals of two weeks, to wild-type (WT) and db/db mice. After vaccination, compared to WT mice, db/db mice showed suppressed T cell responses, increased IgE levels, and a prolonged decrease in weight loss recovery that persisted for over 14 days. Additionally, there were significant changes in serum biochemistry, increased liver weight, and observations of increased cytoplasmic vacuolation db/db mice via H&E staining. These results indicate that hepatotoxicity caused by the mRNA vaccine is more severe in db/db mice. According to a biodistribution analysis utilizing luciferase signals from mRNA encoding firefly luciferase and RT-PCR, db/db mice exhibited a stronger and longer-lasting signal at the injection site and in the liver compared to WT mice. To investigate the reasons for increased hepatotoxicity in db/db mice following mRNA vaccination, we conducted RNA sequencing and compared the results with those of WT mice. The analysis indicated an increase in complement activation and inflammation, as well as a decrease in cell proliferation. Through gene network analysis, we identified genes related to cell cycle regulation and proliferation. To further study the connection between these genes and the hepatotoxicity observed in db/db mice after mRNA vaccination, we plan to conduct additional experiments using siRNA.

***Corresponding author :** Jun-Won Yun

***Keywords :** MRNA vaccine, Type 2 diabetes, Side effect, Liver injury, Anaphylaxis

PS-B-032

Effects of nanoparticles on innate immunity: study in young, old, and subcutaneous tumor mouse models

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Nanoparticles (NPs), such as reduced graphene oxide (rGO) and zinc oxide (ZnO), exhibit promising potential across a wide spectrum of applications, including drug delivery systems (DDS) and cancer therapy. Despite these prospects, their impact on the immune system, particularly on innate immune cells, remains a subject of ongoing investigation and scrutiny. In this comprehensive study, we administered NPs—specifically rGO, carbon black (CB), and ZnO—via various administration routes in BALB/c mice. Our observations revealed diverse patterns of immunotoxicity among different mouse models, including those representing young, old, and subcutaneous tumor conditions. Notably, NPs have been shown to diminish the tumour-killing activity of splenic natural killer (sNK) cells, which may switch to cytokine secretion and inhibitory receptor signalling mechanisms. On the other hand, NPs were observed to enhance the phagocytic capabilities of peritoneal macrophages and activate peritoneal mast cells, indicating an augmented phagocytic response. These dual effects underscore the complexity of NP interactions within the immune system and highlight the need for a nuanced understanding of their immunological impacts. In conclusion, ensuring the safety and efficacy of NP-based strategies necessitates a thorough comprehension of the underlying mechanisms governing their interactions with the innate immune system. This understanding is crucial for optimizing NP applications in biomedical contexts and for mitigating potential adverse effects that may arise from their immunomodulatory properties. Continued research efforts in this area will contribute to advancing NP technology towards safer and more effective therapeutic interventions.

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***Keywords :** Nanoparticle, NK cell, Macrophage, Immunotoxicity, DDS

PS-B-033

RNA sequencing data of mouse 4-cell embryo treated with Nanoplastics

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Nanoplastics, as environmental pollutants, are increasing attention for their potential risks to ecosystems and human health. To understand the effect of NPs in preimplantation embryos, we have treated mouse 1 cell zygotes with NPs and found that NPs exposure caused 2 or 4 cell embryonic arrest and delayed blastocyst formation. To further investigate the mechanism of NPs in mouse preimplantation embryos, fertilized zygotes have been treated with 0, 100 and 1000 μg/mL of NPs and then performed RNA-seq analysis with 4-cell embryos. Differential gene expression analysis and pathway analaysis were performed to interpret the data. Transcriptomic results indicate alterations in the expression of autophagy related genes were up-regulated in 100 μg/mL NPs exposure groups, while in the 1000 μg/mL NPs treated groups, genes associated with blastocyst development and apoptotic signaling pathways were increased. This study suggests that NPs affect early mouse embryo development. NPs exposure induces specific gene expression changes, potentially impacting the embryonic development process. These findings contribute to the understanding of the biological effects of NPs on mammalian embryo development and provide valuable insights into environmental toxicology.

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Keywords : Nanoplastics, Mouse embryo development, Embryo RNA sequencing

PS-B-034

Effects of nanoplastics exposure on oocyte maturation in mouse and cynomolgus monkey

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Toxic environmental substances such as fine dust, microplastics (MPs) and nanoplastics (NPs), have been implicated as causes of infertility and are a serious environmental toxicity problem. Humans are exposed to NPs through ingestion of food and/or inhalation when breathing. In our previous studies, we demonstrated that mouse zygote exposed to NPs exhibited decreased embryo developmental rates, blastocyst formation and implantation rates due to generation of reactive oxygen species (ROS). The maturation of oocytes, including the cytoplasm, nucleus, and mitochondria, is crucial for potential embryonic development because it ensures correct cell division and gene expression during the post-fertilization embryonic development process. However, the most prominent effects of NPs exposure on the maturation of mammalian oocytes has not yet been elucidated. In this study, we investigated the cytotoxic effects of PMMA-NPs exposure on oocyte maturation in both mouse and cynomolgus monkey. As a result, GFP-NPs permeated into the cytoplasm of mouse and monkey oocytes and led to impairment of maturation of oocytes. Additionally, we observed tubulin formation and DNA alignment in NPs-treated oocytes and confirmed that NPs exposure leads to ROS generation, mitochondrial dysfunction, and DNA damage in both mouse and monkey oocytes. These findings suggest that NPs pollution could have harmful effects on female reproductive health across different mammalian species. Moreover, this study holds significance in confirming the impact of NPs exposure not only mice but also on oocyte maturation in primates, which are more similar to humans. This provides valuable insights into potential interspecies differences and underscores the need for further research and regulatory measures to mitigate environmental contamination.

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Keywords : Nanoplastics, Oocyte maturation, Cynomolgus monkey

PS-B-035

Exposure to PMMA nanoplastics through the mouse respiratory system causes lung abnormalities

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Plastic, a ubiquitous material in daily life and industry, is extensively released into the environment. Unlike complete biodegradation, plastic debris fragments into smaller pieces, accumulating as nanoplastics(NPs) (less than 1 μm) in the environment. Human exposure to these NPs can occur through inhalation, ingestion via water and food, and these particles are known to induce cytotoxicity through physical and chemical mechanisms. Polymethyl methacrylate (PMMA), a plastic commonly used in implants and artificial bones, has been identified in human lungs and linked to pulmonary embolism according to prior research. However, the mechanism of the effects of PMMA-NPs detected in the lungs on the lungs is still unclear. In this study, we investigated the effects of inhaled PMMA-NPs on mouse lungs. Mice were exposed to 20 or 100 μg of PMMA-NPs for 28 days via intratracheal intubation and subsequent outcomes were assessed. We observed a reduction in body weight and an accumulation of PMMA-NPs in the lungs of exposed mice. Bronchoalveolar lavage fluid (BALF) analysis revealed an increase in cell count, while serum and BALF levels of inflammatory cytokines were also elevated. Histopathological examination using hematoxylin and eosin staining revealed lung tissue abnormalities, and protein and RNA expression alterations were detected in lung tissues. Collectively, these findings demonstrate that respiratory exposure to PMMA-NPs induces a range of adverse effects in the lungs, including inflammation, tissue damage, and protein expression dysregulation.

Corresponding author : Ji-Su Kim

Keywords : Nanoplastics, PMMA, Lung toxicity, Inflammation, Intratracheal intubation

PS-B-036

Loss of Ninjurin1 alleviates acetaminophen-induced liver injury via enhancing AMPKα-NRF2 pathway

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Acetaminophen (APAP), a widely used pain and fever reliever, is a major contributor to drug-induced liver injury, as its toxic metabolites such as NAPQI induce oxidative stress and hepatic necrosis. While N-acetylcysteine serves as the primary treatment for APAP-induced liver injury (AILI), its efficacy is confined to a narrow window of 8-24 h post-APAP overdose. Beyond this window, liver transplantation emerges as the final recourse, prompting ongoing research to pinpoint novel therapeutic targets aimed at enhancing AILI treatment outcomes. Nerve injury-induced protein 1 (Ninjurin1; Ninj1), initially recognized as an adhesion molecule, has been implicated in liver damage stemming from factors like TNFα and ischemia-reperfusion. Nonetheless, its role in oxidative stress-related liver diseases, including AILI, remains unexplored. In this study, we observed up-regulation of Ninj1 expression in the livers of both human DILI patients and the AILI mouse model. Through the utilization of Ninj1 null mice, hepatocyte-specific Ninj1 KO mice, and myeloid-specific Ninj1 KO mice, we unveiled that the loss of Ninj1 in hepatocytes, rather than myeloid cells, exerts alleviative effects on AILI irrespective of sex dependency. Further *in vitro* experiments demonstrated that Ninj1 deficiency shields hepatocytes from APAP-induced oxidative stress, mitochondrial dysfunctions, and cell death by bolstering NRF2 stability via activation of AMPKα. In summary, our findings imply that Ninj1 likely plays a role in AILI, and its deficiency confers protection against APAP-induced hepatotoxicity through the AMPKα-NRF2 pathway.

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Keywords : Nerve injury-induced protein 1 (Ninj1), Acetaminophen, Hepatocytes, NRF2, AMPKα

PS-B-037

Acute inhalation toxicity test of Dimethyl 1,4-cyclohexanedicarboxylate in SD rats

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To evaluation the acute inhalation toxicity of Dimethyl 1,4-cyclohexanedicarboxylate, SD (Sprague-Dawley) rats (3 males/group and 3 females/group) were exposed to mist aerosols at concentrations of 1 mg/L, 5 mg/L for 4 hours. During the exposure period, the chamber environment and the concentration of the test substance were measured, and the particle size distribution of the aerosol was determined. After exposure, body weight changes and clinical signs were observed for 14 days, followed by necropsy for gross pathological examination. The target concentrations of Dimethyl 1,4-cyclohexanedicarboxylate in the chambers were 1 mg/L and 5 mg/L, with average concentrations of 0.95±0.02 mg/L and 4.78±0.10 mg/L, respectively. The MMAD (Mass Median Aerodynamic Diameter) of the aerosols at concentrations of 1 mg/L and 5 mg/L were 3.391 μm and 2.605 μm, respectively, with GSDs (Geometric Standard Deviations) of 2.1 and 1.8. According to the OECD Guideline for the Testing of Chemicals Section 4 Health Effects Test No. 436 Acute Inhalation Toxicity - Acute Toxic Class Method - Annex 3d, no abnormal signs were observed in any of the test animals exposed to either concentration. Based on these results, the LC50 value of Dimethyl 1,4-cyclohexanedicarboxylate is considered to be greater than 4.78 mg/L. These findings suggest that Dimethyl 1,4-cyclohexanedicarboxylate has low acute inhalation toxicity.

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***Keywords :** Dimethyl 1, 4-cyclohexanedicarboxylate, Acute inhalation, Toxicity, TG 436

PS-B-038

Loranthus tanakae Franch. and Sav. attenuates respiratory inflammation caused by asian sand dust

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Asian sand dust (ASD), generally produced in East Asia, including China, Japan, and Korea, directly leads to the development of pulmonary disease and exacerbates underlying pulmonary diseases. Additionally, it can cause conjunctivitis, rhinitis, and asthma. *Loranthus tanakae* Franch. and Sav. is a traditional herbal medicine applied to improve various inflammatory conditions. Here, we evaluated the curative properties of *L. tanakae* ethanol extract (LTE) against pulmonary inflammation caused by ASD. Additionally, to investigate the mechanism of action of LTE, we performed network pharmacological analysis. ASD was administrated on day 1, 3, and 5 by intranasal instillation, and LTE was orally administered for 6 days. Administration of LTE significantly decreased inflammatory cytokines and the number of inflammatory cells in bronchoalveolar lavage fluid, which was accompanied by a decrease in inflammatory cell accumulation in pulmonary tissue. Administration of LTE decreased the expression of cyclooxygenase (COX)-2 and matrix metalloproteinase (MMP)-9 in mice exposed to ASD with the decline in p65 phosphorylation. Additionally, administration of LTE significantly elevated heme oxygenase (HO)-1 expression in the pulmonary tissue of mice exposed to ASD. These results were consistent with the data of network pharmacological analysis. This experiment showed that LTE attenuated pulmonary inflammation caused by ASD via inhibition of nuclear factor-kappa (NF)-κB and elevation of HO-1. Therefore, LTE may have potential as a therapeutic agent to treat pulmonary inflammation caused by ASD.

***Corresponding author :** In-Sik Shin

***Keywords :** Loranthus tanakae Franch. and Sav., Asian sand dust, Airway inflammation, Nuclear factor-kappa B, Heme Oxygenase-1

PS-B-039

NLRC4 regulates Th2 differentiation in allergic asthma induced by house dust mite

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Allergic asthma, characterized by chronic airway inflammation involving bronchospasm and shortness of breath due to allergic reaction, is associated with T helper (Th) 2 cell responses, which are regulated by GATA-binding protein 3 (GATA3), the key transcription factor for Th2 cell differentiation and function. The NLR family CARD domain-containing 4 (NLRC4) is involved in the formation of NLRC4 inflammasome complex, which activates caspase-1 and facilitates the release of mature interleukin (IL)-1β and IL-18. While NLRC4 has been implicated in response to bacterial pathogens, its role in regulating Th cell differentiation in asthma remains poorly understood. In this study, we used NLRC4 knock-out (KO) and adeno-associated virus (AAV)-mediated NLRC4 overexpression mice to investigate the involvement of NLRC4 in allergic airway inflammation induced by house dust mite (HDM). In NLRC4 KO asthmatic mice, reduced airway hyperresponsiveness (AHR), inflammatory cell counts, inflammatory cytokine levels, immunoglobulin (Ig)E level, and mucus secretion were observed compared with wild-type (WT) asthmatic mice. These changes were accompanied with decreased expression of caspase-1 and IL-1β, as well as a decline in the population of activated T cells and Th2 cells expressing GATA3. Moreover, naïve $CD4^+$ T cells isolated from NLRC4 KO mice under Th2 polarization conditions displayed diminished Th2 activation compared to those from WT mice. Conversely, NLRC4 overexpression mice exhibited exacerbated allergic responses associated with asthma and increased Th2 cell subsets compared to the control mice. Overall, our findings highlight the role of NLRC4 as a transcription factor in regulating Th2 differentiation.

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***Keywords :** NLRC4, Allergic asthma, House dust mite, Th2 differentiation, GATA3

PS-B-040

The effects of Pycnogenol, a pine bark extract on pulmonary inflammation by Asian sand dust in mice

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Asian sand dust (ASD), also called China dust or yellow dust, mainly occurs in East Asia during spring and autumn. Because ASD enters the body mainly through the respiratory system, it can cause respiratory dis orders or worsen underlying diseases. Because of this, it has become an important health concern that threatens the well-being of humans and animals. Pycnogenol (PYC), a standardised extract of French maritime pine bark (Pinus pinaster Aiton), contains several active components, including proanthocyanins. PYC, which is used worldwide as an herbal remedy and as a nutritional and dietary supplement for the management of various disorders including inflammatory and circulatory diseases, has antioxidant, anti-inflammatory, anticancer, and antimicrobial effects. In this study, we investigated the effects of 15 and 30 mg/kg of Pycnogenol (PYC15 and 30 groups), a pine bark extract, on ASD-induced pulmonary inflammation in mice. We evaluated the inflammatory cell counts, inflammatory cytokines, and matrix-metalloproteinase (MMP)-9 expression in animal models. PYC administration significantly decreased inflammatory cell infiltration into lung tissue; this was accompanied by a reduction in the levels of pro-inflammatory mediators including interleukin (IL)-1β ($P < 0.01$), IL-6 ($P < 0.01$) and tumor necrosis factor-α ($P < 0.01$) in bronchoalveolar lavage fluids of ASD-exposed mice (ASD group). Histological analysis revealed that PYC suppressed ASD-induced pulmonary inflammation. Moreover, PYC suppressed the levels of matrix-metalloproteinase (MMP)-9 in the lung tissue of ASD-exposed mice, indi cating that PYC reduced ASD-induced pulmonary inflammation by suppressing MMP-9. Together, these results indicate that PYC as the potential to treat ASD-driven pulmonary inflammation.

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***Keywords :** Airway inflammation, Fine dust, MMP-9, Pinus pinaster Aiton

PS-B-041

TXNIP regulates pulmonary inflammation induced by Asian sand dust

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Asian sand dust (ASD) is a dust storm occurs in spring that blows from the deserts of China and Mongolia to Korea and Japan and contains not only soil particles but also various biochemical components. ASD exposure could induce respiratory disorders and even exacerbate the underlying respiratory diseases. However, underlying mechanism of ASD-induced pulmonary inflammation is still obscure. In this study, we investigate the pulmonary toxicity induced by ASD exposure and further elucidate the underlying mechanism using thioredoxin-interacting protein (TXNIP) knockout (KO) mice and adeno-associated virus (AAV)-mediated TXNIP overexpression transgenic mice. To induce pulmonary inflammation, ASD were intranasally administered into mice on days 1, 3, and 5. As a result, ASD exposure induced pulmonary inflammation as evidenced by increased inflammatory cell counts and cytokines in bronchoalveolar lavage fluid with elevated expression of TXNIP/ NOD-like receptor pyrin domain containing 3 (NLRP3) inflammasome. In addition, ASD-exposed TXNIP KO mice showed ameliorated airway inflammatory responses with downregulation of NLRP3 inflammasome compared to ASD-exposed WT mice. On the other hand, AAV-mediated TXNIP overexpression mice exhibited the aggravated ASD-induced pulmonary inflammation with increased expression of NLRP3 inflammasome compared to AAV-GFP mice. Together, our results indicate that TXNIP plays a critical role in ASD-induced pulmonary inflammation. In the present study, we investigated the effects of ASD on pulmonary inflammation and identify the underlying mechanism focusing on TXNIP signaling pathway.

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***Keywords :** Asian sand dust, Pulmonary inflammation, TXNIP, NLRP3 inflammasome

PS-B-042

Large-scale profiling of coding and long noncoding transcriptomes in the lungs of mice acutely exposed to vaporized CBD or THC

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Cannabis vaping can cause respiratory risks, including lipoid pneumonia and e-cigarette or vaping use-associated lung injury (EVALI), characterized by lipid accumulation and lung inflammation. The precise cellular and molecular mechanisms underlying lung damage from vaping of cannabis, mainly composed of cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC), are not yet known. This study aimed to identify the genes differentially expressed in the lungs by cannabis vaping and their biological functions. After acute exposure of ICR mice to vaporized CBD or THC (Control, n=5; CBD, n=5; THC, n=5), we performed large-scale transcriptome profiling in the lungs using total RNA sequencing technology and analyzed gene ontology (GO) enrichment of genes. Of 424 mRNAs differentially expressed among control, CBD, and THC groups, 22 and 58 were upregulated in CBD and THC groups, respectively, compared with the control group, while 45 and 63 were downregulated in CBD and THC groups, respectively. When comparing between CBD and THC groups, 96 mRNAs were upregulated but 215 were downregulated in THC group. Based on the results of GO enrichment analysis, mRNAs upregulated in the CBD group compared with the THC group were mainly associated with cell adhesion and positive regulation of cell migration. On the contrary, mRNAs upregulated in the THC group compared with the CBD group were related to positive regulation of tumor necrosis factor production and inflammatory response. On the other hand, of 1,540 lncRNAs differentially expressed among control, CBD, and THC groups, 40 and 107 were upregulated in CBD and THC groups, respectively, compared with the control group, while 37 and 228 were downregulated in CBD and THC groups, respectively. These results give novel insight into genes up-/downregulated in the lungs acutely exposed to vaporized CBD or THC and their correlated mechanisms.

***Corresponding author :** Mi Ran Choi, Sang-Rae Lee

***Keywords :** Cannabidiol, Delta-9-tetrahydrocannabinol, Vaping, Transcriptome, Lung

PS-B-043

Acute inhalation toxicity of dipropylene glycol dimethyl ether: a study in Sprague-Dawley rats

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Dipropylene glycol dimethyl ether (CAS No. 111109-77-4) is a colorless liquid used in paint additives, cleaning agents, sealants, and as a viscosity modifier in various industries. Additionally, it is used as a solvent (part of product formulation or mixture) in consumer applications. However, workers and consumers are potentially exposed to this substance through inhalation during use. Data on inhalation toxicity remains insufficient for a comprehensive hazard assessment. Therefore, we conducted an acute inhalation toxicity test using a nose-only inhalation chamber system and a mist generator with filtered, clean, and dry air. Seven-week-old specific pathogen-free Sprague-Dawley rats (3 males and 3 females) were exposed to the test substance for 4 hours at a concentration of 5.19 ± 0.23 mg/L in the chamber. The mass median aerodynamic diameter was 2.935 μm with a geometric standard deviation of 1.5. Clinical signs, including mortality, general appearance, and abnormal behaviors, were observed. Additionally, mean body weight changes and gross necropsy results were recorded. Weakness was observed in all animals immediately after exposure, but all animals had recovered by the next day. There were no abnormal changes in the mean body weight in either sex, and no gross necropsy findings were observed during necropsy. Based on these results, we suggested that dipropylene glycol dimethyl ether is unclassified according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

***Corresponding author :** Yong Soon kim

***Keywords :** Dipropylene glycol dimethyl ether, Acute inhalation toxicity, Sprague-Dawley rat, Aerosol, GHS

PS-B-044

Effects of AMT-XX05 on pathological mechanisms of Alzheimer's disease in murine neuroblastoma Neuro2a cells

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Alzheimer's disease (AD) is a neurodegenerative disorder that heavily impacts daily life, characterized by symptoms like memory loss, impaired judgment, and language difficulties. Although recent treatments for AD have predominantly focused on mitigating symptoms by regulating neurotransmitters, the intricate complexity of AD necessitates the exploration of multi-target approaches in drug development. This study aimed to investigate whether the novel derivative of 2-hydroxy-4-(trifluoromethyl) benzoic acid, AMT-XX05, exhibits multi-targeting effects on Neuro2a cells. Following a 24-hour exposure to AMT-XX05, we assessed cell viability, acetylcholine (ACh) production, acetylcholinesterase (AChE) activity, and the expression of genes associated with AD pathology in Neuro2a cells. Besides, we measured nitric oxide (NO) production in murine microglial BV2 cells. Our results revealed a significant increase in ACh concentration and notable inhibition of AChE activity in Neuro2a cells treated with AMT-XX05. Moreover, AMT-XX05 not only mitigated the production of NO induced by LPS but also led to the down-regulation of key genes such as *App*, *Tau*, *Psen1*, and *Psen2*. In conclusion, AMT-XX05 demonstrates promising multi-target effects on the complex mechanisms involved in AD pathology, suggesting its potential as a novel therapeutic agent for AD.

***Corresponding author :** Mi Ran Choi, Sang-Rae Lee

***Keywords :** Alzheimer's disease, Acetylcholine, AMT-XX05, Multi-targeting effects

PS-B-045

Effects of a salicylic acid derivative, AMT-XX06, on changes of Alzheimer's disease-related factors in murine neuroblastoma Neuro2a cells

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Alzheimer's disease (AD) is a neurodegenerative disease that has a serious impact on daily life, showing various symptoms such as memory loss, language impairment, and decreased judgment. Recently, AD treatments have focused on alleviating symptoms through neurotransmitter regulation. However, considering that AD is caused by multi-factorial mechanisms, multi-target strategies must be proposed to develop new drugs for AD. In this study, we aimed to investigate whether the novel salicylic acid derivative, AMT-XX06, exhibits multi-targeting effects on Neuro2a cells. After exposing Neuro2a cells to AMT-XX06 for 24 h, cell viability, acetylcholine (ACh) production, acetylcholinesterase (AChE) activity, and expression levels of genes involved in AD pathology were analyzed. In addition, nitric oxide (NO) production was measured in murine microglial BV2 cells. The concentration of ACh was significantly increased but the activity of AChE was significantly inhibited in Neuro2a cells exposed to AMT-XX06. Furthermore, AMT-XX06 not only alleviated the production of NO induced by LPS but also led to down-regulation of genes such as *App*, *Tau*, *Psen1*, and *Psen2*. In conclusion, AMT-XX06 exhibits multi-targeting effects on multi-factorial mechanisms involved in AD pathology, suggesting its potential as a new therapeutic drug for AD.

***Corresponding author :** Mi Ran Choi, Sang-Rae Lee

***Keywords :** Alzheimer's disease, Acetylcholine

PS-B-046

Evaluation of blood-brain barrier permeability of liposomal AMT-XX05 in C57BL/6 mice

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The blood-brain barrier (BBB) serves as a critical barrier to protect the brain from toxins and pathogens in the blood, but it also poses a significant limitation in pharmacotherapy by restricting the delivery of therapeutic agents to the brain. Materials science and nanotechnology have been explored to overcome this barrier, including the use of liposomal formulations. Therefore, in this study, we aimed to assess BBB permeability by encapsulating AMT-XX05 in liposomes. The experiment included both liposomal AMT-XX05 and non-liposomal AMT-XX05, administered intraperitoneally (IP) and orally at a dose of 100 mg/kg. One-hour post-administration, the mice were anesthetized and subjected to cardiac perfusion before brain extraction. The brain tissue was homogenized and separated into supernatant and pellet fractions for analysis. A standard curve was prepared by mixing normal brain tissue with known amounts of the therapeutic agent and analyzed alongside the samples using HPLC. Mice administered the liposomal drug intraperitoneally showed decreased clinical signs starting 10 minutes post-administration, although no fatalities were observed. Furthermore, HPLC analysis revealed that liposomal AMT-XX05 was detected at a concentration of 9.18 μg/ml, whereas non-liposomal AMT-XX05 was not detected at all. We have established an evaluation method for BBB permeability and used it to measure the BBB permeability of AMT-XX05. As a result, it was confirmed that the liposomal formulation significantly enhances the brain penetration of AMT-XX05, thereby increasing its potential as a CNS-targeted therapeutic. The evaluation method established in this study will greatly aid in assessing the BBB permeability of various CNS-targeted candidate therapies in the near future.

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***Keywords :** Efficacy Test Center for Mental & Behavioral Disorders, BBB permeability, Liposomes, CNS-targeted therapeutic

PS-B-047

Recombinant human bone morphogenetic protein-2 priming of mesenchymal stem cells ameliorate acute lung injury by inducing regulatory T cells

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Mesenchymal stromal/stem cells (MSCs) possess immunoregulatory properties and their regulatory functions represent a potential therapy for acute lung injury (ALI). However, uncertainties remain with respect to defining MSCs-derived immunomodulatory pathways. Therefore, this study aimed to investigate the mechanism underlying the enhanced effect of human recombinant bone morphogenic protein-2 (rhBMP-2) primed ES-MSCs (MSC^{BMP2}) in promoting Tregs in ALI mice. MSC were preconditioned with 100 ng/ml rhBMP-2 for 24 h, and then administrated to mice by intravenous injection after intratracheal injection of 1 mg/kg LPS. Treating MSCs with rhBMP-2 significantly increased cellular proliferation and migration, and cytokines array reveled that cytokines release by MSC^{BMP2} were associated with migration and growth. MSC^{BMP2} ameliorated LPS induced lung injury and reduced myeloperoxidase activity and permeability in mice exposed to LPS. Levels of inducible nitric oxide synthase were decreased while levels of total glutathione and superoxide dismutase activity were further increased via inhibition of phosphorylated STAT1 in ALI mice treated with MSC^{BMP2}. MSC^{BMP2} treatment increased the protein level of IDO1, indicating an increase in Treg cells, and Foxp3+CD25+ Treg of CD4+ cells were further increased in ALI mice treated with MSC^{BMP2}. In co-culture assays with MSCs and RAW264.7 cells, the protein level of IDO1 was further induced in MSC^{BMP2}. Additionally, cytokine release of IL-10 was enhanced while both IL-6 and TNF-α were further inhibited. In conclusion, these findings suggest that MSC^{BMP2} has therapeutic potential to reduce massive inflammation of respiratory diseases by promoting Treg cells.

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***Keywords :** RhBMP-2, MSC, Acute lung injury, Treg, IDO1

PS-B-048

Major pathological lesion and NOAEL analysis of carcinogenicity test on 190 insecticides

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This study analyzed carcinogenicity test data of 190 insecticides among the pesticide residues used at domestic and foreign to derived the major toxicopathological lesions and NOAEL(No Observed Adverse Effect Level). As a result of the analysis, 196 lesions out of the 190 insecticides were confirmed by carcinogenicity test. Toxicological lesion analysis was performed on four organs containing various lesions. As a result of the analyzing the 196 insecticides with observed lesions, many lesions were observed in order of liver, female reproductive system, thyroid gland and spleen. Of the 196 lesions, 78 lesions were found in the liver, with hepatocellular adenoma(16/78) observed highest incidence. After that, the female reproductive system 19 lesions were found, with endomertrial adenocracinoma(4/19) observed highest incidence. 19 lesions were found in the thyroid gland, with follicular cell adenoma (5/19) observed highest incidence. Finally, in the spleen, 7 lesions were found, with pigmentation (3/7) observed highest incidence. Analysis of 107 NOAEL values among the insecticides indicated that the representative setting bases of NOAEL were clinical chemistry (42.6%), hematology and blood biochemistry (8.8%), organ weight (15.5%), and histopathological factors (33.1%). Especially, among histopathological factors, non-neoplastic lesions accounted for 68 cases, with liver hypertrophy (11 cases) being the most common. Neoplastic lesions accounted for 15 cases, with liver adenoma (3 cases) being the most frequent. The insecticide with the lowest NOAEL was fipronil, announced by JMPR and EFSA, is 0.019 mg/kg bw/day. Through this analysis, evaluating the NOAEL and toxicopathological characteristics of 190 insecticides, it will contribute to providing the essential foundational data for related research and regulation.

***Corresponding author :** Beom Seok Han

***Keywords :** Insecticides, Toxicopathological lesion, NOAEL, Carcinogenicity test

PS-B-049

Major pathological lesion and NOAEL analysis of repeated dose toxicity test of 190 insecticides

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This study analyzed repeated-dose toxicity test data of 190 insecticides among the pesticide residues used at domestic and foreign to derived the major toxicopathological lesions and NOAEL(No Observed Adverse Effect Level). As a result of the analysis, 79 lesions out of the 190 insecticides were confirmed by repeated-dose toxicity test. Toxicological lesion analysis was performed on four organs containing various lesions. As a result of the analyzing the 196 insecticides with observed lesions, many lesions were observed in order of liver, spleen, thymus, and adrenal glands. Of the 79 lesions, 48 lesions were found in the liver, with hepatocellular hypertrophy (21/48) observed highest incidence. After that, the spleen 17 lesions were found, with extramedullary hematopoiesis (8/17) observed highest incidence. After that, the thymus 7 lesions were found, with atrophy (6/7) observed highest incidence. Finally, in the adrenal glands, 7 lesions were found, with vacuolation (3/7) observed the highest incidence. Analysis of 169 NOAEL values among the insecticides indicated that the representative setting bases of NOAEL were clinical chemistry (51.8%), hematology and blood biochemistry (10.9%), organ weight (12.4%), and histopathological factors (24.8%). Especially, among histopathological factors, hepatocellular hypertrophy in the liver was the most frequently with 11 instances, followed by thymus atrophy with 3 instances and liver fatty change with 3 instances. The insecticide with the lowest NOAEL was dieldrin, announced by US EPA, is 0.005 mg/kg bw/day. Through this analysis, evaluating the NOAEL and toxicopathological characteristics of 190 insecticides, it will contribute to providing the essential foundational data for related research and regulation.

Corresponding author **:** Beom Seok Han

Keywords **:** Insecticides, Toxicopathological lesion, NOAEL, Repeated Dose Toxicity test

PS-B-050

Acute inhalation toxicity study of barium carbonate in SD rats

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Barium carbonate (CAS NO. 513-77-9) is used in disinfectants and cleaning agents, as well as in skincare products in the cosmetics industry. It is also being used for the electronics industry, especially in electronic components and special glass. The use of special glass is increasing with the advancement of electronic devices and display technologies, and the use of barium carbonate is also increasing rapidly. In this study, two groups of Sprague-Dawley (SD) rats (3 males and 3 females per group) were exposed to the Barium carbonate at the concentrations of G1(5 mg/L), G2(1 mg/L) for 4 hours by nose-only exposure chambers and observed for 14 days after exposure. Analytical concentrations of test substances were 0.991±0.034, 4.978±0.085 mg/L in G1(5 mg/L), G2(1 mg/L) groups. The MMAD (Mass Median Aerodynamic Diameter) were measured as 4.255, 3.076 μm and GSD (Geometric Standard Deviation) were 2.0, 1.6 in G1(5 mg/L), G2(1 mg/L) groups. The values of T95, T99 chamber were 1.99, 3.06 minutes in the G2(1 mg/L) groups. Examination results showed that there were no toxic symptoms or mortality in any of the animals treated with Barium carbonate during the study period. As a result, LC50 of barium carbonate is proposed at > 5mg/L.

Corresponding author **:** Seong-won Jo

Keywords **:** Barium carbonate, Aerosol, Acute inhalation, Toxicity.

PS-B-051

Maximum tolerated dose (MTD) test of caragana sinica in ICR mice

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Caragana sinica is known to be highly effective in treating circulatory and nervous system diseases in several studies, and its root shell is used as a medicinal ingredient that can promote nerve pain, joint pain, cardiotonic and diuretic action. In addition to these effects, it is necessary to study the effects of natural products on various diseases. The maximum allowable dose (MTD) test is an essential experiment for toxicity assessment before efficacy assessment. The purpose of this study was to evaluate toxicity and observed adverse effect levels (NOAEL) by oral administration of *Caragana sinica* extract to male ICR mice for 21 days. The animals were distributed into 5 groups of 10 mice per group according to their body weight. *Caragana sinica* was orally administered daily for 21 days at a dose of 250, 500, 1000, and 2000 mg/kg (MPK). We also conducted complete blood cell count and serum clinical chemistry test (glucose, TP, ALB, AST, ALT, T-bil, total cholesterol, TG, LDL, HDL, LDH, D-bil and UA). There were no significant differences in mortalities, clinical signs, body weight changes and serum clinical chemistry test in all animals administrated with *Caragana sinica*. The results obtained in this study suggest that *Caragana sinica* did not show any toxic effect in ICR mice and the NOAEL of *Caragana sinica* was regarded as over 2000 mg/kg.

Corresponding author **:** Eun-Kyung Ahn

Keywords **:** Maximum tolerated dose, MTD, Natural product

PS-B-052

Successful tracheal tissue regeneration using biofabricated analogues in rabbit model

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Backgroud/Aim: A wide range of interest has been recently focused on the reconstruction of long-segment tracheal defects, especially in the field of thoracic reconstructive surgery. The aim of this study is to develop a biofabricated analogues treatment method that can be achieved with cells to tracheal disorders or injuries. We tested a decellularized porcine kidney hydrogel tracheal graft with imposing the cells for tracheal transplantation from a porous PCL bellows framework. We successfully demonstrated the potential of a biofabricated analogues graft with luminal collagen stratification for immediate application in emergencies that require an artificial graft.
Methods: As a base material for the construct, porcine decellularization was performed along with its quantification of glycosoaminoglycans (GAGs), collagen, and DNA. Immunohistochemical staining of the decelluarized tissues showed a high preservation of the major extracellular matrix (ECM) components. PCL was used to print a porous framework for the tracheal graft. Ten healthy New Zealand white rabbits underwent end-to-end anastomosis using off-the-shelf tracheal grafts, and the site was evaluated mechanically, endoscopically, and histologically.
Results: The results of this study indicate that re-epithelialization was complete at the anastomosis site at 8 weeks and that circumferential tracheal defect was successfully reconstructed together with complete re-epithelialization on the entire luminal surface of the off-the-shelf graft within 17 weeks.
Conclusion: In this study, we successfully demonstrated the potential of the biofabricated analogues graft with luminal decellularized porcine kidney hydrogel stratification for immediate application in tracheal transplantation. Although a long period of time was confirmed for complete re-epithelialization on the entire luminal surface of the graft, further combination with advanced tissue engineering strategies, such as the application of other enhanced materials, biological factors, or autologous stem cells, can lead to even more remarkable results.

Corresponding author **:** Jae Yeon Lee

Keywords **:** Extracellular matrix, Bioink, Tracheal, Reconstruction, Decellularized biomaterials

PS-B-053

Evaluation of Immunotoxicity in ICR mice following oral administration of polypropylene microplastics

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Exposure to microplastics may be associated with damage of immune system. Polypropylene microplastics (PP-MPs) with a wide range of beneficial applications have not been extensively studied with respect to the immune system. The aim of this investigation is to examine the influence of two different sizes of PP-MPs (5.2 and 23.9 μm diameter) on immune system compo- nents in ICR mice. PP-MPs were administered orally to female and male mice at 0 (corn oil vehicle), 500, 1000, or 2000 mg/kg/d for single and daily for 4-week repeated toxicity test, respectively. No significant differences were observed in number of thymic CD4+, CD8+, CD4+CD8+ T lymphocytes, splenic helper T cells, cytotoxic T cells, and B cells. The ratio of interferon-γ to interleukin-4 in culture supernatants from activated splenocytes ex vivo (48 hr) was lower in females which were repeatedly administered with PP-MPs compared to vehicle irrespective of PP-MPs size and dose. In contrast, the opposite trend was observed in males. Production of tumor necrosis factor-α was upregulated in females that were repeatedly exposed to PP-MPs. The serum IgG2a/IgG1 ratio was lowered in female receiving large-size PP-MPs. Data suggest that immune disturbances resulting in predominant type-2 helper T cell reactivity may occur in mice, especially in females, when repeatedly exposed to PP-MPs. Further investigations with longer exposure periods are necessary to determine the immunotoxicities attributed to PP-MPs. This researched was approved by the NRF(National Research Foundation of Korea) [Assignment number:RS-2023-00212281] and This researched was conducted with support from the Graduate School of Chemical Safety Management funded by the Korea Environment Institute.

***Corresponding author :** Chang Yul Kim

***Keywords :** Cytokines, Gastric, Immunotoxicity, Immunoglobulins, Porypropylene microplastics

PS-B-054

The toxic effects of environmental risk factors(microplastics) on autism spectrum disorder with autism-like behavioral mouse

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In recent years, there has been growing concern about the impact of environmental risk factors on the development and prevalence of autism spectrum disorder. Several studies have indicated that exposure to microplastics, which are prevalent in both terrestrial and marine environments, may have toxic effects on individuals with autism spectrum disorder. The study aims at evaluating the impact of Pb transmitted to offspring through placental and lactational exposure in dams on autism spectrum disorder. This evaluation will include behavioral experiments, assessment of fluid/cellular immune functions, and analysis of neuroimmune markers in the brain. BTBR T+tf/J mice (hereafter BTBR, 8 weeks old) were used as the experimental group, with C57BL/6 (B6, 8 weeks old) mice as the control group. PE-MPs was transmitted to neonates through pregnant dams per placental transfer and breastfeeding, and their behavioral experiments, as well as fluid/cellular immune functions, were evaluated. Passive avoidance results revealed that groups administered with PE-MPs at 1000ug/L showed a relatively decreased retention time compared to the control group. BTBR blood IgE levels were significantly higher than those of the control group, both in dams and neonates B6, and the lymphocyte ratio was also relatively higher, suggesting the presence of nonspecific humoral immune enhancement in BTBR. BTBR and B6 exhibit opposing tendencies in immunological indicators, indicating that ASD may manifest immune dysfunctions. This researched was approved by the NRF(National Research Foundation of Korea) [Assignment number:RS-2023-00212281] and This researched was conducted with support from the Graduate School of Chemical Safety Management funded by the Korea Environment Institute.

***Corresponding author :** Chang Yul Kim

***Keywords :** Autism spectrum disorder, Behavior test, BTBR, Microplastic, Humoral immunity

PS-B-055

Enhancing liver cancer metastasis detection through biomarker analysis in metastatic mouse models

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Liver cancer is associated with high incidence and mortality rates, with a 5-year survival rate of approximately 20% for regional and 3% for distant metastatic stages. Considering the increasing economic burden caused by liver cancer, early detection of metastatic liver cancer is crucial to overcome this disease. Therefore, identifying biomarkers for early detection of liver cancer metastasis is essential. Our study aimed to identify lipid biomarkers that consistently increased in metastatic tissues between the tail vein injection method and a sponteneously metastasizing mouse model currently used in metastatic cancer research. Liver tissues from experimental and spontaneous metastatic mouse models were analyzed using hematoxylin (H)-staining, matrix-assisted laser desorption/ionization (MALDI)-time of flight (TOF) mass spectrometry, MALDI-mass spectrometry imaging (MSI), and MALDI-MS/MS. H-staining confirmed metastatic lesions histopathologically, while MALDI-TOF analyzed lipid masses in liver tissues. Peaks showing significantly increased intensity in metastatic lesions compared to normal tissue were identified at m/z 725.6, 734.6, 735.6, 741.6, 742.6, 744.6, 756.6, and 772.6. Structural analysis of these peaks using MALDI-MS/MS revealed sphingomyelins (SM) [SM(d18:0/16:0)], phosphatidylcholines (PC) [PC(32:0), PC(31:1), PC(31:0)], and phosphatidylethanolamines (PE) [PE(36:2)], confirmed through the METASPACE annotation platform and Lipid Maps® lipid database. MALDI-MSI confirmed these peaks as red and yellow in metastatic lesions, consistently observed in both experimental and spontaneous metastatic models. These findings suggest the potential use of these identified lipid biomarkers for early detection of liver cancer metastasis, potentially enabling intervention at earlier stages of disease progression.

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***Keywords :** Metastasis, Liver cancer, Lipid biomarker, MALDI-TOF, MALDI-MSI

PS-B-056

Efficacy of canine stem cell-derived ex vivo vesicles treatment in canine atopic and allergic dermatitis

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Canine atopic dermatitis (cAD) is an inflammatory skin disease caused by an imbalance of T lymphocytes, characterized by severe pruritus and skin barrier dysfunction. There are several approaches to treat cAD, immunomodulatory therapies are commonly used, but there is a high risk of recurrence when treatment is stopped and a lack of research on the possible side effects of long-term treatment. This study evaluated the therapeutic efficacy of canine stem cell-derived ex vivo vesicles, GCEV-001, in an in vivo cAD model. GCEV-001 reduced clinical symptoms of cAD as assessed by the Draize skin irritation scoring system (DDISS), such as erythema (CON: 0±0, AD (AD+PBS): 2.6±0.6, T1 (AD+GCEV-001): 1.1±0.3, p=0.0044). GCEV-001 reduces mast cells bind to immunoglobulin E (IgE) and release inflammatory mediators process mast cell degranulation (CON: 6.4±1.5, AD: 18.2±3.4, T1: 6.5±3.7, T1 vs. AD p=0.0017). Also, GCEV-001 also attenuated IgE and OVA-specific IgE expression levels in skin and plasma (skin IgE CON: 42.0±5.0, AD: 65.3±10.4, T1: 34.9±9.5 ng/mL, skin OVA-specific IgE CON: 3.5±0.2, AD: 6.0±0.9, T1: 3.8±1.6 μg/mL and plasma IgE CON: 2.9±0.2, AD: 14.3±1.6, T1: 6.0±4.0 μg/mL, plasma OVA-specific IgE: CON: 8.7±0.1, AD: 12.1±1.4, T1: 11.4±1.9 μg/mL). Interestingly, GCEV-001 attenuated IL-4 and IL-31-mediated pruritus and attenuated CCL17 levels involved in Th2 cell migration (CON: 0.0±0.0, AD: 2.0±0.3, T1: -0.5±2.2 (log2 fold)). Taken together, GCEV-001 demonstrated immunomodulatory effects by modulating T lymphocytes responses, we suggest its potential as a therapeutic agent for canine atopic and allergic dermatitis.

***Corresponding author :** Jeong Ho Hwang

***Keywords :** Canine atopic dermatitis, Toxicology, Stem cell-derived ex vivo vesicles, Canine atopic dermatitis therapeutic

PS-B-057

Surface conjugation of microspheres carrying rapamycin on mesenchymal stem cells exerts improved anti-fibrotic effects against pulmonary fibrosis

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Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease with a poor prognosis characterized by progressive pulmonary fibrosis. Current treatments for pulmonary fibrosis have been reported to slightly delay the progression of fibrosis, therefore, promising drugs that can significantly reduce or reverse fibrosis should be developed. Mesenchymal stem cells (MSCs) have been reported to have an anti-fibrotic effect by producing various paracrine factors, and MSCs therapy could be an alternative treatment. Rapamycin has been demonstrated to have anti-fibrotic activity in animal models of lung fibrosis by regulating cell growth and the fibrosis progression through the inhibition of the mTOR signaling pathway. In this study, we aimed to investigate the anti-fibrotic efficacy of MSCs with rapamycin using surface microsphere-conjugating techniques. Lung fibroblasts were co-cultured with MSCs using trans-well in the presence or absence of rapamycin, and the expression of markers related with myofibroblast differentiation in fibroblasts were determined by western blotting. Production of anti-fibrotic paracrine factors from MSCs were analyzed by ELISA. In addition, rapamycin microspheres were conjugated to the surface of MSCs using polydopamine coating, then added to fibroblasts treated with TGF-β1, and the markers of myofibroblast differentiation were measured. We found that MSCs reduced TGF-β1-induced fibrosis of lung fibroblasts, determined by the expression of α-SMA, collagen and fibronectin. Furthermore, we found that rapamycin elevated the production of MSC-derived anti-fibrotic factors such as HGF and PGE_2. And rapamycin-mediated enhancement of anti-fibrotic abilities of MSCs was dependent on PGE_2 production. Co-treatment of rapamycin with MSCs reduced fibrosis *in vitro*. In addition, MSCs conjugated with rapamycin-loaded microspheres exhibited higher inhibitory effect against fibrosis compared to sole treatment of MSCs or rapamycin. These results suggest that MSCs conjugated with rapamycin-loaded microspheres on their surface might exert improved therapeutic efficacy against pulmonary fibrosis.

***Corresponding author :** Hyung-Sik Kim

***Keywords :** Idiopathic pulmonary fibrosis, Mesenchymal stem cell, Microsphere, Rapamycin

PS-B-058

Single oral dose toxicity study of Vaccinium oldhamii in Sprague-Dawley rats

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Vaccinium oldhamii (VO) is a deciduous shrub that grows to a height of 1~4 m and is native to eastern China, Japan and Korea. VO, which is wild blueberries, have been used in Korea and China as folk medicines to treat inflammation, gonorrhea, vomiting, diarrhea, and skin eruptions. Also, its fruit has been reported to have various pharmacological activities such a physiological activity and antioxidant, antimicrobial, and anti-inflammatory effect. The objective of this study was to evaluate the acute toxicity of water extract from the fruit of VO (VOW) by a single oral dose in male and female Sprague-Dawley rats. The mortality and changes on body weight, clinical signs and gross observation were monitored during 14 days after single oral treatment of VOW at dose levels 0, 1,250, 2,500, and 5,000 mg/kg according to KFDA Guidelines. After single oral treatment of VOW, we could not find any mortality and toxicological evidences up to 5,000 mg/kg treated group, the limited dosages in rodents, on the body and organ weights, clinical signs, gross and histopathological observations. The results obtained in this study suggest that the approximate lethal dose (ALD) of VOW in both male and female rats is over 5,000 mg/kg, so this finding would be expected to provide scientific evidence for the safety of VOW.

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***Keywords :** Vaccinium oldhamii, Toxicity study, Approximate lethal dose, KFDA Guidelines, Limit test

PS-B-059

Angelica keiskei extract alleviates colitis via attenuating colonic mucosa injury and regulating pro-inflammatory cytokines production

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Angelica keiskei is a perennial plant of the Umbelliferae family that has been widely cultivated throughout Asia. Angelica keiskei possesses anti-inflammatory and anti-oxidative properties and has been documented to have beneficial effects against diabetes mellitus, obesity, and hypertension. We sought to determine whether angelica root extract, which contains 4-hydroxydericin and xanthoangelol, which are known anti-inflammatory agents, has an anti-inflammatory effect in an animal model of colitis. So, this study aimed to investigate the anti-inflammatory effects of angelica root ethanol extract (AKE) against DSS-induced colitis in mice. The results demonstrated that AKE significantly relieved the loss of body weight, shortening of colon length. The serum cytokine profile demonstrated that tumor necrosis factor-α, interleukin (IL)-1β and IL-6 was significantly lower in the AKE group than in the DSS-induced group. Moreover, AKE ameliorated colonic edema, mucosal damage, and neutrophil infiltration into colonic intestinal tissue in response to DSS challenge. These results demonstrate for the first time that UA (ulcerative colitis) has an ameliorative effect on DSS-induced colonic inflammation in mice. In the future, the therapeutic potentials of UA as an effective complementary modality for the treatment of ulcerative colitis.

***Corresponding author :** Chan Hee Park

***Keywords :** Angelica keiskei, Inflammatory bowel disease, Ulcerative colitis, Dextran sulfate sodium

PS-B-060

Oral repeated dose range finding study of purple corn husk extract in sprague-dawley rats

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The purpose of this study was to evaluate the approximate toxicity by systemic exposure of the test article, when Purple Corn Husk Extract oral administered to Sprague-Dawley rats once daily for 28-days and to setting dosages in a subsequent 90 days repeated dose toxicity study. The study was conducted by setting the test group administered with the test article, Purple Corn Husk Extract(PCHE) at 5,000 mg/kg as high-dose group, and mid-dose and low dose group were set to 2,500 mg/kg and 1,250 mg/kg. Also, we were set a control group to compare with the test-article and vehicle. During observation period, clinical signs observation, body weights, food consumption and drinking water consumption measurements were performed. After the observation period, hematology, blood biochemistry, organ weight measurements and necropsy findings were performed. As a results of the body weights, food consumptions, water consumption measurements and organ weight measurements and necropsy findings no abnormal change were observed in the test article groups administration. There were no significant toxicological change when Purple Corn Husk Extract oral administered to Sprague-Dawley rats once daily for 28-days. So, it is considered appropriate to set 5,000 mg/kg or less as a high-dose group in order to observe toxicity changes caused by the test article in 90 days repeated toxicity study.

***Corresponding author :** Kiyeon Lee

***Keywords :** Purple Corn, Husk, Toxicity

PS-B-061

Protective effects of Sicyos angulatus on binge drinking-induced liver injury through regulation of gut integrity in mice

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Alcoholic liver injury (ALI) is a leading cause of severe liver disease, but current treatments are mostly supportive and do not directly addressing alcohol metabolism. Binge drinking induces ALI through oxidative stress and inflammation, causing significant hepatic and intestinal damage. Alcohol-induced oxidative stress damages intestinal cells and disrupts junctional proteins, increasing intestinal permeability and causing dysbiosis. This leaky gut condition triggers inflammatory responses via endotoxins, including lipopolysaccharides (LPS), which promote alcoholic liver disease. *Sicyos angulatus* (SA), a summer annual vine in the *Cucurbitaceae* family, is known to have anti-inflammatory and antioxidative effects, but its efficacy on ALI has not yet been reported. In this study, we induced ALI by administering a single oral dose of binge alcohol (6 g/kg) to mice pre-treated with either vehicle or SA for four days. The SA-treated group exhibited significantly lower levels of plasma ALT and AST, markers of liver injury, compared to the control group. However, there were no significant changes in hepatic fat accumulation or the expression levels of alcohol metabolism-related genes. Nonetheless, the number of TUNEL-positive hepatocyte and total ROS levels in mitochondrial fraction of liver were significantly reduced in the SA-treated group, suggesting that SA might indirectly protect against liver injury through alternative mechanisms. We confirmed that SA protects against alcohol-induced disruption of gut integrity. This was evidenced by increased expression of tight junction-related genes in ileum and colon, and reduced LPS levels in blood of the SA-treated group. Additionally, *in vitro* studies using Caco-2, human colon carcinoma cell line, showed that pre-treatment with SA followed by ethanol exposure resulted in reduced tight junction protein disruption compared to the vehicle group. Overall, these results demonstrate that SA can protect against hepatic damage caused by binge drinking by preventing leaky gut, suggesting its potential as an agent for regulating gut barrier function.

Corresponding author **:** Yong-Hoon Kim, Chul-Ho Lee

Keywords **:** Sicyos angulatus, Alcoholic liver injury, Gut-liver axis, Tight junction, Binge drinking

PS-B-062

Discovery and identification of tastants in kimchi using bitter taste receptor activation

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Taste is classified into five types, each of which has evolved to play its respective role in mammalian survival. A taste receptor or tastant is a type of cellular receptor which facilitates the sensation of taste. When food or other substances enter the mouth, molecules interact with saliva and are bound to taste receptors in the oral cavity and other locations. Molecules which give a sensation of taste are considered. Sour taste is one of the important ways to judge whether food has gone bad, and the sour taste receptor (PKD2L1) is the gene behind it. The gustatory system consists of taste receptor cells in taste buds. Taste buds, in turn, are contained in structures called papillae. There are three types of papillae involved in taste: fungiform papillae, foliate papillae, and circumvallate papillae. Here, we investigated whether L-pyroglutamic acid interacts with sour taste receptors through electrophysiology and mutation experiments using Xenopus oocytes. R299 of hPKD2L1 was revealed to be involved in L-pyroglutamic acid binding in a concentration-dependent manner. As a result, it is possible to objectify the change in signal intensity according to the concentration of L-pyroglutamic acid, an active ingredient involved in the taste of kimchi, at the molecular level. Since the taste of other ingredients can also be measured with the method used in this experiment, it is expected that an objective database of taste can be created.

Corresponding author **:** Junho Lee

Keywords **:** Tastants

PS-B-063

Physiologically-active composition based on Rosa multiflora Thunb and Zizyphus jujuba Miller

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Sleep is an essential component of quality of life. The majority of people experience sleep problems that impact their quality of life. Melatonin is currently a representative sleep aid. However, it is classified as a prescription drug in most countries, and consumers cannot purchase it to improve their sleep. This sleep induction experiment in mice aimed to identify a natural combination product (NCP) that can create synergistic sleep-promoting effects. Based on the mechanism of action of sleep, we investigated whether phenomenological indicators of sleep quality change according to the intake of NCP. The sleep onset and sleep time of the mice that consumed the NCP found by this study were improved compared to the existing sleep aids. The mean melatonin level in the blood increased by 197% compared to the control. To our knowledge, this is the first study to demonstrate that Rosa multiflora Thunb. (Yeongsil) can promote sleep similarly to Zizyphus jujuba Miller (Sanjoin). The results indicate a preclinical study of NCPs containing Rosa multiflora Thunb and Zizyphus jujuba Miller developed by us showed significant differences in sleep incubation and duration depending on melatonin concentrations. Our results also suggest that increased melatonin concentrations in the blood are likely to improve sleep quality, especially regarding incubation periods.

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Keywords **:** Melatonin receptor

PS-B-064

Biochemical studies of the structure and function of the N-methyl-D-aspartate subtype of glutamate receptors by Ergot

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The N-methyl-D-aspartate receptors (NMDARs) mediate fast excitatory currents leading to depolarization. Postsynaptic NMDARs are ionotropic glutamate receptors that mediate excitatory glutamate or glycine signaling in the CNS and play a primary role in long-term potentiation, which is a major form of use-dependent synaptic plasticity. The overstimulation of NMDARs mediates excessive Ca2+ influx to postsynaptic neurons and facilitates more production of ROS, which induces neuronal apoptosis. To confirm the induced inward currents by the coapplication of glutamate and ergotamine on NMDARs, a two-electrode voltage clamp (TEVC) was conducted. The ergotamine-mediated inhibitory effects of NR1a/NR2A subunits were explored among four different kinds of recombinant NMDA subunits. In silico docking modeling was performed to confirm the main binding site of ergotamine. The ergotamine-mediated inhibitory effect on the NR1a/NR2A subunits has concentration-dependent, reversible, and voltage-independent properties. The major binding sites were V169 of the NR1a subunit and N466 of the NR2A subunit. Ergotamine effectively inhibited NR1a/NR2A subunit among the subtypes of NMDAR. This inhibition effect can prevent excessive Ca2+ influx, which prevents neuronal death.

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Keywords **:** N-methyl-D-aspartate

PS-B-065

Repellent interactions with olfactory receptors and ionotropic receptors analyzed by molecular modeling receptors to find repellents

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The olfactory nervous system recognizes and distinguishes many different chemicals in the general living environment. Insects have evolved a group of odorant-gated ion channels composed of highly-developed olfactory receptors capable of distinguishing and distribution between various chemicals with symbolic or evasive specificities. Recently, aphid genomes related to olfaction, including olfactory receptors and proteins, have been identified and olfactory receptors have been reported that are differentially differentiated from Drosophila. The genome of the olfactory receptor has a very conservative sequence and a systematic signaling system. A representative receptor, odorant-gated ion channels comprised of a highly conserved co-receptor (Orco) has a homotetramer channel structure with four subunits arranged symmetrically around the central hole. It has a very similar structure to the 7-transmembrane receptor present in the human body and has a very similar structural form and gating mechanism to receptors of neurotransmitters. In this study, whole cell voltage clamp recording was performed with cell expression system of OR65 gene, which is a subtype of olfactory receptor isolated from Drosophila. After the successful expression of this receptor, microbial culture extract of microorganism, a harmful insect inducer, was used to investigate whether olfactory receptor activity was regulated. The activity of the receptor was confirmed in the recording media diluted 10,000 times with the microbial culture extract. Therefore, it is possible to identify attractant or repellent substance using the olfactory receptor activity regulating system of insects. Through this study, new attractant shows the attracting phenomenon by activating insect receptor OR65, The results of the scientific analysis of the performance of the extracts are presented.

***Corresponding author :** Junho Lee

***Keywords :** Olfactory receptors

PS-B-066

Network pharmacology and molecular docking analyses of mechanisms underlying effects of the kaempferol

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Monoamine serotonin is a major neurotransmitter that acts on a wide range of central nervous system and peripheral nervous system functions and is known to have a role in various processes. Recently, it has been found that 5-HT is involved in cognitive and memory functions through interaction with cholinergic pathways. The natural flavonoid kaempferol extracted from Cudrania tricuspidata is a secondary metabolite of the plant. Recently studies have confirmed that kaempferol possesses a neuroprotective effect because of its strong antioxidant activity. It has been confirmed that kaempferol is involved in the serotonergic pathway through an in vivo test. However, these results need to be confirmed at the molecular level, because the exact mechanism that is involved in such effects of kaempferol has not yet been elucidated. Therefore, the objective of this study is to confirm the interaction of kaempferol with 5-HT3A through electrophysiological studies at the molecular level using kaempferol extracted from Cudrania tricuspidata. This study confirmed the interaction between 5-HT3A and kaempferol at the molecular level. kaempferol inhibited 5-HT3A receptors in a concentration-dependent and voltage-independent manner. Site-directed mutagenesis and molecular-docking studies confirmed that the binding sites D177 and F199 are the major binding sites of human 5-HT3A receptors of kaempferol.

***Corresponding author :** Junho Lee

***Keywords :** N-methyl-D-aspartate antioxidant, Ergot alkaloid, Ergotamine, Free reactive oxygen species, Neuronal disease, Two-electrode voltage clamp

PS-B-067

Discovery and application of Medical Fluorophore 33: a novel theranostic agent for cancer therapy and imaging in mice of colorectal cancer

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Fluorescent dyes have garnered significant attention as theranostic platforms owing to their inherent characteristics. In this study, we present the discovery of Medical Fluorophore 33 (MF33), a novel and potent theranostic agent with a phenaleno-isoquinolinium salt structure that can serve as a cancer therapeutic strategy. The synthesis of MF33 is readily achievable through a simple Rh(III)-catalyzed reaction. Moreover, MF33 displayed strong fluorescence signals, excellent microsomal stability, and high biocompatibility in vivo. It induces significant apoptosis in cancer cells via the p53/p21/caspase-3 signaling pathway, leading to selective cytotoxicity in various cancer cells. In vivo fluorescence imaging with MF33 enabled the visualization of sentinel lymph nodes in living mice. Notably, repeated intraperitoneal administration of MF33 resulted in antitumor activity in mice with colorectal cancer. Collectively, our findings suggest that phenaleno-isoquinolinium salt-based MF33 is a viable theranostic agent for biomedical imaging and cancer treatment.

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***Keywords :** Cancer therapy, Fluorescent dye, Phenaleno-isoquinolinium, Sentinel lymph nodes, Theranostic

PS-C-001

Polymicrobial enteric infection and treatment in common marmoset (Callithrix jacchus), especially Enteropathogenic Escherichia coli (EPEC)

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Enteropathogenic *Escherichia coli* (EPEC) is a pathogenic *E. coli* strain in common marmosets, capable of causing inflammation in their intestines and damaging the mucosa. Seoul National University Hospital Marmoset Model Network Center (SNUH-MMNC) has implemented microbial monitoring of all marmosets' fecal samples in the colony. Newly imported marmosets from Europe showed bloody diarrhea during quarantine, and then exhibited bloody diarrhea again 18 days after the quarantine period ended. Hematological findings revealed leukocytosis ($12.53x10^3$ cells/μL), with a particularly elevated neutrophil count ($10.06x10^3$ cells/μL). Additionally, serum biochemistry analysis showed hypoalbuminemia (3.0%), elevated creatinine (0.78 mg/dL), and elevated CPK (2361 U/L) compared to reference values, raising suspicion of infection. Bacterial pathogen monitoring from the bloody diarrhea sample tested positive for *Clostridium perfringens*, EPEC, and *Helicobacter spp*. Intramuscular injection of metoclopramide hydrochloride hydrate (MHH) to regulate gastrointestinal motility and per oral administration of the macrolide antibiotic azithromycin hydrate (AzH), which is effective against gram-positive/negative bacteria with a low risk of drug resistance were treated for marmoset. Within 4 days of initiating antibiotic treatment, diarrhea resolved into soft stools, and normal stools were observed after 1 week. Antibiotic therapy was continued for a total of 15 days, with tapering of the antibiotic dose from day 13 onward. From the start of antibiotic administration, EPEC tests were negative, and remained negative in stool samples during and after the course of antibiotic treatment. We report the first case of EPEC infection in SNUH-MMNC marmoset colony, which was successfully treated, and consider that our treatment regimen can be proposed as a good guideline for quality control of marmoset colonies.

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Keywords : Common Marmoset, Enteropathogenic Escherichia coli (EPEC), Microbial monitoring , Azithromycin hydrate , Metoclopramide hydrochloride hydrate

PS-C-002

Comparison of Marmoset Fecal Bacterial Monitoring according to Origin from Japan and Europe

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Seoul National University Hospital Marmoset Model Network Center (SNUH-MMNC) has been maintaining a marmoset breeding colony originated from CLEA Japan since 2013, conducting quality control including health examination and microbiological monitoring. Recently additional breeding colonies were imported from Europe. In this report, we aimed to compare the status of fecal microbiological monitoring between marmosets from Japan and Europe. *Klebsiella pneumoniae* and *Clostridium perfringens* were identified in colonies from both Japan and Europe. However, the incidence was much higher in the colony from Japan than in the marmosets from Europe. *Helicobacter spp*. and Enteropathogenic *Escherichia coli* (EPEC) were exclusively detected in marmosets from Europe. Additionally, *Campylobacter spp*. was detected in one individual marmoset from Europe. From these findings, we are able to provide valuable insights into the microbiological profiles of marmosets imported from different origins, specifically Japan and Europe. Furthermore, we are conducting eradication procedures with appropriate antibiotic treatments, and we will standardize these procedures to apply them to the marmoset quality control enhancement data. In the future, we plan to implement more stringent quarantine and monitoring processes for newly imported marmosets to prevent the introduction and spread of pathogens. These enhanced protocols will not only improve the health and welfare of our colonies but also ensure the reliability and validity of our research outcomes.

***Corresponding author :** Byeong-Cheol Kang

Keywords : Marmoset, Microbiological monitoring, Klebsiella pneumoniae, Clostridium perfringens, Enteropathogenic Escherichia coli

PS-C-003

Heat-killed Limosilactobacillus Reuteri modulates the growth performance and inflammation of weaning pigs via microbiota composition and intestinal stem cell activity management

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The weaning period is a critical phase in the growth of pigs, significantly impacting their viability and overall performance, with implications for the pig industry's production efficacy. This transition is typically marked by stressors that may cause reduced feed intake, diarrhea, heightened susceptibility to pathogens, and increased mortality rates. To mitigate these negative effects, the use of feed additives such as probiotics and postbiotics has been explored. This study examines the effects of administering live and heat-killed (HK) Limosilactobacillus Reuteri on the growth performance and health of weaning pigs. We found that HK L. Reuteri administration during the initial 0-14 days post-weaning led to increased body weight and reduced diarrhea rates, whereas live L. Reuteri showed no significant difference compared to the control group. HK L. Reuteri also contributed to decreased systemic inflammatory cytokines IL-1β and IL-6, corresponding with the reduction in diarrhea rate. Moreover, the expression of intestinal health markers Lgr5, Muc2, and Lyz1 was enhanced, indicating improved intestinal cell function. Pigs treated with HK L. Reuteri also showed higher intestinal organoid forming efficiency and increased levels of short-chain fatty acids (SCFA), such as butyric acid and valeric acid, in the colonic digesta, which are beneficial for gut health. These findings suggest that HK L. Reuteri has significant potential for managing the weaning period in pigs by improving growth performance, reducing diarrhea rates, modulating inflammatory responses, and enhancing intestinal integrity and function. This study highlights HK L. Reuteri as a potent candidate for enhancing health during the critical weaning phase of pigs.

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Keywords : Probiotics, Postbiotics, Anti-inflammatory, Microbiome, Organoid

PS-C-004

Changes in gut microbiota after radioactive iodine therapy

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Background/Aim: Iodine-131 (I-131) is a radioactive isotope widely used as a treatment for thyroid diseases. This study to identify whether there were changes in intestinal microorganisms after radioactive iodine treatment, in addition to known side effects such as sialadenitis and gastritis using mice.
Method: Based on the 1.11 – 7.40 MBq dose administered therapeutically to humans, C57BL/6 male mice were orally injected with saline, low dose I-131 (0.46 MBq), and high dose I-131 (3.05 MBq). Two weeks after injection, fecal samples were harvested for Microbiome Taxonomic Profiling (MTP) data. Each tissue was extracted over time to confirm the amount of distribution within the tissue and then performed biodistribution-based dosimetry analysis using the OLINDA/EXM 1.1 software with a focus on intestines. To quantify villi height ileum tissue was stained with hematoxylin and eosin (H&E).
Results: In the MTP analysis, the Firmicutes/Bacteroidetes (F/B) ratio gradually decreased with increasing I-131 dose: 2.54 (control), 1.00 (low-dose; p=0.1875), and 0.76 (high-dose; p=0.1280), respectively. The *in vivo* tissue distribution results showed an overall similar distribution pattern except for the difference in the initial time. The high-dose I-131 group resulted in higher whole-body effective dose compared to low-dose group, but there were no differences in intestinal absorbed dose. Histological analysis focusing on the ileum revealed increased villi length in the treatment group compared to the control group.
Conclusions: After oral administration of I-131 to mice, we confirmed the ratio of intestinal microorganisms and histological changes according to radioactive dose without differences in intestinal absorbed dose. Based on this study, further research on changes in intestinal microorganisms after I-131 treatment will be of great help in the follow-up management of patients.

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Keywords : Iodine Therapy, Gut microbiota, Biodistribution, Dosimetry, Histological anaylsis

PS-C-005

Anti-tumor effects of heat-killed Lactobacillus plantarum NCHBL-004 on syngenic melanoma mice model

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This study aimed to assess the anti-tumor effects of heat-killed lactobacilli, specifically *Lactobacillus plantarum*, *Lactobacillus kunkeei*, and *Lactobacillus reuteri* isolated from honey bee intestine in a syngenic mouse melanoma model. The strains were administered daily via intraperitoneal injection starting in 10 days post-implantation of the murine melanoma cell line B16F10 in C57BL/6J mice. Results revealed a significant reduction in tumor size and weight in the *L. plantarum* group compared to the PBS group, while *L. kunkeei* and *L. reuteri* groups did not exhibit the same effect. *L. plantarum* group demonstrated an increase in IFNγ^+ CD4$^+$, IFNγ^+ CD8$^+$, and IFNγ^+ NK1.1$^+$ cell populations, along with the highest cytotoxic T lymphocyte activity. In-vitro studies on murine bone marrow derived dendritic cells stimulated with the heat killed lactobacilli strains showed that *L. plantarum* induced the highest IL-12 / IL-10 cytokine ratio and increased populations of IFN-γ^+ CD4$^+$, IFN-γ^+ CD8$^+$, and IFN- γ^+ NK1.1$^+$ cells compared to other groups. Remarkably, anti-tumor effects of *L. plantarum* were abolished in TLR2 knock-out mice syngenic melanoma model, indicating that the anti-tumor capacity of *L. plantarum* is attributed to TLR2 ligands present in the bacterial wall. In summary, our findings affirm that heat-killed *L. plantarum* possesses potent anti-tumor effects on melanoma, mediated through the stimulation of host TLR2. This suggests that purified TLR2 ligands from *L. plantarum* could hold promise as potential therapeutic agents for melanoma treatment.

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***Keywords :** Probiotics, Lactoabcillus species, Melanoma, Bone marrow derived dendritic cells, Toll-like receptor 2

PS-C-006

Entamoeba muris infection induces intestinal Inflammation and Gut Microbiota changes

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E. muris, a highly infectious intestinal protozoan, is commonly found in laboratory housing environments, maintaining direct life cycles and spreading through the fecal-oral route. Since there are no reported pathogenic effects of *E. muris*, infections in laboratory animal facilities are often overlooked. Therefore, this study aimed to investigate the impact of *E. muris* infection on the host. A naturally infected donor mouse with *E. muris* was discovered through fecal examination in the animal facility. Cecal contents from this donor mouse were processed using Ficoll isolation and HCl treatment to purify *E. muris*. The purified *E. muris* was then used to infect female BALB/c mice (immunocompetent) and BALB/c Nude mice (T cell-deficient) via oral gavage. gDNA was extracted from feces for quantification of *E. muris* using qPCR. The amount of *E. muris* in feces increased up to 28 day post infection (dpi), peaking at 35 dpi. At 45 dpi, increased cell death, cell proliferation, and the infiltration of immune cells, including regulatory T cells, were observed in the colons of infected mice via H&E and immunohistochemistry (IHC) analyses. However, *E. muris* colonization was significantly lower or absent in T cell-deficient BALB/c Nude mice or mice depleted of T-cells using CD4/CD8 depletion antibodies, compared to immunocompetent mice. Additionally, metagenome amplicon sequencing of fecal samples demonstrated that *E. muris* infection altered the composition of gut microbiota. *E. muris* infection induces intestinal lesions and alters the intestinal microbiome, withcolonization being more effective in mice with intact T-cell immunity. Overall, our study representsthe first report of *E. muris* pathogenicity in laboratory mice, highlighting the complex interactions among host immunity, *E. muris*, and the gut microbiota.

***Corresponding author :** Jun Won Park

***Keywords :** Host-Parasite Interactions, Immunity, Microbiota, Parasite, Pathogenicity

PS-C-007

Generation of Germ-free Lgr5GFP reporter mice to determine microbiome-stem cell interaction in gastrointestinal tract

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Background: Leucine-rich repeat-containing G protein-coupled receptor 5 (Lgr5) was first traced and revealed their identity as a marker of intestinal stem cells (ISCs) in 2007. Followed studies have found that Lgr5 marks homeostatic adult stem cells in multiple tissues, such as the pyloric antrum of the stomach, myoepithelial cells of the mammary gland, and outer bulge cells of hair follicles. Since then, recent studies have established newly generated mouse (Lgr^{5DTR}, Lgr5$^{2A\text{-}Cre}$) system and organoid culture to reveal Lgr5+ stem cell behavior in various tissues. Although the role of microbiome-host interactions in the GI tract has previously been studied, their effect on the Lgr5$^+$ adult stem cells in homeostatic and injury contexts still remains unclear.
Method: While germ-free mouse models are generally exhibited as the gold standard for studies of the microbiota, here we compare and describe gut microbiome interaction with Lgr5$^+$ host stem cell by generation of novel germfree (GF) Lgr5$^{EGFP\text{-}IRES\text{-}creERT2}$-Rosa26^{tdTomato} mice.
Result: In homeostasis, GF mice displayed divergence in the gastrointestinal tract. Lgr5$^+$ ISCs are known to reside in specific region called the crypt of Lieberkühn. In single crypt, proliferative Lgr5$^+$ ISCs were reduced in GF mice, and we also noticed a declined cellular migration of crypt-villus axis due to lineage traced of Lgr5 and their progeny labelled with tdTomato. Overall, GF mice showed decelerated proliferation, and epithelial turn over rate compared to specific pathogen free (SPF) Lgr5$^{EGFP\text{-}IRES\text{-}creERT2}$-Rosa26^{tdTomato} mice.
Conclusion: Our observation elucidates that specific microbiota or microbial metabolites such as short-chain fatty acid (SCFA) may have interacted with Lgr5$^+$ intestinal stem cells (ISCs) for intestinal homeostasis and tissue renewal. This work significantly contributes to advancing our knowledge of the interplay between Lgr5$^+$ stem cells and the microbiome, providing a nuanced perspective on the factors influencing tissue health and repair. These findings have the potential to guide future research directions and inspire the development of novel therapeutic approaches.

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***Keywords :** Germfree, LGR5, Microbiome, Intestinal stem cells

PS-C-008

Metagenomic sequencing of the gut microbiome in BALB/c mice administered fermented soybean for 60 days

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The human gut hosts diverse microbes that ferment indigestible food, providing nutrients and energy while maintaining immune balance. However, the rise of instant and convenient foods in modern society can harm this microbial ecosystem. Therefore, we have four groups of BALB/c male mice (control and treated) that were fed fermented soybeans at a dose of 1000 mg/kg for 30 and 60 days. Metagenomic sequencing was then performed on the mice stool samples. The classification was conducted using MIrROR, a custom platform for analyzing 16S-23S rRNA operon sequences. The database was built by downloading bacterial genomes from NCBI and collecting sequences amplified by 16S-23S rRNA operon primers, followed by extensive curation. NanoFilt was used to filter reads with a quality score of 7 or higher and lengths between 3,000 and 7,000 bp. Porechop was then used to remove adapter and barcode sequences, allowing for sample demultiplexing. Metagenomic analysis results showed that the diversity of microbial species increased in the fermented soybean group compared to the control group. Additionally, acute toxicity assessment determined that an oral dose of 2,000 mg/kg was mildly toxic to mice. In conclusion, this study demonstrates safe intake concentrations and benefits for the gut health of fermented soybeans.

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***Keywords :** Metagenome, Fermented soybeans, Acute oral toxicity, Gut microbiota, Sequencing

PS-C-009

Cell penetrating peptide nucleic acid platform for rapid therapeutics development against new emerging pandemic virus

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Coronaviruses, such as SARS-CoV-2, which caused the most recent global COVID-19 pandemic, are highly pathogenic respiratory viruses that have a significant negative influence on mortality and public health around the globe. Worldwide research has been done in an effort to find a cure for diseases caused by coronaviruses. Recently, reports of antisense oligonucleotides (ASOs) that target the SARS-CoV-2 genome with potential therapeutic uses have surfaced. ASOs based on peptide nucleic acids (PNAs) have been suggested as excellent treatment candidates for antivirus therapeutic agent. In this work, OliPass corporation created PNA (also known as OliPass PNA or OPNA), which was formed from PNA by attaching a cationic lipid moiety to the nucleobase. OPNA has good cell permeability. The conserved sequences of SARS-CoV-2 were targeted by sense and antisense oligonucleotides. PNA oligomers were created using the solid phase peptide synthesis (SPPS) method, which was slightly modified from the Olipass patent method and is based on Fmoc-chemistry. a mixture of OPNA targeting a conserved region of SARS-CoV-2 were treated at 3 hours before infection, and 1 hour post infection, and the virus titers in the culture supernatant were measured daily from 1 to 3 dpi. In addition, in vivo test performed to antiviral effect using Syrian golden hamsters. The ultimate anti-viral impact was observed from 1 to 3 dpi. Viral gene including RdRp was reduced in the therapeutics group. The combination of OPNA targeting multiple regions greatly reduced CPE at three days post SARS-CoV-2 infection confirming their efficacy to control viral infection. In vivo test also showed antiviral effect in the Syrian golden hamsters. A PNA ASO platform with exceptional chemical stability, high binding affinity, and cellular permeability has been created in this study. In the future, this might be a potential therapeutic agent to fight pandemic viral diseases.

***Corresponding author :** Chiho Yu

***Keywords :** Antisense oligonucleotide, SARS-CoV-2, Peptide nucleic acid

PS-C-010

R51-3, a Ricin vaccine, protects rabbits against ricin toxin

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Ricin toxin is a 64 kDa protein produced by castor beans. Ricin toxin is glycoprotein consisting of two distinct subunits, RTA and RTB. The RTA is a ribosome inactivating protein (RIP) that inhibits protein synthesis in mammalian cells. The RTB is a lectin, which binds to galactose residues on the surface of cells. Because of its wide availability and extraordinary toxicity, ricin represents a potential agent for use in bioterrorism and is classified by the CDC as a caterory B bioterrorism threat. Ten New Zealand white rabbits (flve females and five males) were injected intramuscularly three times, once every two weeks with R51-3. As a control, six New Zealand white rabbits (three females and three males) were injected intramuscularly with PBS only. Two weeks after the last injection, all rabbits were challenged by an intramuscular injection of 42.2 ug/kg of ricin, a dose corresponding to 20-fold the LD50 of ricin. Animals were monitored daily signs of morbidity and mortality throughout the study. Ten of ten animals vaccinated with R51-3 survived challenge with 20 LD50 of ricin. In contrast all control rabbits died within 24 hours following challenge with ricin toxin. In this study, we established a lethal rabbit model for ricin toxin, which may facilitate in vivo studies on the evaluation of cadidate drugs against ricin toxin. R51-3 given intramuscularly protected rabbits against intramuscular administered ricin toxin.

***Corresponding author :** Gyeung-Haeng Hur

***Keywords :** Ricin, Vaccine, Rabbit, LD50

PS-C-011

Anti-Viral activity of novel mRNA Antibodies against SARS-CoV-2 delta

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As with the Coronavirus Disease 2019 (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in 2022, rapid development of vaccines and treatments for new or re-emerging infectious diseases is needed. While traditional monoclonal antibody (mAb) technologies have limitations in terms of rapid development, mRNA-based antibody platform technologies that can dramatically shorten the development period has rapidly evolved in recent years. Here, we discovered SARS-CoV-2 delta-specific mRNA-antibodies using single B cell technologies, and *in vitro* plaque reduction neutralization test (PRNT) and *in vivo* efficacy tests were performed to confirm the neutralizing effects of the mRNA-antibody candidates. The treatments DW-S-Ab-9 or DW-S-Ab-10 were shown to have significant antiviral efficacy, and further molecular biological and histopathological analyses of both substances have also shown efficacy. Therefore, we have confirmed the effectiveness of the mRNA-antibody platform against viruses, and it may be used to develop more diverse infectious disease treatments in future studies.

***Corresponding author :** Chiho Yu

***Keywords :** SARS-CoV-2, Therapeutics, MRNA antibody

PS-C-012

Exploring immunological defense mechanisms against Sendai virus infection

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This study was conducted to find the immunological defense mechanism against Sendai virus infection through repeated administration of lipopolysaccharide (LPS). First, to determine the LPS concentration, 0.1μg and 8μg of LPS were administrated four times repeatedly, and then inoculated at $2x10^6$pfu/mouse of Sendai virus via intubation-mediated intratracheal instillation (IMIT). In changes in body weight, the 8μg LPS group showed a lower value than the 0.1μg LPS group, and there was a significant difference compared to the virus control group. However, there was no difference in spleen-weight changes between the LPS group and the virus control group. Next, to determine the infective dose of Sendai virus, when inoculated at $1x10^4$, $1x10^5$, and $1x10^6$pfu/mouse of Sendai virus via IMIT, body-weight changes was found to be lower in 8μg LPS group than in the virus control group. In particular, when Sendai virus was administrated at $1x10^6$pfu/mouse, there was a significant difference in the body-weight changes and survival rate between the 8μg LPS group and virus control group, respectively. However, when only LPS was administered without infection, the change in lung weight significantly increased in the 8μg group compared to the normal control group. Finally, as a result of reducing the LPS administration to 4ug, there was a significant difference in the body-weight changes and survival rate between the 4μg LPS group and virus control group, respectively. In conclusion, it was confirmed that repeated administration of LPS causes antiviral effect *in vivo*, and this experiment can be used for research on the immunological defense mechanisms of viral pneumonia.

***Corresponding author :** Yang-Kyu Choi

***Keywords :** Sendai virus, Lipopolysaccharides, Intubation-mediated Intratracheal Instillation, C57BL/6N

PS-C-013

The oral administration of Bacillus velezensis KD1 enhances influenza vaccine efficacy in mice

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Influenza is a severe respiratory illness that continues to pose a global health threat. Although the best prevention against influenza is the vaccination, its efficacy is relatively modest. Therefore, developing novel strategies to enhance vaccine effectiveness is important to prevent potential future influenza pandemics. Recent several studies suggest that the gut microbiome plays a pivotal role in regulating the vaccine-induced immune responses, although the exact mechanisms are not fully understood. In this study, we investigated the potential of *Bacillus velezensis* KD1 (B. KD1), isolated from the traditional Korean fermented foods, to enhance influenza vaccine efficacy. Upon oral administration with B. KD1, mice exhibited significantly higher levels of the vaccine-induced antibodies compared to the PBS-administered control group. Interestingly, metabolite analysis revealed notable alteration in metabolic pathways such as Sphingolipid metabolism, Glycolysis/Gluconeogenesis, and Pentose phosphate pathway in fecal and serum samples from mice administered with B. KD1. Particularly, there were significant increases in Glucosylsphingosine and Phosphoethanolamine levels. Taken together, our results suggest that B. KD1 enhances influenza vaccine efficacy by improving humoral immune responses, which is potentially mediated by metabolic modulation.

***Corresponding author :** Young-Jin Seo

***Keywords :** Influenza, Vaccine, Gut microbiome, Humoral immunity, Metabolomic analysis

PS-C-014

Probiotic Lactobacillus sakei regulates intestinal mucosal homeostasis through NOD2 signaling-mediated epithelial proliferation and IL-10 production from stromal cells

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Nucleotide-binding oligomerization domain 2 (NOD2) is an intracellular pattern recognition receptor that senses bacterial peptidoglycan and supports the survival of LGR5+ intestinal stem cells (ISCs) through its activation. The regeneration of the intestinal mucosal barrier is maintained by the continuous differentiation and proliferation of ISCs under both physiological and pathological conditions. However, little is known about the regulatory effect of intestinal microbiota on its ability to epithelial homeostasis and regeneration. In this study, we aimed to investigate the regulatory effect of microbiota on the proliferation of intestinal epithelial cells. We found that one of probiotics, *Lactobacillus sakei* stimulated epithelial cells to secret IL-22 through Nod2 and then induced phosphorylation of STAT3 to accelerate the production of anti-microbial peptides and the proliferation of intestinal epithelial cells, leading to epithelial regeneration. Furthermore, we found that *Lactobacillus sakei* stimulated IL-10 production from intestinal stromal cells of lamina propria, indicating that the probiotics might support the anti-inflammatory responses when the epithelial barrier is disrupted. Moreover, *Lactobacillus sakei* induced secretion of IL-10 from stromal cells to accelerate the proliferation of intestinal epithelial cells. Taken together, these results suggest a novel mechanism by which the intestinal microbiota can support the homeostasis and regeneration of intestinal epithelium.

***Corresponding author :** Hyung-Sik Kim

***Keywords :** Probiotics, Lactobacillus, Intestinal mucosal, Nod-like receptor2, Interleukine-22

PS-C-015

Exploring novel natural inhibitors against the leptospira interrogans GroEL protein: a structure-based virtual screening and molecular dynamics approach

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Leptospira interrogans is the causative agent of leptospirosis, an emerging zoonotic disease characterized by biofilm formation on abiotic surfaces. The disease poses significant health risks in canines due to its diverse serotypes and contagious nature, yet specific antiviral treatments remain unavailable. The GroEL protein, implicated in Leptospira biofilm formation, represents a promising druggable target for therapeutic screening. Here, we aimed to identify potent inhibitors capable of disrupting GroEL function in *L. interrogans*. Leveraging GroEL's conserved importance in pathogenesis and high immunogenicity, we employed a structure-based virtual screening approach targeting GroEL with a dataset of natural compounds (n = 54,3503) from the Life Chemicals database. Virtual screening identified five promising compounds-F3385-2019, F1243-0200, F3139-0927, F2801-0179, and F1864-0208, with binding affinities of − 10.343 kcal/mol, − 9.778 kcal/mol, − 8.445 kcal/mol, − 8.364 kcal/mol, and − 8.257 kcal/mol, respectively. These compounds underwent validation through physiochemical properties and density functional theory (DFT). Subsequently, molecular dynamics (MD) simulations over 100 ns confirmed the structural stability of all five complexes, assessed through root mean square deviation (RMSD), root mean square fluctuation (RMSF), radius of gyration (Rg), solvent accessible surface area (SASA), hydrogen bonds, and principal component analysis (PCA). Furthermore, MM-PBSA calculations indicated strong binding affinities for all five compounds, particularly F3385-2019, F1243-0200, F2801-0179, and F1864-0208, positioning them as promising GroEL inhibitors. These findings suggest that these compounds warrant further investigation as potential candidates for natural therapeutics in combating leptospirosis effectively.

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***Keywords :** Leptospira interrogans, GroEL protein, Biofilm formation, Virtual screening, Molecular dynamics simulations

PS-C-016

De novo Interleukin-10 production gained by priming with Lactobacillus sakei CVL-001 boosts the immunomodulatory abilities of human mesenchymal stem cells

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Mesenchymal stem cells (MSCs) hold therapeutic promise for treating inflammatory bowel disease (IBD) due to their immunosuppressive properties. Currently, pre-conditioning strategies with several beneficial agents have been applied to enhance the efficacy of MSCs in treating IBDs. Probiotics are increasingly acknowledged as a supplemental therapy for IBD; however, the potential benefits of probiotics on MSCs-based therapy remain largely unexplored. In this study, we hypothesized that pre-treatment of MSCs with *Lactobacillus sakei* CVL-001 (*L. sakei* CVL-001), a representative probiotic strain, could enhance the efficacy of MSCs in treating IBD. In line with this hypothesis, we observed that treatment with *L. sakei* CVL-001 induced the secretion of the anti-inflammatory cytokine, Interleukin (IL)-10 from MSCs through activation of the STAT3 signaling pathway. IL-10 release from *L. sakei* CVL-001-treated MSCs (MSC+*L. sakei* CVL-001) reduced the expression of pro-inflammatory genes in LPS/IFN-γ -induced M1 macrophages. Interestingly, co-culturing MSCs with *L. sakei* CVL-001 enhanced the expression of M2-like phenotype in undifferentiated macrophages. In addition, MSC+*L. sakei* CVL001 reduced the proliferation and IL-2 production of Concanavalin A (Con A)-activated Jurkat cells, as well as the proliferation of splenocytes. These results indicate that MSC+*L. sakei* CVL-001 possess enhanced immunosuppressive effects on both macrophages and activated T cells. Furthermore, in the dextran sulfate sodium (DSS)-induced colitis mouse model, the treatment with *L. sakei* CVL-001 enhanced the protective effects of MSCs against IBD symptoms. In conclusion, our findings suggest that probiotics, such as *L. sakei* CVL-001, can improve the immunomodulatory effects of human MSCs for IBD therapy.

***Corresponding author :** Hyung-Sik Kim

***Keywords :** Lactobacilllus sakei CVL-001, Mesenchymal Stem Cells, Interleukin 10, Immunomodulation, Inflammatory Bowel Diseases

PS-C-017

Development and analytical evaluation of an indirect ELISA with recombinant nucleocapsid of Sendai virus

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Sendai virus (SeV) causes a highly contagious respiratory tract infection in laboratory rodents such as mice and rats. Consequently, SeV infection causes a significant problem for the breeding and upkeep of laboratory animals as well as for the execution of animal experiments. As a diagnostic method for SeV infection, the enzyme-linked immunosorbent assay (ELISA) and the bead-based multiplexed fluorogenic immunoassay (MIFA) are commonly used. Despite their widespread use, these methods present certain inconveniences, including prolonged reaction times, multiple washing steps, and the use of strips coated with negative antigens (tissue control). Here, we have developed an indirect ELISA (i-ELISA) utilizing a recombinant nucleocapsid (N) antigen expressed in *Escherichia coli* (*E. coli*), and optimized the ELISA conditions, including reaction and washing times, for single-well testing. Our results showed that the performance of LADPro® SeV Ab i-ELISA demonstrated a sensitivity of 100% and specificity of 100% using a cut-off value of 0.3 with 22 positive samples and 23 negative samples. Moreover, no cross-reactivity was observed in common mouse pathogens. Taken together, LADPro® SeV Ab i-ELISA, which offers enhanced user suitability, is comparable to the conventional approach in terms of performance.

Corresponding author **:** Dong Sook Min

Keywords **:** Sendai virus, Nucleocapsid, Indirect ELISA

PS-C-018

Efficacy evaluation of NK cell therapy in SARS-CoV-2 infected mice

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Natural killer (NK) cells are innate immune cells that recognize and remove abnormal cells, such as virus-infected cells and cancer cells. NK cell function is regulated by multiple encoded receptors. During viral infections, host cells can become sensitive to NK cell-mediated recognition through the upregulation of self-encoded molecules induced by infection and/or a variety of mechanisms, including cellular stress responses associated with combined NK cell-activating receptors, such as cytotoxic receptors, C-lectin like receptors, and co-activated receptors. Recently, several studies have reported on the potential of NK cells as a treatment for viral infections. In this study, we isolated NK cells from peripheral blood mononuclear cells donated by healthy individuals and induced their proliferation and activation. When NK cells were co-cultured with SARS-CoV-2 infected Vero E6, a significant reduction in virus titer was observed. Administration of NK cells in mice prior to SARS-CoV-2 infection led to increased survival rate, indicating the antiviral activity of NK cells. Furthermore, analysis of cytokine secretion in human lung cells infected with SARS-CoV-2 revealed an increase in MIP-3 alpha secretion. when treating NK cells with MIP-3 alpha during differentiation, we observed an increase in NK cell proliferation.

Corresponding author **:** Yong Han Lee

Keywords **:** NK cell, SARS-CoV-2, ACE2-Tg

PS-C-019

Combination of Lacticaseibacillus paracasei BEPC22 and Lactiplantibacillus plantarum BELP53 attenuates fat accumulation and alters the metabolome and gut microbiota in mice with high-fat diet-induced obesity

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This study evaluated the effects of formulations with Lacticaseibacillus paracasei BEPC22 and Lactiplantibacillus plantarum BELP53 on adiposity, the alteration of microbiota, and the metabolome in high-fat diet-fed mice. The strains were selected based on their fat and glucose absorption inhibitory activities and potential metabolic interactions. The optimal ratio of the two strains in the probiotic formulation was determined based on their adipocyte differentiation inhibitory activities. Treatment of formulations with BEPC22 and BELP53 for 10 weeks decreased body weight gain at 6 weeks; it also decreased the food efficiency ratio, white adipose tissue volume, and adipocyte size. Moreover, it decreased the expression of the lipogenic gene Ppar-γ in the liver, while significantly increasing the expression of the fat oxidation gene Ppar-α in the white adipose tissue. Notably, treatment with a combination of the two strains significantly reduced the plasma levels of the obesity hormone leptin and altered the microbiota and metabolome. The omics data also indicated the alteration of anti-obesity microbes and metabolites such as Akkermansia and indolelactic acid, respectively. These findings suggest that treatment with a combination of BEPC22 and BELP53 exerts synergistic beneficial effects against obesity.

Corresponding author **:** KilSoo Kim, Seokjin Kim

Keywords **:** Probiotics, Microbiota, Metabolome, Obesity

PS-D-001

Regulation of Chi3l1 expression in the mice uterus through estrogen receptor alpha

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In the uterus, responses to ovarian hormones like estrogen and progesterone lead to dynamic changes. Chitinase-like proteins (CLPs) in the glycoside hydrolase family 18 vary across species due to mutations in the enzymatic active site of chitinase. Chitinase-3 like 1 (Chi3l1), extensively studied in human and mice for immune regulation, saw increased mRNA expression with 17β-estradiol in ovariectomized wild-type mice, not in ERα knock-out or uterus-specific ERα conditional knock-out mice in microarray data. Chi3l1 mRNA and protein peaked during proestrus, declining by diestrus in the mouse estrous cycle. 17β-estradiol notably raised Chi3l1 levels in ovariectomized mice, particularly after 24 hours, but progesterone didn't affect Chi3l1 expression. Additionally, Chi3l1 was found exclusively in the luminal and glandular epithelial cells of the uterus, consistent with informatics analysis. By isolating primary uterine epithelial and stromal cells, we corroborated that Chi3l1 expression surged solely within the epithelial cells upon exposure to estrogen. Also, with uterine epithelial cell organoid, we verify the expression of Chi3l1 is induced by estrogen. Our findings unveil that estrogen can prompt an elevation in Chi3l1 mRNA and protein levels in uterine epithelial cells. Considering Chi3l1's involvement in epithelial-mesenchymal transition and angiogenesis, this suggests a potential crucial role for Chi3l1 in orchestrating the dynamic changes in the uterus triggered by estrogen.

Corresponding author **:** Youngsok Choi

Keywords **:** Uterus, Estrogen, Chi3l1, Immune regulation, Inflammation

PS-D-002

Efficacy study in a rat peripheral neuropathy (L5 spinal nerve ligation) model

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Neuropathic pain is an intractable pain caused by damage or functional abnormalities of the somatosensory system. 7%-10% of the global population is estimated to be affected by neuropathic pain, among which 20-25% of affected individuals have chronic pain. Complex aspects of neuropathic pain make it difficult to be completely cured, and chronically lasting pain significantly reduces patients' quality of life. Characterization of peripheral neuropathic pain model and development of evaluation methods for neuropathic pain behaviors exploiting human pain diseases are essential for discovering new mechanisms and novel treatments. This study evaluated mechanical and thermal allodynia in the rat L5 spinal nerve ligation (SNL) model. The rats were divided into three groups: sham-operated control, SNL model, and SNL model treated with pregabalin. Mechanical allodynia was measured 7, 22, 29, and 36 days post-surgery using the Von Frey test. Thermal allodynia was measured 25 and 32 days post-surgery using the Hargreaves test. The pregabalin (30 mg/kg, PO) was treated an hour before the Von Frey and Hargreaves test. Body weight was measured during entire experimental period. Compared to the sham-operated control group, the SNL group displayed significant mechanical and thermal allodynia in the ipsilateral hind paw. The Pregabalin-treated SNL group displayed significant reversion of mechanical and thermal allodynia. There were no significant differences in weight between the three groups. These results suggest that the L5 SNL model is suitable for evaluating novel treatment of neuropathic pain.

Corresponding author **:** Woori Jo

Keywords **:** Peripheral neuropathy, L5 spinal nerve ligation model, Von Frey test, Hargreaves test

PS-D-003

Genome-wide CRISPR screening to identify host factors for brain infection of SARS-CoV-2

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(Background & Aim) SARS-CoV-2, which causes Coronavirus disease 2019 (COVID-19), has been reported to infect the brain in addition to the lungs in certain cases, potentially contributing to increased lethality and long COVID. However, the mechanisms underlying brain infection remain largely unknow. To identify host factors essential for the brain infection, we conducted a genome-wide CRISPR/Cas9 knockout (KO) screen in human neuroblastoma cells. (Results) Our previous studies using COVID-19 mouse models revealed that brain infection by SARS-CoV-2 is not necessarily dependent on hACE2 expression. To uncover mechanisms of brain infection independent of hACE2, we infected human neuroblastoma cells, which exhibit low ACE2 expression, with SARS-CoV-2. Infection with Wuhan strain of SARS-CoV-2 at a concentration of 8x10^6 TCID50/ml resulted in approximately 2% infection rate, as confirmed by FACS analysis. In contrast, Vero-E6 cells, which are prone to infection, exhibited an infection rate of 39.61% at a concentration of 8x10^2 TCID50/ml. We performed two independent genome-wide CRISPR/Cas9 knockout screens using a lentiviral KO library with 90,709 sgRNAs targeting human genes in SK-N-SH cells expressing Cas9. Genomic DNA from surviving cells was harvested 7 days post-infection (DPI), and gRNA abundance was determined by NGS. We evaluated CRISPR hits and searched for genes targeted by gRNAs enriched and depleted. Additionally, by comparing these hits with those identified from genome-wide KO screening in the infection-prone Vero-E6 cells, we identified potential host factor candidates contributing to infection. RNA sequencing analyses were performed on mRNA extracted from the virally infected library cells, and the integration of amplicon NGS data with RNA-seq results identified pathways that are recurrently involved. (Conclusion) This study suggests potential host factors and pathways involved in brain infection, emphasizing the necessity for functional validation.

Corresponding author **:** Ho Young Lee , Je Kyung Seong, Jun Won Park

Keywords **:** SARS-CoV-2 , CRISPR-Associated Protein 9 , Angiotensin-Converting Enzyme 2 , Brain

PS-D-004

Mouse models for dynamics of epithelial cell plasticity during gastric carcinogenesis and metastasis

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Cancer cell plasticity is intricately interlaced with processes such as epithelial-mesenchymal transition (EMT) and mesenchymal-to-epithelial transition (MET), and the acquisition of stem cell-like characteristics. This study demonstrated the dynamics of epithelial cancer cell plasticity in GEM gastric cancer (GC) models, particularly focusing on context-dependent MET/EMT processes and their association with cancer stem cell (CSC) properties. Previous research showed that *Cdh1*$^{f/+}$;*Trp53*$^{f/f}$(ChetP) mice do not form GC, whereas the Smad4-deficient *Cdh1*$^{f/+}$;*Trp53*$^{f/f}$;*Smad4*$^{f/f}$(ChetPS) model exhibits complete loss of the remaining E-cadherin expression from the single *Cdh1* allele, leading to a loss of epithelial cell characteristics and cellular polarity, which in turn induces diffuse-type GC and metastasis. Additionally, ChetPS primary cancer cells (S1), established from E-cadherin-deficient cancer exhibited a partial EMT state (E-cadherin$^+$/Vimentin$^+$) and were characterized by the expression of cancer stem cell marker CD44 but not CD133, SCA-1 and ST2. Metastatic cancer cells (S1M), cultured from lung metastases formed after transplantation of S1, acquired heterogeneity, resulting in two subtypes showing different tumorigenesis, metastasis, and drug resistance: predominantly E-cadherin-negative cells (advanced EMT CSCs properties; E-cadherin-/Vimentin$^+$/CD133$^-$/ST2$^+$) and a minority of E-cadherin-positive cells (partial EMT state; E-cadherin$^+$/Vimentin$^+$/CD133$^+$/ST2$^-$). When S1M E-cadherin-negative cells were transplanted into mice, E-cadherin-positive cells became dominant. This dominance was influenced by whether the mice were immunocompetent or immunodeficient SCID mice, suggesting that the tumor microenvironment related to immunity may dynamically regulate the ratio of these subpopulations. The findings from this study, using mouse and cell models established by our team, demonstrate that the tumor microenvironment modulates EMT/MET states and CSC properties in gastric cancer cells. These results underscore the necessity for further investigation into the specific elements of the tumor microenvironment that influence epithelial cancer cell plasticity and heterogeneity.

Corresponding author **:** Jun Won Park

Keywords **:** Epithelial-Mesenchymal Transition, Tumor microenvironment, Cancer stem cell

PS-D-005

Immunization against SARS-CoV-2 immunologically inhibits metastatic colonization

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Background and Aims: Clinical cancer remission accompanied by an intense immune response after SARS-CoV-2 infection has been reported. Based on these clinical findings, we hypothesized that SARS-CoV-2 immunization would inflame the tumor microenvironment to reduce metastasis.
Results: To test our hypothesis, we utilized two SARS-CoV-2 immunization mouse models: immunization through infection and full recovery, and immunization with inactivated SARS-CoV-2 whole virus administration. Then, we challenged the immunized mice with melanoma and gastric cancer cells via intravenous (i.v.) injection to form metastatic colonization in the lung. Significantly, SARS-CoV-2 immunization reduced metastatic colonization in the lung. This reduction was characterized by increased infiltration and higher activation of dendritic cells (DC) and cytotoxic T lymphocytes (CTL), along with a reduction in myeloid-derived suppressor cells (MDSCs). Additionally, we observed the increase in pro-inflammatory cytokines, including CXCL1, which enhanced CTL cell function. Furthermore, we observed an increase in cancer- specific T cell activity and sensitization of tumors to anti-PD1 therapy following SARS-CoV-2 immunization. Interestingly, we identified antigen mimicry between SARS-CoV-2 and cancer peptides displayed by MHC, including TMCO6 (human: 292-299, mouse: 286-293) which shares homology with SARS-CoV-2 nucleocapsid amino acids (219 -228). Immunization with the inactivated SARS-CoV-2 whole virus or SARS-CoV-2 N (219-228) peptide led to a substantial decrease in metastatic colonization in TMCO6-over cancer cells, increasing the reactivity of SARS-CoV-2-specific CTLs to cancer cells.
Conclusion: Our findings reveal that immunization against SARS-CoV-2 immunologically inhibits metastatic colonization by strengthening anti-tumor innate immunity and cancer-specific CTL responses. Additionally, we found molecular mimicry between SARS-CoV-2 and cancer peptides.

***Corresponding author :** Je Kyung Seong, Jun Won Park

***Keywords :** COVID-19, Metastasis, Cytotoxic T cell, Dendritic cell, TMCO6

PS-D-006

Establishing rat endometrial organoids and verifying functional mimicry of uterine tissue

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Endometrial organoids recapitulate the complex structure and function of the endometrium and enable endometrial development and related diseases and inter-maternal interface studies, thereby minimizing ethical concerns in vivo experiments. However, in rat model, despite their similarity to humans and their various preferred experimental advantages over mouse models, studies associated with female genitals using rat models have been mainly conducted through embryonic stem cells, 2D culture cells, and in vivo models, and the establishment and study of endometrial organoids have been mainly conducted in humans and mice. Therefore, we established rat endometrial organoids, which have not been established to date. The established organoids showed morphological similarity with uterine tissue through immunohistochemistry (IHC) analysis , and it was verified that they could be cultured for a long time with possibility of freezing and thawing without cell senescence. We also confirmed that the organoid formation rate correlated with plasma progesterone hormone levels. In addition, the reactivity of progesterone receptor (PR), estrogen alpha receptor (ER) and CD163 according to the treatment of sexual steroids was analyzed in organoids by real-time PCR to investigate the actual uterine functional mimicry derived from it. In conclusion, rat endometrial organoids established in this study will be utilized as optimal alternative models for various female genital related research. This study was supported by BK21 FOUR Future Veterinary Medicine Leading Education and Research Center, NRF-2021R1A5A1033157 and IBS (550-20240037).

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***Keywords :** Adult stem cells (ASC), Endometrium, Organoids, Rat, Uterus

PS-D-007

Leptin receptor deficiency promotes carbon tetrachloride-induced liver tumor incidence in mice

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Leptin, as a key metabolic hormone, mediates its effects by binding to its receptor, leptin receptor (Lepr). Previous studies have revealed that the expression of Lepr is upregulated in human hepatocellular carcinoma (HCC) tissues. However, the role of Lepr in the liver tumorigenesis remains poorly understood. Here we tested the hypothesis that Lepr protects from liver tumor progression. In this study, we used Lepr-deficient mice (Leprdb/Korl) generated by CRISPR/CAS9 gene editing. Six-week-old male Leprdb/Korl and wild-type (WT) were given intraperitoneal injections with the carcinogen carbon tetrachloride (CCl4) for 24 weeks. Most of the CCl4-treated Leprdb/Korl mice had a higher tumor burden indicated by higher nodule numbers, larger nodule sizes, worsened liver pathology, and higher serum alpha-fetoprotein levels when compared with the CCl4-treated WT mice. Specifically, hepatocellular adenoma developed in 6 out 7 of the treated Leprdb/Korl mice, and HCC was found in only one nodule. The increased expression of genes/proteins, such as Lcn2, Epcam, Muc1, and Ggals3 that are associated with human tumorigenesis was observed in the livers of tumorigenic Leprdb/Korl mice. Interestingly, hepatic expression of cytochrome p450 2e1, which plays a suppressive role in HCC, was decreased in the CCl4-treated Leprdb/Korl mice compared to the treated WT mice. Bioinformatic analyses of genes with differential expression in RNA-seq data predicted an increase in cancer, chemical carcinogenesis, and drug metabolism pathways, etc. In addition, some somatic mutations were identified by Exome-seq in the CCl4-treated Leprdb/Korl mice. These findings suggest that CCl4-induced liver tumor can be promoted in Leprdb/Korl mice and disruption of leptin signaling via Lepr may affect liver tumorigenesis.

***Corresponding author :** Jong Kwon Lee

***Keywords :** Leprdb/Korl mice, Leptin receptor, Carbon tetrachloride, Liver tumor, Cytochrome p450 2e1

PS-D-008

Regulation of anti-inflammatory adipose foamy macrophages by growth differentiation factor 15 and β2-adrenergic receptor in alcohol-related liver disease

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Background: Alcohol-related liver disease (ALD) is a major cause of liver-related morbidity and mortality worldwide. Adipose tissue (AT) exacerbates ALD by releasing free fatty acids (FFAs), with foamy macrophages in AT contributing to lipid metabolism and inflammatory responses. Growth differentiation factor 15 (GDF15) and beta-2 adrenergic receptor (ADRB2) have been identified as key regulators of anti-inflammatory functions in macrophages. This study investigates the effects of GDF15 and ADRB2 on foamy AT macrophages (ATMs) in ALD.
Methods: Wild-type mice were fed a Lieber-DeCarli liquid ethanol (EtOH) diet (4.5%) for 8 weeks. Biochemical, histopathological, and bulk RNA-sequencing analyses were performed. Flow cytometry and single-cell RNA sequencing (scRNA-seq) were conducted on freshly isolated stromal vascular fractions (SVFs) from AT. *In vitro* experiments involved treating primary AT macrophages or RAW 264.7 cells with recombinant GDF15 and an ADRB2 agonist.
Results: Bulk-seq data revealed increasing lipid catabolism-related genes in AT, indicating adipocyte lipolysis, and serum FFA and catecholamine levels were increased. As alcohol metabolism occurred via CYP2E1 in AT, which increases ROS level, leading to an elevated level of GDF15 in adipocytes. Histology analysis confirmed formation of crown-like structures around injured adipocytes, where macrophages were infiltrated. Flow cytometry revealed most of these macrophages were fat droplet-storing F4/80^{high} macrophages (foamy ATMs). These foamy ATMs showed elevated ADRB2 expression, which suggested the role of ADRB2 in foamy macrophages. Moreover, scRNA-seq of SVFs revealed an increase in F4/80^{high} Trem2^{+} foamy macrophages with elevated expression of anti-inflammatory markers (*Adrb2, Trem2, Arg1*), and lipid storage-related genes. *In vitro*, EtOH exposure increased GDF15 expression in adipocytes, whereas treatment of GDF15 increased *Cd36* expression and ADRB2 agonist promoted anti-inflammatory foamy macrophages.
Conclusion: Our study revealed that alcohol intake induces the production of GDF15 in adipocytes and increases ADRB2 expression in neighboring ATMs. This process enhances the uptake of FFAs, promoting fat storage, and exerting anti-inflammatory properties in foamy ATMs. Thus, GDF15 and ADRB2 in AT may be therapeutic targets for ALD intervention.

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***Keywords :** Alcohol-related liver disease, B2-adrenergic receptor, Growth/differentiation factor 15, Foamy macrophage, Free fatty acid

PS-D-009

Lethal SARS-CoV-2 infection reduces tissue-resident macrophages and increases M2 macrophages accompanied by fibrotic reaction in the liver of COVID-19 mouse models

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Background and aims: Although SARS-CoV-2 is known to primarily target the lung, multiple lines of evidence suggest that SARS-CoV-2 infection affects extrapulmonary organ dysfunction, including in the liver. Tissue resident macrophages (TRMs) play important roles in maintaining tissue homeostasis, controlling infection, and resolving inflammation. Here, we investigated TRM changes in extrapulmonary organs and its mechanism in a COVID-19 mouse model.
Results: 10^5 PFU of SARS-CoV-2 caused severe weight loss and decreased body temperature at 7 days post infection (DPI) in K18-hACE2 mice, which could be defined as lethal. As a result of H&E and IHC analyses, no infection or inflammatory response was detected in extrapulmonary organs including the liver, kidney, heart, and intestine. Based on IHC analysis of F4/80, we found significant reductions of TRMs in these organs. In contrast, a non-lethal dose of SARS-CoV-2 10^2 PFU did not cause a reduction of TRMs. However, influenza A-infected mice with similar lethality to 10^5 PFU SARS-CoV-2-infected mice did not show a decrease in TRMs, implying that it might be a specific feature of SARS-CoV-2 infection rather than a nonspecific response to the lethal condition. IHC analysis of the apoptosis marker cleaved caspase-3 showed a significant increase in apoptosis of TRM in the liver of lethally SARS-CoV-2-infected mice. IF analyses showed an increase in the number of M2 macrophages in the same liver samples. Additionally, Sirius red staining and α-SMA IHC analysis revealed an increased fibrotic reaction in these livers.
Conclusion: We found that lethal SARS-CoV-2 infection might induce dysregulation of macrophage homeostasis in COVID-19 mouse models.

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***Keywords :** K18-hACE2, TRMs

PS-D-010

Humanized mice applying CD47;Prkcd;IL2rg triple KO mice exhibit enhanced human immune cell engraftment and reduced GvHD symptoms

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Recently, humanized mice (hu-mice) models, which are engrafted with human hematopoietic cells or lymphoid tissues in immunodeficient mice, have been widely used for various human diseases studies. Representative hu-mice models are human peripheral blood mononuclear cells (PBMC) and CD34+ hematopoietic stem cells (HSC) engrafted models. Each model has its own advantages and disadvantages, but variable immune cell transplantation efficacy and the occurrence of lethal graft-versus-host disease (GvHD) are common limitations. To overcome the limitations, we generated CD47; Prkdc;IL2rg triple KO mice (STKO) using NOD-Prkdc^{null}IL2rg^{null} mice (SID). Because CD47 is functionally known as a "don't-eat-me" signal and plays an important role in transplantation of human tissues and cells, we expected improved human cell engraftment and GvHD development in STKO mice. In HSC hu-mice analysis, the transplantation efficacy was enhanced that hCD45 of STKO exceeded 50% at 8 weeks after HSC transplantation, which was more than 50% enhanced than that of SID. By the time of last measurement (40 weeks), the engraftment of hCD45 as well as hCD3 in STKO were significantly enhanced than SID. Considering the body weight change, the survival rate, and clinical symptoms, GvHD was reduced in STKO. Similarly, the PBMC hu-mice studies showed that human leukocyte engraftment efficacy of human leukocytes and GvHD symptoms were improved in STKO. Especially, in the study applying low-dose PBMC to 4-weeks-old mice, long-term studies (over 10 weeks) were possible with minimal clinical signs despite the significant human leukocyte engraftment. Considering these results, STKO mice could be an alternative platform for generating humanized mice.

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***Keywords :** CD47, Graft-versus-host disease, Hematopoietic stem cells, Peripheral blood mononuclear cells , Humanized mice

PS-D-011

Male infertility phenotype in Ehf knock-out mice

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Ehf is a member of the epithelial-specific ETS subfamily and is a transcription factor specifically expressed in epithelial tissues (Kar and Gutierrez-Harmann, 2013). Recent studies have reported that Ehf promotes proliferation in gastric, thyroid, and ovarian cancer cell models and plays a crucial role in maintaining epidermal and intestinal homeostasis. However, no studies have been conducted on the expression and influence of Ehf on reproductive system in mammals. In this study, we conducted cross-mating experiments among different genotypic pairs of mice (Ehf+/+, Ehf+/-, Ehf-/-) aged over 8 weeks to investigate the impact of Ehf deficiency on male fertility in Ehf-/- mice. The results demonstrated that although Ehf-deficient mice were born normally, Ehf-deficient male mice were infertile and unable to produce offspring. Subsequently, we examined sperm viability and morphology. In in vitro fertilization experiments using fresh sperm and unfertilized WT oocytes, Ehf-/- sperm showed the lowest fertilization ability compared to Ehf+/+ sperm. Morphologically, many Ehf-/- sperm exhibited heads separated from tails, and tail fragments were observed. Additionally, the mRNA levels of CFTR, which mediates the transport of intracellular chloride ions across the membrane and facilitates bicarbonate secretion in the principal cells of the mouse epididymis (Andrology, 2019), decreased in cauda epididymis of Ehf-/- compared to Ehf+/+. These results suggest that the expression pattern of CFTR in the epididymis of Ehf-/- mice affects the epididymal lumen environment, causing issues in the process of sperm formation and contributing to infertility.

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***Keywords :** Ehf, Infertility, Sperm, CFTR

PS-D-012

TXNIP in Kupffer cells regulates liver injury, inflammation and fibrosis

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Kupffer cells play a crucial role in regulating the pathogenesis of chronic liver diseases such as metabolic dysfunction associated fatty liver disease (MAFLD), metabolic associated steatoheptitis (MASH) and alcoholic liver disease (ALD). Thioredoxin-interacting protein (TXNIP), a key mediator of cellular stress response metabolism, is involved in the development of various liver diseases. In this study, we investigated the role of TXNIP in Kupffer cells in the development of liver injury, inflammation and fibrosis. Myeloid specific TXNIP deficient mice (*TXNIP^{iLyz}*) and wild-type (WT) mice were administered intraperitoneal injections of carbon tetrachloride (CCL4) for 16 weeks. We also isolated Kupffer cells from *TXNIP^{iLyz}* and WT mice and then treated them with lipopolysaccharide (LPS). As a result, *TXNIP^{iLyz}* mice showed decreased levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and downregulated hepatic inflammatory cytokines such as tumor necrosis factor α (TNFα), interleukin-6 (IL-6) and IL-1β. *TXNIP^{iLyz}* mice also exhibited decreased positive areas of Sirius red staining and α-smooth muscle actin (αSMA). The level of TNF-α, IL-6, IL-1β and transforming growth factor β (TGF-β) were lower in LPS treated Kupffer cells isolated from *TXNIP^{iLyz}* mice than in LPS treated Kupffer cells isolated from WT mice. In consequence, our findings suggest that TXNIP in Kupffer cells regulates liver injury, inflammation and fibrosis, indicating that targeting TXNIP could be an effective strategy for mitigating liver disease

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***Keywords :** Kupffer cells, TXNIP, Liver fibrosis, Liver inflammation

PS-D-013

Regulation of ERa-induced IL36a in mouse uterus

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The uterus experiences intricate cyclical changes driven by the ovarian sex hormones, estrogen and progesterone. In mice, this estrous cycle includes the proestrus, estrus, metestrus, and diestrus phases. Precise temporal regulation of immune function in the uterine endometrium is essential, with endometrial steroid hormones modulating the inflammatory process. Diseases such as endometrial cancer and endometriosis are related to this immune regulation. RNA-seq data has confirmed that the IL36α expression in mouse uterine epithelial cells is regulated through estrogen receptor alpha (ERα)-dependent signaling. It was observed that the expression of the IL36α, which belongs to the IL1 family of pro-inflammatory cytokines involved in immune modulation, is significantly lower in endometrial cancer. Despite the connections between the IL36 subfamily and conditions like cancer or psoriasis, uterus-specific expression patterns remain unclear. Our findings indicate that IL36α expression peaks during the estrus phase of the normal estrous cycle, driven by estrogen, as shown by treatment with 17β-estradiol in ovariectomized mice. A similar pattern is observed at the IL36α protein level. Treatment with an ERα antagonist confirmed that this action is mediated by ERα. Immunofluorescence revealed exclusive localization of IL36α in mouse endometrial epithelial cells. Furthermore, mouse endometrial primary cells were isolated, demonstrating specific expression in epithelial cells in vitro. To explore the relationship with endometrial cancer, IL36α recombinant protein was administered to Ishikawa cells, showing differences in proliferation. Future studies will utilize IL36α knockout mice to investigate the role of IL36α in antitumor regulation within the uterus.

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***Keywords :** Uterus, Interleukin 36 alpha, Endometrial cancer

PS-D-014

Simultaneous mutation of Abhd14a and Tmem115 drives gastric tumor while displaying vulnerability to Wnt inhibitors

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Gastric cancer (GC) is a prevalent and lethal malignancy. Despite advancements in genome sequencing, which have identified frequently occurring mutations, the functional validation of these candidate driver genes remains largely unknown. Here, we performed in vivo CRISPR-Cas9 knockout (KO) screening in mouse stomach organoids to functionally validate GC driver gene mutations. Using genomic profiles of human GC, we identified the 18 most frequently mutated genes, excluding well-known driver gene mutations such as Smad4, Cdh1, Tgfbr, and Fbxw7. We created a pool of gRNA vectors targeting these genes, with each gene targeted by two gRNAs. The 36 gRNAs were pooled and transduced into *Trp53* KO mouse stomach organoids expressing Cas9, then implanted into immunodeficient NSG mice. The organoids formed tumors in 18% of injections (2/11), whereas *Trp53* KO organoids did not (0/8). In these two tumors, quantitative PCR analysis revealed that the frequency of *Rfc4, Tmem115, Abhd14a, Apc, Kctd7, Twf2*, and *Slc2a1* KO clones was enriched. Interestingly, analysis of TCGA GC patient data indicated that among these five genes, Abhd14a and Tmem115 simultaneously exhibited deep deletions and were mutually exclusive with already known driver gene mutations. Based on these findings, we individually and doubly knocked out *Abhd14a* and *Tmem115* in organoids and implanted them into NSG mice. Only the double KO led to tumor formation in 50% of injections (4/8), whereas single KO did not (0/10). RNA sequencing of the double KO organoids showed activation of the Wnt signaling pathway, which was confirmed by reporter assays. Additionally, increased sensitivity to Wnt inhibitors in the double knockout organoids was observed. The combined mutation of *Abhd14a* and *Tmem115*, functionally validated as a novel driver gene combination in GC, synergistically enhances tumorigenesis and activates the Wnt signaling pathway. This combination potentially increases susceptibility to Wnt inhibition, highlighting a promising therapeutic target for GC.

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***Keywords :** CRISPR-Associated Protein 9, Mutation, Stomach Neoplasms, Wnt Signaling Pathway

PS-D-015

Antidiuretic activity and safety of cephalotocin, an oxytocin/vasopressin-related peptide from octopus

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Cephalotocin is a peptide belonging to the oxytocin/vasopressin superfamily and was first isolated from a marine mollusk Octopus vulgaris. It differs from the antidiuretic hormone arginine vasopressin by two amino acids. Our previous study showed that cephalotocin selectively activates human vasopressin receptor types 1b and 2. While reducing the possibility of vasopressin receptor 1a-mediated side effects, cephalotocin has an significant antidiuretic effect: decreased urine output and increased urine osmolarity when intravenously injected into rats. In this study, we confirmed the antidiuretic activity of cephalotocin by measuring osmolarity of spot urine in normal C57BL/6 mice and in an experimental model of polyuria. Next, the safety of CPT was evaluated through acute toxicity test. There were no signs of acute toxicity in the mice administered a single oral dose of cephalotocin and in the mice used to confirm antidiuretic activity. Lastly, we analyzed the stability of cephalotocin over time under various temperature conditions. It is measured that the cephalotocin maintains its purity in frozen powder form and in aqueous solution over a period of time. In conclusion, we expect that cephalotocin can be developed into a pharmaceutical or health functional food ingredient for treating urological diseases such as nocturia, enuresis, and diabetes insipidus.

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***Keywords :** Cephaltocin, Vasopressin receptor, Antidiuretic, Nocturia, Polyuria

PS-D-016

TXNIP regulates the autophagy of liver sinusoidal endothelial cells

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Liver sinusoidal endothelial cells (LSECs) constitute the liver's first barrier of defense because of their unique position lining the sinusoidal lumen and LSECs fenestrae is critical to maintaining homeostasis in the liver parenchyma. Because of their localization in blood vessels, they are the first cell type to sense and respond to any environmental perturbation, and they have been shown to orchestrate the cellular response to liver injury. Autophagy is an endogenous protective system that can maintain LSECs differentiation and function. In the previous study, we found that thioredoxin interacting protein (TXNIP), a stress-response gene, is a key factor in regulating LSECs phenotype and function. In this study, we investigated the role of TXNIP in LSECs autophagy. We isolated primary LSECs from *Txnip*-knockout (KO) and wild-type (WT) mice and then treated them with lipopolysaccharide (LPS). Deletion of *Txnip* impaired LPS-induced LSECs autophagy as evidenced by decreased conversion of microtubule-associated proteins light chain 3B (LC3B-I) to LC3B-II and increased p62 (sequestosome-1) expression. In addition, the mRNA expression levels of the autophagy-related genes, unc-51 like autophagy activating kinase 1 (Ulk1/Atg1a), Ulk2/Atg1b, Atg2a, Atg3, Atg7, GABA type A receptor-associated protein-like 2 (Gabarapl2/Atg8), Atg12, and Atg13 was decreased in LPS-treated *Txnip*-deficient LSECs. Rapamycin treatment restored autophagy in LPS-treated *Txnip*-deficient LSECs, while leupeptin and chloroquine treatments accelerated autophagy in LPS-treated *Txnip*-deficient LSECs. In conclusion, our findings suggest that TXNIP in LSECs may be a potential target for enhancing endothelial autophagy, which can be beneficial in maintaining LSECs differentiation and function.

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***Keywords :** Liver sinusoidal endothelial cells, Autophagy, Differentiation, TXNIP, MAP1LC3B

PS-D-017

Hepatitis B virus X protein (HBx) induced an unbalanced metabolism of cholesterol and fibrosis in the high fat, high glucose liver

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Hepatitis B virus (HBV) is a significant causative agent in the pathogenesis of hepatocellular carcinoma (HCC) and is characterized by its persistent nature post-infection [1]. The HBV X protein (HBx) acts as a multifunctional transactivator during liver infection [2]. While HBx transgenic (Tg) mice have been employed to explore the mechanisms involved in HCC progression during aging, limited attention has been paid to the susceptibility of infected livers to external stimuli. This study aims to elucidate the increased susceptibility of chronic hepatitis B (CHB) patients' livers to diets high in fats and glucose. Through histological and molecular evaluations of HBx Tg mice fed a fructose-palmitate-cholesterol (FPC) diet, our research uncovered that HBx exacerbates the progression of fibrosis. Morphological assessment of hepatocyte zones revealed an augmentation in microvesicular steatosis score in zone 3 and elevated serum cholesterol levels in the presence of HBx. Analysis of RNA expression indicated a notable decrease in the expression of Cyp1a2, a gene essential for cholesterol homeostasis and predominantly expressed in zone 3, under the influence of HBx. These results suggest that HBx influences cholesterol metabolism. Consequently, individuals with CHB carrying HBx may undergo accelerated fibrosis and perturbed cholesterol metabolism when exposed to high-fat, high-glucose diets, leading to expedited liver damage compared to those lacking HBx. These findings emphasize the heightened risk of liver injury in CHB patients under dietary stress, highlighting the significance of careful dietary management in this population.

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***Keywords :** Hepatitis B virus X protein, Fibrosis, Cholesterol metabolism, Transgenic mice , Fructose-palmitate-cholesterol diet

PS-D-018

Adenosylhomocysteinase-like 1 regulates nutrient-induced insulin sensitivity through a calcium-dependent brown adipocyte activation

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Brown adipose tissue (BAT) combusts energy sources to produce heat in adult humans. The recent identification offers a new strategy to increase nutrient supply to mitochondria and reactivation of BAT to combat obesity and associated metabolic diseases in adult humans. According to a previous paper, *Inositol 1,4,5-trisphosphate receptors (InsP3Rs)* located in the endoplasmic reticulum (ER)-mitochondrial contacts (ERMCs) are essential for calcium transfer to mitochondria to facilitate oxidative metabolism. *Adenosylhomocysteinase-like 1 (Ahcyl1)* is a binding partner of IP3Rs and regulates calcium release, while whether and how *Ahcyl1* regulates calcium-dependent heat production is unknown. Here, we describe the elevated mitochondrial oxidative metabolism through increased calcium transfer and its effect on nutrient utilization in response to insulin signaling using BAT-specific *Ahcyl1* KO mice (cKO; $Ucp1^{Cre/+}$; $Ahcyl1^{fl/fl}$) and the *Ahcyl1* KO immortalized brown preadipocyte (iBPA) cell line. We found the gradually increased binding affinity between AHCYL1 and IP3Rs during the prolonged cold exposure period despite decreased expression levels of *Ahcyl1* and *Itprs* in iBAT of 8-week-old wild-type mice. After cold stimulation, we observed increased calcium-dependent dephosphorylation of PDH-E1α levels and upregulated UCP1 levels in cKO mice. These findings were also supported by the upregulated oxygen consumption rates in KO cells. This was because of enhanced lipid utilization with simultaneous lipolysis and nutrient-sensing kinase mTOR activation to supply fatty acid for mitochondrial uncoupled respiration in cKO iBAT. Finally, we test the insulin responsibility induced by refeeding the normal chow or high-fat diet after fasting. cKO mice revealed improved insulin sensitivity with upregulated p-AKT levels in epididymal white adipose tissue and elevated whole-body energy expenditure compared to control littermates. Our findings suggest that the increased sensitive calcium signaling in brown adipocytes could be a promising avenue for enhancing whole-body metabolism, offering a potential strategy to combat diet-induced obesity and insulin resistance.

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***Keywords :** Brown adipose tissue, Insulin sensitivity, Adenosylhomocysteinase-like 1, Calcium, Inositol 1, 4, 5-trisphosphate receptor

PS-D-019

Generation of mouse models using virus-like particles-packaged CRISPR ribonucleoproteins

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Genetically engineered mouse models (GEMMs) are essential to research on the causes and treatment of diseases and basic research. Although the production of GEMMs has been greatly simplified since the development of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology, it still relies on inefficient methods such as microinjection and electroporation, which require skilled technicians, complex machinery, and many zygote donor mice. Here, we addressed these challenges by achieving targeted mutagenesis through the use of virus-like particle (VLP) –packaged CRISPR ribonucleoproteins (RNPs). We cultured zygotes obtained through natural mating, traditionally used for GEMM production, with VLP-packaged CRISPR RNPs during in vitro culture to test whether the editing efficiency varies depending on the culture time and concentration of the VLP-packaged CRISPR RNPs. Moreover, to generate GEMM using a small number of mice, we applied VLP-packaged CRISPR RNPs to in vitro fertilization (IVF). We conducted experiments by varying the concentration of VLP-packaged CRISPR RNPs in sperm pre-incubation, fertilization, or post-fertilization culture. Using zygotes obtained through natural mating, we found that overnight culture with a high concentration of VLP-packaged CRISPR RNPs resulted in high editing efficiency without hindering developmental rates. Additionally, treating zygotes obtained through IVF with VLP-packaged CRISPR RNPs during the culture stage was necessary to achieve high editing efficiency without hindering developmental rates. Finally, we treated zygotes obtained from natural mating and IVF with VLP-packaged CRISPR RNPs to generate *Plin1*- and *Tyr*- knockout (KO) mice. We then confirmed germline transmission and phenotype. This method further simplifies and accelerates GEMM generation using a small number of mice without requiring specialized techniques or equipment.

***Corresponding author :** Kyoungmi Kim, Je Kyung Seong

***Keywords :** Genetically engineered mouse models, Clustered Regularly Interspaced Short Palindromic Repeats, Virus-Like Particle, In Vitro Fertilization

PS-D-020

Establishing a clinically relevant mouse model of acute kidney injury using the Small Animal Radiation Research Platform (SARRP)

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Radiation is significant modality for anti-cancer therapy, but tissue injury are common side effects. Although radiation nephropathy has been characterized by numerous animal studies, it is necessary to clinically relevant, more advanced irradiation technique are definitely needed in a preclinical setting. The goal of this study is to create an optimal mouse model of radiation-induced acute kidney injury(AKI) using the SARRP that mimics clinical radiation oncology treatment conditions. BALB/c mice were irradiated with a radiation dose(30Gy) determined based on the results of serum analysis and immunohistochemical staining in three ways: 1. A single arc using CT scanning(K1, one kidney), 2. Two arcs and two single static beams using CT scanning(K2, both kidneys), and 3. X-ray and a single static beam(AI, abdominal irradiation including the kidneys). They then determined which method most effectively induced AKI five days after irradiation. The results showed that the K2 group showed significant weight loss compared to the K1 and AI groups($p<0.001$ and $p<0.05$, respectively), and significant renal atrophy compared to the K1 group($p<0.05$). BUN levels in serum were significantly increased in the K2 group compared to the sham group and the K1 group($p<0.05$, $p<0.01$, respectively). H&E staining showed that the K2 group had the most severe damage, including granular casts and renal tubular necrosis. The AKI index of the K2 group was assessed as significantly increased compared to all groups. The K2 group had increased expression of novel biomarkers of AKI (NGAL, Kim-1) and DNA damage markers (γ-H2AX, MDA, caspase-3) compared to K1 and AI. This is the first AKI model created using SARRP that delivers calculated doses to the kidney and decreases irradiation of extra-renal tissue in a clinically relevant manner, which is expected to improve the accuracy of research in this area by reducing the gap between clinical and non-clinical studies.

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***Keywords :** AKI, Kidney, Mouse , Radiation, SARRP

PS-D-021

Compositional changes in fecal microbiota in a C57BL/6-Tg (NSE-haSyn) mice as novel Parkinson's disease model

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The gut–brain axis (GBA) in Parkinson's disease (PD) has only been investigated in limited mice models despite dysbiosis of the gut microbiota being considered one of the major treatment targets for neurodegenerative disease. Therefore, this study examined the compositional changes of fecal microbiota in novel transgenic (Tg) mice overexpressing human α-synuclein (hαSyn) proteins under the neuron-specifc enolase (NSE) promoter to analyze the potential as GBA model. The expression level of the αSyn proteins was significantly higher in the substantia nigra and striatum of NSE-hαSyn Tg mice than the Non-Tg mice, while those of tyrosine hydroxylase (TH) were decreased in the same group. In addition, a decrease of 72.7% in the fall times and a 3.8-fold increase in the fall number was detected in NSE-hαSyn Tg mice. The villus thickness and crypt length on the histological structure of the gastrointestinal (GI) tract decreased in NSE-hαSyn Tg mice. Furthermore, the NSE-hαSyn Tg mice exhibited a significant increase in 11 genera, including Scatolibacter, Clostridium, Feifania, Lachnoclostridium, and Acetatifactor population, and a decrease in only two genera in Ligilactobacillus and Sangeribacter population during enhancement of microbiota richness and diversity. Therefore, the motor coordination and balance dysfunction of NSE-hαSyn Tg mice may be associated with compositional changes in gut microbiota. In addition, these mice have potential as a novel mouse model for GBA study.

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***Keywords :** Parkinson's disease, A-Synuclein, Gut–brain axis, Microbiota, Transgenic mice

PS-D-022

LRIG1 represents pancreatic acinar cells capable of expansion in homeostasis and regeneration

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The exocrine pancreas is primarily composed of long-lived acinar cells and is generally considered to lack adult pancreatic stem cells. However, several studies labeling pancreatic acinar cells with stem cell markers such as Bmi1 and Dclk1 have demonstrated distinct lineage patterns, indicating the existence of progenitor-like subpopulations among acinar cells. Recent single-cell RNA-sequencing studies further support that acinar cells represent a heterogeneous population. Lrig1 is known as negative regulator of EGFR and marker of proliferative and quiescent stem cells in the skin and intestine. Here, we investigated whether Lrig1 can represent proliferative property of pancreatic acinar cell. Long-term (1 year) lineage tracing was performed using Lrig1-CreERT2/+;R26R-mTmG mice to examine whether the Lrig1-marked cells are capable of renewing pancreatic acinar cells. To confirm whether the Lrig1-marked cells are pancreatic acinar progenitor cells, we additionally conducted lineage tracing of randomly marked acinar cells using Mist1-creERT2/+;R26R-mTmG mice, as Mist1 is a marker of all pancreatic acinar cells. In the exocrine pancreas, Lrig1 expression was limited to the acinar cells and not observed in the ductal cells. During homeostasis, long-term lineage tracing showed that the Lrig1-marked acinar cells renewed the pancreas by forming expanding clones and randomly marked acinar cells also form these clones. Moreover, following caerulein-induced pancreatitis injury in Lrig1/mTmG mice, Lrig1-marked acinar cells rapidly formed large clones to regenerate the damaged pancreatic acinar cells. Taken together, our findings suggest that Lrig1 expression represents pancreatic acinar cells are facultative progenitor in the mouse exocrine pancreas.

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***Keywords :** Pancreas, Proliferation, Lrig1, Lineage tracing

PS-D-023

Novel role of ALPI gene associated with constipation caused by complement component 3 deficiency

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Complement component 3 (C3) deficiency has recently been reported as one of the novel causes of constipation. To identify a unique gene specific to constipation caused by C3 deficiency, the total RNA extracted from the mid colon of C3 knockout (C3 KO) mice was hybridized to oligo-nucleotide microarrays, and the function of the candidate gene was verified in *in vitro* and *in vivo* models. There was a significant reduction in the number of stools, gastrointestinal (GI) transit, colon length, mucosal layer thickness, and muscle layer thickness in the C3 KO mice. Overall, compared to the wild type (WT), 1,237 genes were upregulated, and 1,292 genes were downregulated in the C3 KO mice. Of these, the major genes included were lysine (K)-specific demethylase 5D (*KDM5D*), olfactory receptor 870 (*Olfr870*), pancreatic lipase (*PNLIP*), and alkaline phosphatase intestinal (*ALPI*). Specifically, the *ALPI* gene was selected as a novel gene candidate based on alterations during loperamide (Lop)-induced constipation and intestinal bowel disease (IBD). The upregulation of *ALPI* expression treated with acetate recovered the expression level of mucin-related genes in primary epithelial cells of C3 KO mice as well as most phenotypes of constipation in C3 KO mice. These results indicate that several gene functional groups and individual genes serve as novel biomarkers in constipation caused by C3 deficiency. Also, the present results indicate that *ALPI* plays an important role as the novel gene associated with C3 deficiency-induced constipation.

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***Keywords :** Constipation, Microarray analysis, Complement C3, C3 knockout, ALPI

PS-D-024

Laparoscopic ovum-pick up in common marmoset

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Ovum pick-up (OPU) by laparotomy is important procedure and general method in transgenic research of marmoset (*Callithrix jaccus*). OPU using laparoscopy can provide several advantages such as minimal incisions, less pain, faster recovery and good quality of oocytes. The ovaries were stimulated using the modified follicular stimulation protocol with cloprostenol, menotrophin and human chorionic gonadotropin (hCG) by monitoring plasma progesterone and hCG levels. The donor animal was anesthetized using ketamine induction and isoflurane maintenance, and the abdomen was insufflated with CO_2 to a pressure of 8 mmHg using Veress needle. A modified 3.5-mm cannula for telescope (0°, 3-mm diameter, 14-cm length) was placed at 0.3-cm caudal to the umbilical scar, and two modified 2-mm cannulae for grasper and aspiration needle were inserted in a nonvascular area, paramedian to the midline and at the level of the inguinal fold. The oocytes were aspirated from over 2-mm or greater follicles on ovaries which were identified by a telescope. Collected oocytes were maturated for 24 h using modified HP-POM (Cosmo Bio USA, CA, USA), and fertilized in modified TYH medium (LSI Medience Corporation, Tokyo, Japan) for 19 h with spermatozoa which were collected from healthy and an experienced male marmoset using noninvasive penile vibrostimulation. Fertilized oocytes were cultured in modified Cleav™ and Blast™ media (CooperSurgical., CT, USA) until reach blastocyst. The oocytes were incubated at 38°C in humidified atmosphere containing 5% CO_2, 5% O_2 and 90% N_2. Eight oocytes were obtained by OPU from a female marmoset, and 6 oocytes were maturated and fertilized with collected spermatozoa (rate: 75% - 6/8), and 3 oocytes were developed to blastocyst (rate: 50% - 3/6). The developed laparoscopic OPU system for common marmoset may be efficient for OPU and collected oocytes were fertilized and developed to blastocysts as relatively high rate.

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***Keywords :** Assisted reproductive technology, Non-human primate, Minimally invasive, Monkey, Embryo

PS-D-025

The medical screening of causative factors for osteoporosis in Macaca fascicularis

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Osteoporosis is a skeletal disease characterized by diminished bone mineral density (BMD) and mass, remaining silent until fractures occur. The structure and elasticity of the bone matrix could be deteriorated by an imbalance derived from decreased bone formation and increased resorption. The factors influencing osteoporosis include sex, age, body size, dietary habits, medications and hormonal fluctuations. Diagnostic methods involve direct measurement of BMD through dual-energy X-ray absorptiometry (DXA) and the analysis of bone turnover markers, which indirectly assess bone formation and resorption in body fluids. In the present study, we conduct medical screening that involves weight-for-height indices (WHI), and reports of blood hematology and biochemistry to identify crab-eating monkeys (*Macaca fascicularis*) at higher risk of developing an osteoporosis. We aim to analyze the patterns of numerical changes throughout stages of aging in *Macaca fascicularis* for each sex before proceeding analysis with bone turnover markers. Blood analyses carried out on 157 monkeys (58 males, 99 females) to examine 20 hematological and 16 biochemical parameters. We confirmed that WHI calculated from weight in kilograms accurate to one decimal, height measured from its bottom to head while seating, and abdominal circumference. The results of the screening could be used for valuable data for selecting candidates for control and experimental groups, testing the ability of bone turnover biomarkers, and verifying a spontaneous model of osteoporosis.

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***Keywords :** Macaca fascicularis, Osteoporosis, Medical screening

PS-D-026

Cannabinoid receptor 1 antagonist (AM251) reduces pancreatic β-cell apoptosis in STZ-induced diabetic female mice

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Diabetes is mainly caused by problems in glucose metabolism and pancreatic β-cell dysfunction, leading to insulin resistance. Previous studies have shown that the onset of diabetes varies by gender, making it a critical factor in research. Other research has found that excessive activation of cannabinoid receptors is strongly associated with diabetes. This study investigated the relationship between sex and cannabinoid receptor activity by administering the cannabinoid receptor 1 antagonist (AM251) to streptozotocin (STZ)-induced diabetic mice. During the experiment, both male and female STZ groups showed impaired FBG and glucose tolerance compared to the control. However, after 4 weeks, the STZ+AM groups showed reduced FBG levels compared to 1 week before, with females showing particularly improved glucose tolerance. In the STZ group, pancreatic β-cell function and insulin sensitivity were impaired, while insulin resistance increased. In contrast, STZ+AM groups, especially females, showed improved pancreatic β-cell function and insulin sensitivity. The glucagon/insulin ratio, which indicates changes in pancreatic cell composition, increased significantly in both male and female STZ and STZ+AM groups compared to the control at 2 weeks. After 4 weeks, the F-STZ+AM groups showed a significant decrease compared to the F-STZ group. The expression of PDX-1, a marker of β-cell proliferation, increased significantly in the STZ+AM groups at 2 weeks, consistent with the increased insulin expression. This suggests that β-cell proliferation initially affected insulin secretion and, over time, β-cell apoptosis decreased, particularly in females. These results indicate that administration of the cannabinoid receptor 1 antagonist AM251 to STZ-induced diabetic mice attenuates diabetes and has a more pronounced effect in females.

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***Keywords :** Diabetes, Cannabinoid receptor 1, AM251, Apoptosis, Sex differences

PS-D-027

MRI-based investigation about Focal induction of reactive astrocytes in cortex

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This study aimed to develop and evaluate a focal reactive astrocyte mouse model for neurostimulation research. To induce focal astrocyte reactivity in the primary motor cortex (M1), we employed inducible diphtheria toxin receptor (iDTR) mice and directly administered AAV5-GFAP-mCherry-Cre viral vectors into the M1 region. Astrocyte-specific reactivity was induced by intraperitoneally administering diphtheria toxin (DT). Immunohistochemistry (IHC) and confocal microscopy analyses targeting GFAP and NeuN revealed pronounced astrocyte reactivity within the M1, while neurons in the same region showed no significant changes. In this study, we performed in vivo diffusion tensor imaging (DTI) using a 7T animal MRI scanner to evaluate the M1 region. Analysis of the DTI images showed the changes in fractional anisotropy (FA) values and mean diffusivity (MD) values. These findings were consistent with IHC results, showing that changes in FA and MD values corresponded to the observed alterations from IHC. The concordance between DTI results and IHC results suggests that DTI analysis might serve as an effective non-invasive histological alternative for detecting neuronal and astrocytic changes in the motor cortex (M1) of the mouse brain. In conclusion, we successfully established a mouse model with focal astrocyte reactivity in the primary motor cortex (M1) and demonstrated that diffusion tensor imaging is a valuable and reliable tool for non-invasively detecting histological changes in the brain.

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***Keywords :** DTI, M1

PS-D-028

Extracts of Dipterocarpus tuberculatus have a great potential as an effective anti-obesity treatment in Lep knockout mice

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Dipterocarpus tuberculatus (*D. tuberculatus*) extracts have been extensively studied for their therapeutic benefits in addressing inflammation, photoaging, and gastritis. However, their potential role in combating obesity is still being explored. To investigate this potential, we conducted a study where we administered a methanol extract of *D. tuberculatus* (MED) orally to Lep knockout (KO) mice over a duration of 4 weeks. The aim was to thoroughly examine the therapeutic effects of MED on various obesity-related parameters, including weight gain, fat accumulation, lipid metabolism, inflammatory response, and β-oxidation. Our results showed that MED administration led to a significant reduction in several key areas including weight gain and food intake were markedly decreased among the MED-treated Lep KO mice compared to controls, and total cholesterol and triglyceride levels were significantly lowered. Additionally, reductions in fat mass and the sizes of adipocytes were observed, indicating decreased fat accumulation. MED treatment also resulted in reduced liver weight and a decrease in the number of lipid droplets in liver tissues, suggesting improved liver health and reduced fat deposition. The molecular mechanisms behind these effects were explored, revealing that the expression levels of genes associated with adipogenesis and lipogenesis were significantly downregulated in the MED-treated group, while genes related to lipolysis were also affected. MED exhibited notable anti-inflammatory effects by downregulating the iNOS-mediated COX-2 induction pathway and the inflammasome pathway, leading to lower levels of inflammatory cytokines in the liver. An increase in β -oxidation was noted, indicating enhanced breakdown of fatty acids in the MED-treated mice. In summary, MED effectively reduces weight gain, fat accumulation, and inflammation while enhancing lipid metabolism and fatty acid breakdown. These results underscore the potential of MED as a promising anti-obesity treatment, providing a multifaceted approach to managing obesity and its related complications.

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***Keywords :** Dipterocarpus tuberculatus , Anti-obesity, Lipogenesis, Lipolysis, Inflammasome

PS-D-029

DGCR8 is essential for the differentiation of myeloid cells within the bone marrow microenvironment

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MicroRNAs are small regulatory RNAs that regulate protein expression and have key roles in various biological processes, including cell proliferation, differentiation, development, apoptosis, metabolism, cancer, and hematopoiesis. The production of normal microRNAs requires enzymes such as DGCR8 and DICER. DGCR8, a double-stranded RNA binding protein, is involved in the miRNA biogenesis pathway by interacting with DROSHA. DGCR8 is also important for stem cell homeostasis. Deletion of Dicer in bone marrow microenvironments leads to myeloid dysplasia and acute myeloid leukemia in mice. In this study, we report that deleting Dgcr8 in the bone marrow microenvironment (Dgcr8Δ/Δ) is crucial for maintaining mature hematopoietic lineage cells in the blood, resulting in increased myeloid cells and decreased B cells in the bone marrow. Additionally, hematopoietic stem cells (HSCs) did not survive at the Dgcr8Δ/Δ setting under transplantation stress. Furthermore, under transplantation conditions, Dgcr8Δ/Δ recipient mice showed myeloid expansion in the bone marrow. Our findings indicate that DGCR8 is important for myeloid cell differentiation within the hematopoietic system.

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***Keywords :** MicroRNA, DGCR8, DICER

PS-D-030

Protective effects of green pine cone extract on the HCl/ethanol-induced acute gastritis model

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Gastritis refers to a condition in which the gastric mucosa is inflamed, and is generally characterized by inflammatory cells found within the lamina propria of the stomach. Extracts of green pine cones are known to have high antioxidant and anti-inflammatory properties. Our study evaluated the protective effect of green pine cone (GPC) extract on HCl/ethanol-induced acute gastritis model. To achieve this, ICR mice were firstly divided into 2 groups; No group (normal group) and gastritis group (HCl treated group). And then, gastritis groups further divided into four groups; Vehicle treated group (HCl+dH_2O treated group), Low concentration GPC (LGPC) treated group (HCl+50 mg/kg GPC), Mid concentration GPC (MGPC) treated group (HCl+100 mg/kg GPC), High concentration (HGPC)treated group (HCl+ 200 mg/kg GPC treated group). They were administrated with appropriate amount of GPC or dH_2O for 2 weeks, and finally treated with 70% EtOH in in 150 mM HCl solution for 1 hour. Firstly, the stomach lesion index was significantly decreased with dose-dependent manner in GPC treated group compared to Vehicle treated group, while a significant decrease in the level of mucosal injury, edema and the number of inflammatory cells was similarly detected in the same group. Also, GPC treatment induced the decrease on the transcription levels of four inflammatory cytokine genes including IL-6, IL-1b, TNF-a and TGF-b. However, any significant toxicity was not detected in three GPC treated group. Overall, the results of this study suggest that GPC may have anti-gastritis activity through the inhibition of inflammatory cytokine expression.

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***Keywords :** Green pine cone, Gastritis, Inflammatory cytokines, Stomach injuries

PS-D-031

Therapeutic strategies of FXR signaling and one carbon metabolism for the treatment of colorectal cancer

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Colorectal cancer (CRC) is one of the most prevalent cancers with a poor prognosis, and bile acids are a significant risk factor. Bile acids, produced by the liver to aid in the digestion of dietary lipids, have toxic properties due to their detergent-like nature. Studies have shown a link between continuous bile acid exposure and CRC, particularly involving the farnesoid X receptor (FXR). FXR deficiency is often observed in CRC, indicating that restoring or activating FXR might be a viable treatment approach. However, while FXR activation reduces the number of intestinal cancer stem cells and slows cancer progression, it does not induce cell death, and the exact mechanism remains unclear. We hypothesized that cells activated by FXR utilize an alternative survival pathway. Our study revealed that FXR activation upregulates one-carbon (1C) metabolism genes, which are involved in processes such as nucleotide synthesis and reactive oxygen species (ROS) regulation and are linked to several cancers. Previous research has underscored the importance of 1C metabolic genes in promoting cancer proliferation by maintaining cellular functions. By analyzing clinical data from Colon Adenocarcinoma (COAD) patients, particularly TCGA-COAD data, we found consistent expression patterns of specific 1C metabolic genes following FXR activation. Importantly, patients with high expression levels of both ATF4 and 1C metabolic genes had poorer prognoses, indicating that the 1C metabolism pathway is crucial for cancer survival. We suggest that CRC cells, despite reduced proliferation due to FXR activation, survive via the 1C metabolic pathway. Our findings propose new therapeutic strategies for CRC by targeting FXR and its associated metabolic pathways, potentially improving patient outcomes.

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***Keywords :** Colorectal cancer, FXR, 1c metabolism

PS-D-032

Estrogen-P2ry2 orchestrates MAPK signaling in mouse uterus and promotes epithelial-mesenchymal transition in endometrial cancer cell

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Elucidating the molecular intricacies governing uterine development and function is crucial for reproductive success and addressing uterine pathologies. The interplay between estrogen-related cytokines, growth factors, and receptors maintains a robust uterine microenvironment. The purinergic Receptor P2Y, G-protein coupled 2 (P2ry2), regulates immune responses, inflammation, and cellular processes like migration, proliferation, and apoptosis. This study investigates the estrogen-mediated regulation and mechanisms of P2ry2 expression in the mouse uterus, using both in vivo and in vitro models, to understand the P2ry2 signaling pathway and its role in endometrial carcinoma cells. Our findings revealed a dynamic pattern of P2ry2 expression, which increased during the proestrus and estrus stages of the estrous cycle and decreased during metestrus and diestrus. P2ry2 expression rapidly elevated during the early time points following estradiol administration, an effect that was diminished by the ERα antagonist ICI 182,780, indicating that estrogen activated P2ry2 through ERα. Furthermore, we identified that estrogen and inhibitor treatments regulated MAPK-related genes in mouse uterine epithelial cells. Specifically, estrogen treatment gradually induced phosphorylation of Erk1/2 and Stat3, which were inhibited by an ATP antagonist, a P2ry2 antagonist and a MEK inhibitor. Additionally, P2ry2 induced cell migration and epithelial-mesenchymal transition (EMT) in Ishikawa cells, confirmed through wound healing assays and Western blot analysis. Our research elucidates the regulation and downstream signaling pathway of estrogen-induced P2ry2 in the mouse uterus and shows that P2ry2 induces cell migration and EMT in endometrial cancer cells. These findings suggest that targeting the P2ry2 signaling pathway could offer novel therapeutic strategies for treating endometrial cancer and various uterine disorders.

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***Keywords :** P2ry2, Estrogen, EMT, Uterus, Endometrial cancer

PS-D-033

3D organotypic culture of human follicle dermal papilla cells and their implantation for enhanced hair follicle regeneration

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Human follicle dermal papilla cells (HFDPC) are a population of cells located in the bulge of the hair follicle that play a significant role in the morphogenesis and regeneration of hair growth. In addition, they possess unique characteristics such as aggregation behavior, the ability to regenerate hair follicles, and growth factor induction. Recent advancements in various three-dimensional (3D) biological model systems, including spheroids and organoids, can be used to restore the original phenotype and induce hair follicle formation. Here, we developed a 169-well organoid plate that employs the hanging drop system to generate HFDPC organoids. HFDPC organoids exhibit 3D spherical formation, higher monodispersity, and can be mass-produced in a single culture plate. Interestingly, when we implanted HFDPC organoids into the wounds on mice, they demonstrated significant enhancement of hair follicle regeneration compared to HFDPC spheroids. Therefore, we believe that HFDPC organoids produced using the 169-well organoid plate have significant potential for hair follicle formation, particularly in the fields of regenerative medicine and tissue engineering.

***Corresponding author :** Sung-Min Kang

***Keywords :** Organoid, Hanging drop, Human follicle dermal papilla cell hair follicle regeneration

PS-D-034

Characterization of age-dependent phenotypes in a C57BL/6-Tg(NSE-hPS2*N141I)Korl mice as Alzheimer's diseases model

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To evaluate its potential as an Alzheimer's model animals, alterations on their phenotypes including behavioral changes, Ab accumulation, shrink of hippocampus, neuronal cell deaths and mTOR signaling pathway were analyzed in C57BL/6-Tg (NSE-hPS2*N141I)Korl mice with three different ages. In Morris water maze test, the time of first enter to target were higher in all age of Tg mice than Non-Tg mice, while the resting time in zone and times of target crossing were lower in the same group. Also, in passive avoidance test, the time of first enter to dark box were significantly decreased in 12- and 14-month-old mice compared to Non-Tg mice. The region of cortex and hippocampus were significantly shirked in the cortex and hippocampus of 14-month-old mice during ex vivo magnetic resonance imaging (MRI) analyses. The accumulation level of Ab were significantly increased in the cortex and hippocampus of 12- and 14-month-old mice compared to those of Non-Tg mice although 10-month-old mice showed constant level. Furthermore, the phosphorylation level of mTOR were remarkably enhanced in only hippocampus of 14-month-old mice, while the significant increase on the cleavage of Cas-3 were detected in the cortex of the same mice. Therefore, the results of the present study suggest that C57BL/6-Tg(NSE-hPS2*N141I) Korl mice with 14-month-old age may exhibit significant phenotypes for Alzheimer's disease. In addition, this model animal has the potential to be used to evaluate the therapeutic effects of medicine for Alzheimer's disease.

***Corresponding author :** Dae Youn Hwang

***Keywords :** Alzheimer's disease, Transgenic mice, Presenilin 2, Abeta, MRI

PS-D-035

Loss of ChREBP heightens susceptibility to osmotic diarrhea and compromises gut barrier function under PEG Treatment

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Osmotic diarrhea, a common condition in humans, is often caused by food intolerance, malabsorption, and the widespread use of laxatives. Carbohydrate response element-binding protein (ChREBP) is a transcription factor predominantly expressed in the liver, adipose tissue, and intestine. In ChREBP knockout (KO) mice, a high-fructose diet leads to osmotic diarrhea due to changes in gut microbiota and short-chain fatty acids. To elucidate the mechanisms underlying osmotic stress-induced diarrhea, ChREBP KO mice were administered 10% polyethylene glycol 3350 (PEG) in their drinking water and subsequently analyzed for intestinal disease phenotypes. PEG-treated ChREBP KO mice exhibited significant body weight loss and increased diarrhea. These mice also showed heightened gut permeability and motility. qPCR analysis revealed elevated expression of TNF-α in the small intestine of PEG-treated ChREBP KO mice compared to wild-type (WT) controls. While PEG treatment did not affect cell viability in Caco2bbe cells, it directly induced permeability through activated JNK signaling. ChREBP levels remained unchanged in PEG-treated Caco2bbe cells, although ChoRE luciferase reporter activity decreased. Overexpression of ChREBP/Mlx in Caco2bbe cells improved barrier integrity and reduced PEG-induced JNK signaling. Our findings (1) demonstrate that ChREBP gene deletion increases susceptibility to PEG-induced osmotic diarrhea and (2) underscore the crucial role of ChREBP in maintaining intestinal barrier integrity against osmotic stress-induced leaky gut. This work was funded by the Basic Science Research Program via the National Research Foundation, by the Ministry of Education [2022R1I1A1A01071897] to SH, and by the Ministry of Education, Science, and Technology [2022R1A2C1012833] to J-YC.

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***Keywords :** ChREBP, Osmotic stress, Gut barrier, Permeability

PS-D-036

Aortic inflammation and Wnt signaling undergo activation in the context of spondyloarthritis in the HLA-B27 transgenic rat model

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Introduction: Despite the well-documented link between cardiovascular (CV) disease and spondyloarthritis (SpA), no animal studies have empirically validated this connection or integrated SpA, vascular inflammation, and Wnt signaling into a single study. This study examines these associations using the HLA-B27 transgenic (TG) rat model, which closely mirrors human SpA.
Methods: Six-week-old HLA-B27 TG rats were injected with *M. tuberculosis* in incomplete Freund's adjuvant, while control Lewis rats received phosphate-buffered saline. At seven weeks, HLA-B27 TG rats were classified into two groups: F1 G0 (no arthritis) and F1 G6 (severe arthritis). Both groups, along with control rats (Ctrl G0 and Ctrl G6), were analyzed for aortic protein levels. Histological examination of tail spine samples graded inflammation, bone destruction, and osteoproliferation.
Results: All F1 G6 rats developed clinical arthritis, with 60% also exhibiting spondylitis. Histological analysis revealed a correlation between inflammation and osteoproliferation in F1 G6 rats ($r2 = 0.7992$, $p = 0.041$). Aortic protein levels were significantly higher in F1 G6 rats compared to Ctrl G6 rats, with increased expressions of WNT3, LRP5, WNT5, Runt-related transcription factor 2, TNFα, and IL-17 (all $p = 0.009$, except TNFα at $p = 0.028$). Elevated levels of WNT3, LRP5, WNT5, matrix metalloproteinase 3, TNFα, IL-17, and IL-23 were also observed in F1 G6 compared to F1 G0 rats (all $p < 0.05$).
Conclusion: These findings suggest that arthritis and spondylitis in SpA may contribute to the development of CV disease by activating Wnt signaling, MMP3, and inflammatory pathways in the CV system.

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***Corresponding author :** Seong-Ryul Kwon

***Keywords :** Inflammation, Spondyloarthritis, Cardiovascular disease, Wnt Signaling Pathway, Mmp3 Metalloproteinase

PS-D-037

Inhibition of Kxxx as a potential therapeutic strategy for kidney fibrosis

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Kidney fibrosis is a common pathological condition that leads to chronic kidney disease (CKD) and eventually renal failure. Renal failure is a critical condition that leaves patients with only two treatment options: dialysis or kidney transplantation, both of which significantly impact patients' quality of life and pose substantial healthcare burdens. Therefore, understanding the underlying mechanisms of kidney fibrosis and finding new therapeutic targets is paramount. In this study, we investigated the role of Kxxx in renal fibrosis. We found that the absence of Kxxx confers a protective effect against renal fibrosis. In vitro experiments, we demonstrated that Kxxx promotes epithelial-mesenchymal transition (EMT), a critical process in fibrosis development. Using a unilateral ureteral obstruction (UUO) mouse model, we observed that Kxxx knockout mice exhibited significantly less kidney fibrosis than wild-type controls. Similarly, in a folic acid-induced renal fibrosis mouse model, Kxxx knockout mice showed reduced fibrosis, confirming the protective effect of Kxxx deficiency. To further elucidate the mechanisms by which Kxxx influences fibrosis, we performed RNA sequencing and identified an increase in fibrosis-related RNA levels in the presence of Kxxx. Additionally, we confirmed the elevated expression of several fibrosis-associated proteins. Investigation into the EMT signaling pathways revealed that Kxxx activates the PI3K and Erk pathways, which are components of the TGF-β/non-SMAD signaling axis known to contribute to fibrosis. These findings suggest that Kxxx is a critical regulator of kidney fibrosis and that its inhibition could be a potential therapeutic strategy for preventing or treating renal fibrosis. Further studies are needed to fully understand the role of PI3K and Erk pathways in Kxxx-mediated fibrosis and to explore their potential as therapeutic targets.

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***Keywords :** Renal fibrosis, Epithelial-to-mesenchymal transition(EMT), PI3K, Erk

PS-D-038

Protective effects of Cxxx overexpression on cardiometabolic syndrom in western diet-induced Ldlr-/- mice

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Cardiometabolic syndrome (CMS), mainly characterized by abdominal adiposity, insulin resistance, hypertension, and dyslipidemia, is a complex interplay of metabolic dysfunctions with approximately 25% prevalence in adults globally. People with CMS are 2-3 times more likely to die from atherosclerotic cardiovascular diseases than those who do not have the syndrome. It is now known that abdominal adiposity is a significant contributor to increased cardiometabolic risk. A recent study showed that a designer cytokine combining signaling features of IL-6 family cytokines evoked significant protective effects against diet-induced metabolic disorders in mice. Cxxx is a member of the IL-6 cytokine family, characterized by its use of gp130 as a signal-transducing subunit in its receptor complex. Thus, we hypothesized that Cxxx, IL-6 family cytokine, could prevent cardiometabolic syndrome, including abdominal adiposity and atherosclerosis. LDL receptor knockout (Ldlr-/-) mice were fed a Western diet (WD) for 20 weeks to model cardiometabolic syndrome. Concurrently, mice were intravenously administered either AAV-ctrl or AAV-cxxx. The body weight of these mice was monitored throughout the 20 weeks, revealing that Cxxx overexpressing mice exhibited significantly lower weight gain than control mice. Despite no significant differences in food intake, DEXA analysis showed a lower fat percentage in the Cxxx overexpressing mice. Metabolic cages analysis indicated higher energy consumption in Cxxx overexpressing mice than in controls. Additionally, plasma levels of inflammatory biomarkers, such as MCP-1 and IL-6, decreased at 4 and 20 weeks of the WD in Cxxx-overexpressing mice. Furthermore, quantifying plaque area in the aortic arch and aorta indicated a significant reduction in plaque size in Cxxx-overexpressing mice compared to controls. Thus, our data suggest that Cxxx can potentially be a novel strategy for preventing cardiometabolic syndrome.

***Corresponding author :** Min ji Cho, Jong-Gil Park

***Keywords :** Cardiometabolic Syndrome, Abdominal Adiposity, Cytokine, Inflammation

PS-D-039

DGAT2 in adipocytes mitigates MAFLD by suppressing hepatocyte inflammation

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MAFLD (Metabolic dysfunction-associated fatty liver disease) is known to arise from issues within the adipose tissue-liver axis, highlighting the importance of targeting adipose tissue function for treatment. DGAT2 (acyl-CoA:diacylglycerol acyltransferase 2), crucial for storing fatty acids synthesized via de novo lipogenesis, plays a key role in hepatic steatosis where triglycerides are predominantly stored. However, whether DGAT2 in adipocytes is responsible for lipid accumulation of hepatocyte and progression to fibrosis is currently unknown. To investigate the role of DGAT2 in adipocyte, we generated preadipocyte-specific *Dgat2* knockout mice and induced MAFLD by feeding HFMCD diet. Compared to normal mice, the *Dgat2* knockout mice showed increased lipid accumulation, macrophage infiltration, and fibrosis through tissue staining, confirming the progression to MASH. To explore the mechanism of *Dgat2* deficiency-induced progression to MASH, we conducted in vitro experiments using the 3T3-L1 cell line. Upon inducing an inflammatory response with LPS treatment, continuous upregulation of NF-κB was observed in *Dgat2*-deficient cells. Furthermore, in co-culture experiments with adipocytes and hepatocytes, we analyzed adipokine secretion to elucidate how DGAT2-dependent adipocyte mitigate these effects. Our study demonstrated the molecular mechanism by which adipocyte control hepatocyte lipid accumulation and inflammation by altering the patterns of adipokines. These findings suggest that targeting adipokine secretion through adipocyte could offer a novel strategy to treat MAFLD by curbing lipid accumulation and inflammatory responses in liver.

***Corresponding author :** Ji Eun Lee

***Keywords :** MAFLD, Adipocyte, Inflammation, Adipokine

PS-D-040

Anticancer activity of marine peptides derived green sea algae, bryopsis plumose in non-small cell lung cancer

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Developing new anti-cancer agents with minimal toxicity is notably challenging for cancer therapeutics. The discovery of peptides, whether derived from natural sources or synthesized, presents a promising approach for developing next-generation anti-cancer agents characterized by their remarkable selectivity and specificity. For screening anti-cancer peptide(ACP)s from Bryopsis plumosa, cDNA sequences were cut off below 200 bp (< 60 amino acids) to remove long sequences. A total of 77 distinct peptides, < 50 amino acids in length, are analyzed. The peptides for developing anticancer drugs were screened based on the prediction of ACP tools, such as CancerPPD and AntiCP 2.0, which generated sequence information on potent ACPs. Similarity analysis of the selected peptide sequence was performed using a self-constructed anti-cancer peptide database. We synthesized 30 ACPs predicted peptides and anticancer activities of the candidates were experimentally measured in lung cancer cell lines. Interestingly, MP06 and 28 peptides exhibited significant suppression of proliferative and metastatic effects in adenocarcinoma types compared to non-cancerous cell lines. To investigate the invasion and spread of cancer cells, we used zebrafish embryo xenografted with non-small cell lung cell line A549. The invasion of lung cancer cells in zebrafish embryos was markedly inhibited by MP06. Moreover, anti-angiogenic effect of MP06 was further investigated regarding vascular tube formation in a zebrafish model. Tumor volume was significantly reduced in MP28 treated mice to the control mice in mouse xenografted with non-small cell lung cell line A549. These findings the potential of MPs as a therapeutic agent against lung cancer, offering promise in combating the aggressive tumor behavior characteristic of lung cancer.

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***Corresponding author :** Jeiha Lee

***Keywords :** Anticancer peptide, Cancer, Xenograft, Zebrafish

PS-D-041

Study on copper-binding peptides in Wilson`s disease and copper metabolism

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Copper (Cu) is an essential mineral for humans and various organisms, playing crucial roles in metabolic activities and peripheral nerve functions within cells. However, excessive exposure to copper can lead to toxicity, causing cellular or organ damage and triggering diseases such as Wilson's disease. Wilson`s disease is a rare genetic condition that occurs when your body accumulates too much copper, especially in the liver and brain. Understanding copper dynamics and toxic mechanisms in the body is crucial for preventing or treating copper-induced toxicity. In this study, we identified peptides with high copper-binding affinity by analyzing the activity and structure of genes obtained from the genome of the octopus (Cephalopods), known for their advanced copper metabolism. To investigate the biological effects of copper and the copper removal efficacy of these peptides, we used zebrafish (Danio rerio), an animal model highly similar to humans. Zebrafish are widely utilized in various research fields such as early development, human genetic diseases, gene function studies, toxicity testing, and drug screening. In this study, we examined the effects of copper and peptides on survival rates, growth, and various organs including the nervous system, circulatory system, liver, and skin in animal models and cell assays. In the future, we hope to confirm the stability and efficiency of the copper-binding peptide in rodents so that it can be effectively applied to copper metabolic disorders such as Wilson's disease.

Corresponding author **:** Seung-Hyun Jung

Keywords **:** Copper, Peptide, Wilson`s disease, Zebrafish

PS-D-042

Proteasome-associated deubiquitinases regulate both the cell proliferation and the mitochondrial dysfuntion in pancreatic ductal cancer cells

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The Ubiquitin-Proteasome System (UPS) is a crucial protein degradation pathway composed of various elements, including E1, E2, and E3 enzymes, ubiquitin, and the proteasome. Bortezomib, one of the FDA-approved proteasome inhibitors, extends its therapeutic targets beyond Multiple Myeloma, showcasing its potential impact on solid malignancies. Meanwhile, in the context of rapidly dividing cancer cells, particularly those harboring KRAS mutations like pancreatic cancer, the accelerated cell cycle not only intensifies proteotoxic stress but also sets the stage for intricate molecular responses. Analyzing the TCGA and GTEx databases, we found that pancreatic cancer patients with high KRAS mutation frequencies show a distinct pattern of highly upregulated expression of specific deubiquitinase genes, which also correlates with cell cycle regulation and mitochondrial function. This correlation not only accentuates the link between genetic alterations and cancer pathogenesis but also unveils potential avenues for targeted interventions in the intricate landscape of pancreatic cancer biology. Patients with elevated expression levels of these genes have a higher mortality rate, indicating their pivotal role in orchestrating the cell cycle and mitochondria dynamics in pancreatic cancer cells. To further explore this hypothesis, mRNA sequencing was conducted, confirming the intricate connection between these genes and cell cycle pathways. The sequencing also revealed significant correlations with mitochondrial function. This poster comprehensively analyses these genes, highlighting their profound relevance in governing the complexities of the cell cycle and influencing mitochondrial function in the context of pancreatic cancer cells.

Corresponding author **:** Sungsoon Fang

Keywords **:** Ubiquitin Proteasome System, Deubiquitinase, Pancreatic Cancer, Oxidative Phosphorylation, Cell Proliferation

PS-D-043

Age-dependent changes in the immuno-environment of uteri of diet-induced obesity mice

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Obesity is considered the root of many diseases, and as people age, obesity-related diseases pose a growing threat to health in various ways. Obesity can negatively impact the female reproductive system, leading to issues such as menstrual disorders, infertility, miscarriage, and poor pregnancy outcomes. However, there is limited research on the impact of obesity on the female reproductive system according to age. This study investigates how obesity affects the immune environment in the uterus of mice according to age. ICR-young mice (8-week-old) were divided into two groups: one fed a high-fat diet (HFD, 60% fat) and the other a normal diet (ND, 10% fat) for 4 weeks. ICR-old mice (56-week-old) were also similarly divided into two groups. To conduct fluorescence-activated cell sorting (FACS) experiments using isolated cells from the mouse uterus, four mice were pooled together to prepare uterine stromal cell (USC) samples (n=3 in ND and HFD groups each). To synchronize the estrous cycle of the mice to diestrus, mice received an injection of 5 IU of PMSG, and USC and uterine tissues were collected 72 hours after the injection. Immunofluorescence staining was conducted on uterine cryosections to further analyze the FACS results. FACS analyses demonstrated that monocytes ($CD11b^+$ cells), macrophages ($F4/80^+$ cells), and two types of macrophages, M1 ($CD80^+$ cells) and M2 ($CD206^+$ cells), were significantly decreased in the HFD group compared to the ND group in both old and young mice. Age-related comparisons of the immune environment showed that the number of immune cells in old mice was less than in young mice. Immunofluorescence staining of uterine cryosections showed that monocytes were predominantly localized within the endometrium. Collectively, the results show that a short-term HFD of 4 weeks was sufficient to decrease certain immune cell populations in uteri and that age influences changes in the uterine immune environment. The reduction of uterine immune cells due to age and HFD may serve as parameters to assess fertility conditions in females.

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Keywords **:** Obesity, Aging, Immune system, Reproduction, Uterus

PS-D-044

Effects of high-fat diet on the expression of necroptosis effectors in the mouse ovary

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Obesity is considered a cause of various health issues, including impaired reproductive functions. Excessive fat accumulation increases lipids in the bloodstream, entering cells and causing lipotoxicity. Increased intracellular lipid accumulation can also enhance inflammatory responses, triggering necroptosis, a cell death pathway mediated by pro-inflammatory cytokines. Necroptosis is initiated by stimulation by pro- inflammatory cytokines and executed by sequential actions of Receptor-Interacting Serine/Threonine-Protein Kinase 1 (RIPK1), Receptor-Interacting Serine/Threonine Kinase 3 (RIPK3), and Mixed Lineage Kinase domain Like pseudokinase (MLKL). Phosphorylated MLKL is known as a marker of necroptotic activation. There is limited research on the role of necroptosis in female reproductive functions. In this study, we investigated if short-term exposure to a high-fat diet (HFD) could influence necroptosis in the mouse ovary. C57BL/6J mice (6-week-old) were fed a high-fat diet (HFD, 60% fat) or a normal diet (ND, 10% fat) for 4 weeks. Mice received 10 IU PMSG and total ovary and granulosa cells (GCs) were used for further experiments 48 hours later. We performed quantitative PCR (qPCR), western blot, and immunofluorescence staining. qPCR results of Ripk1, Ripk3, and Mlkl showed no significant differences between ND and HFD ovaries. We executed western blot analyses and confirmed that necroptotic activation is observed in whole ovaries but there were no significant differences between ND and HFD groups. Immunofluorescence confirmed that pMLKL is localized in GCs. The results indicate that necroptosis may be active in GCs. Our findings show that the mouse ovary and GCs are the potential sites of necroptosis, but a high-fat diet of 4 weeks did not significantly influence the status of necroptosis. Whether prolonged exposure to HFD influences necroptosis distinctly requires further investigation.

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Keywords **:** Necroptosis, Obesity, Reproduction, Ovary, Granulosa cell

PS-D-045

TXNIP deficiency in liver sinusoidal endothelial cells enhances liver regeneration and modulates inflammation

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Liver sinusoidal endothelial cells (LSECs) are essential for liver regeneration. Thioredoxin-interacting protein (TXNIP),which is a type of alpha-arrestin, is involved in various cellular functions such as cell proliferation, apoptosis, glycolysis, and redox state regulation. *Txnip* total knockout mice reportedly exhibited faster liver regeneration. Moreover, both human and mouse LSECs reportedly express TXNIP. These results suggest a link between TXNIP and liver regeneration, particularly related to LSECs. However, the precise underlying mechanisms remain elusive. In this study, we describe that mice with LSEC-specific *Txnip* knockout (KO) displayed accelerated liver regeneration after partial hepatectomy (PHx) 6–72 h post-surgery, compared to the controls. The cell cycle was initiated earlier in KO mice, accompanied by increased mitogen levels such as those of hepatocyte growth factor (HGF), interleukin-6 (IL-6), and tumor necrosis factor α (TNF-α). Notably, KO mice exhibited a diminished inflammatory response compared to the controls coupled with reduced inflammatory cytokine expression, (such as that of the C-X-C motif chemokine ligand 1 (CXCL1) and its receptor, C-X-C motif chemokine receptor 2 (CXCR2)) and reduced neutrophil infiltration. To investigate the cellular basis of these differential responses, we isolated hepatocytes, LSECs, Kupffer cells, and hepatic stellate cells (HSCs) after PHx and compared their profiles. As early as 3 h post-PHx, control mice exhibited increased *Cxcl1* and *Cxcr2* expressions in the hepatocytes and LSECs, respectively, whereas KO mice exhibited lower expression levels. Six hours post-PHx, *Hgf* expression was enhanced both in HSCs and LSECs, with a more significant increase observed in KO mice than in the controls. In this study, we established a newly described function of TXNIP in LSECs by modulating inflammatory and regenerative responses of the liver upon surgical resection. These results provide a better understanding of the mechanisms underlying liver recovery and regeneration following transplantation surgery

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***Keywords :** Liver sinusoidal endothelial cells, TXNIP, Liver regeneration, Hartial hepatectomy

PS-D-046

Evaluation of the Xeno pig as a distinct breed: Genetic comparison with MGH, Landrace, and Yorkshire/Landrace Breeds

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Background / Aim: This study aimed to evaluate the potential of the Xeno pig, a hybrid between the alpha 1,3-galactosyltransferase gene knock-out Chicago miniature pig and Landrace, as a distinct pig breed. We compared its genetic characteristics with those of the MGH (a miniature pig breed fixed for xenotransplantation), Landrace (LR), and Yorkshire/Landrace (Y/L) breeds to assess its uniqueness.
Methods: Genetic diversity and relationships were analyzed using 48,136 SNP markers through Principal Component Analysis (PCA), Multidimensional Scaling (MDS), phylogenetic tree analysis, and heatmap analysis. The Xeno breed, specifically pigs from the 6th to 9th generations, were analyzed using gDNA extracted from ear tissue, while gDNA for the other breeds was extracted from blood samples. The founder generation was created by crossing the knock-out Chicago miniature pig with Landrace, and subsequent generations were produced by interbreeding hybrid pigs.
Results: MDS and phylogenetic tree analyses revealed that the Xeno and MGH breeds are genetically distinct from the LR and Y/L breeds, indicating different ancestral origins. The heatmap analysis showed a decreasing trend in genetic diversity within breeds, ranking from MGH to Xeno, LR, and Y/L. The Xeno breed exhibited low genetic diversity similar to the MGH pigs, suggesting a narrow genetic base and potential genetic vulnerability. Notably, the phylogenetic tree analysis indicated that the Xeno pigs, despite their hybrid origin, clustered closer to a different pig lineage than the LR lineage, suggesting a significant influence of this other lineage on the genetic makeup of the Xeno breed.
Conclusions: Our findings suggest that the Xeno breed is genetically distinct from the LR and Y/L breeds, supporting its potential as a unique pig breed. The Xeno breed, like the MGH pigs, shows lower genetic diversity and a closer genetic relationship to a different pig lineage, highlighting its distinct genetic identity. These results are valuable for breed improvement and managing genetic resources effectively.

***Corresponding author :** Keon Bong Oh

***Keywords :** Genetic diversity, Pig breeds, Xeno Pig, SNP markers, Phylogenetic analysis

PS-D-047

ADSSL1-Induced autophagy promotes myogenic fusion for differentiation

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Distal myopathy, a group of heterogeneous genetic diseases, has been linked to mutations in adenylosuccinate synthase-like 1 (ADSSL1) found in some patients, suggesting a potential association. However, the underlying mechanisms related to these mutations have not yet been studied. To uncover the pathology involving ADSSL1, we conducted a loss-of-function study using the C2C12 mouse myoblast cell line and C57BL6/J mice. Our findings indicate that depletion of ADSSL1 impairs muscle differentiation by downregulating key regulators such as myogenin and desmin. Given that ADSSL1 catalyzes the conversion of IMP to AMP, and AMP-activated protein kinase (AMPK) promotes autophagy through the mTOR-ULK1 signaling pathway, we hypothesized that ADSSL1 is involved in autophagy by activating AMPK for myogenic fusion. Our results demonstrate that ADSSL1 is essential for AMPK activation and autophagy during the differentiation of C2C12 cells. In ADSSL1 knockout mice, calf muscle mass decreased, leading to reduced mobility. Collectively, these findings suggest that understanding the mechanism by which ADSSL1 regulates myogenic fusion is crucial for elucidating the pathogenesis of myopathy.

***Corresponding author :** Ji Eun Lee

***Keywords :** Myopathy, Autophagy, Knockout model, Adenylosuccinate synthase-like 1 (ADSSL1), Myogenic differentiation

PS-D-048

Impact of THEMIS deficiency on treg functionality and its role in atopy dermatitis suppression

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Themis, a thymocyte-expressed molecule involved in T cell receptor (TCR) signal transduction, plays a crucial role in thymocyte development and T cell lineage specificity. Recent studies have indicated that THEMIS is implicated in multiple autoimmune diseases, including celiac disease, inflammatory bowel disease (IBD), and multiple sclerosis. However, its function in regulatory T cells (Tregs) and its impact on atopic dermatitis (AD) have only recently begun to be explored. This study investigates the effects of THEMIS deficiency on Treg cell functionality and its subsequent role in suppressing atopic dermatitis. Using THEMIS knockout (KO) mice models, we observed significantly milder symptoms of AD compared to wild-type (WT) mice. Our findings reveal an increased population and enhanced suppressive function of Treg cells in THEMIS KO mice. Specifically, THEMIS KO Tregs exhibited higher stability of FOXP3 in inflammatory conditions (IL-4, IL-6) and demonstrated a marked difference in the differentiation of Treg cells from naïve T cells in vitro, though not in vivo. Furthermore, transcriptome and epigenetic analyses, including RNA-seq and ATAC-seq, highlighted key differences in gene expression and chromatin accessibility between KO and WT Tregs. Notably, THEMIS KO Tregs maintained increased stability and suppressive function, implicating THEMIS as a potential therapeutic target for AD. In summary, our study underscores the importance of THEMIS in T cell biology and its potential as a therapeutic target for atopic dermatitis by modulating Treg cell functionality and stability.

***Corresponding author :** Kyung Won Kim, Myung hyun Sohn, Ho-keun Kwon

***Keywords :** Themis, Treg, Atopic dermatitis

PS-D-049

Anti-obesity and anti-diabetic effect of fermented fig extracts on high-fat diet fed mice

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This study assesses the effects of fermented fig (FF, *Ficus carica L.*) on obesity and diabetes using a mice model. The fig fermentation process utilized the lactic acid bacterium *Lactobacillus plantarum* BT-LP-01, separation from fig peels. Antioxidant assessments indicated that FF demonstrated significant DPPH and ABTS radical scavenging activities and was abundant in total polyphenols content (TP) and total flavonoids content (TF). Mice induced with obesity and diabetes via a high-fat diet (HFD) were subsequently treated with FF at doses of 50, 125, and 250 mg/kg over eight weeks. Green tea extracts (GTE, 50 mg/kg) served as a positive control. In the FF-fed groups, significant reductions in body and organ weights, and food intake were observed compared to the HFD group. The FF groups demonstrated improved recovery in liver color and reduced abdominal fat at a macroscopic aspect. FF administration led to a significant recovery of lipid metabolism markers and liver function compared to the HFD group. Also, serum C-peptide and insulin levels were reduced in FF-fed mice. FF-administered mice showed significant recovery of fasting blood glucose, intraperitoneal glucose tolerance test (IPGTT), and area under the curve (AUC) levels. Moreover, FF-fed groups showed decreased expression of fatty acid synthase (FAS), CCAAT/enhancer-binding protein α (C/EBPα), and fatty acid-binding protein 4 (FABP4), as well as a significant increase expression of the acetyl-CoA (ACC) in the mice liver. These findings indicate the potential of FF in reducing adipogenesis, body weight, blood glucose levels, and lipid-related factors. These findings indicate that FF effectively treats obesity and diabetes.

***Corresponding author :** Jungkee Kwon

***Keywords :** Ficus carica, Anti-obesity, Anti-diabetic, Hyperglycemia, Lipid metabolism

PS-D-050

Anti-NAFLD effects of Fermented gold kiwifruit via activation of AMPK signaling pathway

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Non-alcoholic fatty liver disease (NAFLD) is characterized by excessive fat accumulation in the liver of individuals who consume little or no alcohol. In this study, we used mice fed a high-fat diet (HFD) to establish a NAFLD animal model. In this study, we prepared FGK powder using two strains of lactic acid bacteria, *Lactococcus lactis* VI-01 and *Lactobacillus paracasei* VI-02, isolated and cultured from Gold kiwi peel. Fermented gold kiwi (FGK), known for its high content of organic acids and elevated antioxidant activity, was administered three concentrations (50, 125, and 250 mg/kg) orally to the NAFLD mice for 8 weeks, while a normal control group (NFD) received a standard diet. Body weight and food intake were monitored weekly. Biochemical and histopathological examinations post-experiment revealed that FGK reduced serum levels of ALT, AST, total cholesterol, triglycerides, and glucose. Fasting blood glucose measurements at weeks 4 and 8 indicated significant reductions in the FGK 250 group, with similar trends observed in the IPGTT. Hematoxylin and eosin-stained (H&E) liver sections from FGK-administered mice exhibited fewer NAFLD-consistent lesions. FGK treatment activated the SIRT1/AMPK pathway and inhibited the expression of inflammatory cytokines such as IL-1β, IL-6, and TNF-α in liver tissue. Our findings demonstrate that FGK administration can mitigate the severity of NAFLD, inhibit fat synthesis, promote fat breakdown, and suppress inflammation in HFD-induced obese mice. These results suggest FGK's potential as a therapeutic agent against NAFLD.

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***Keywords :** NAFLD, High fat-diet, AMPK pathway, Metabolic syndrome

PS-D-051

Cirsium japonicum (CJ) extracts prevent STZ-induced diabetic rats: inhibition of RAGE/AGEs signaling pathway

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The study explores the potential therapeutic benefits of Cirsium japonicum (CJ) in preventing diabetic complications, focusing on both liver and kidney health associated with advanced glycation end-products (AGEs). Using a streptozotocin (STZ)-induced diabetic model in Sprague-Dawley rats, CJ (administered at doses of 50 and 100 mg/kg) was given orally for 4 weeks. The results showed that CJ treatment led to a significant reduction in key diabetic markers, such as blood glucose levels, reactive oxygen species (ROS), and lactate dehydrogenase (LDH), compared to rats treated only with STZ. In the liver tissues of STZ-treated rats, there was a marked increase in biomarkers associated with AGE induction and formation, which were notably reduced in the CJ-treated rats. This reduction effectively alleviated oxidative stress, inflammation, and AGE accumulation in the liver. Furthermore, CJ treatment demonstrated significant improvements in diabetic nephropathy markers, showing a reduction in renal oxidative stress, inflammation, and AGE-related complications in the kidneys of STZ-induced diabetic rats. These findings indicate that CJ possesses strong anti-oxidation, anti-inflammation, and anti-AGE properties, making it a promising natural remedy for mitigating diabetes-induced damage to both the liver and kidneys. By reducing oxidative stress and inflammation, CJ helps to protect these vital organs from the detrimental effects of diabetes. This study highlights the therapeutic potential of CJ in preventing and treating diabetic complications, suggesting that it could be an effective natural treatment option for managing diabetes and its associated complications in both the liver and kidneys.

***Corresponding author :** Sokho Kim, Jungkee Kwon

***Keywords :** Diabetic, Cirsium japonicum, Advanced glycation of products, Streptozocotin

PS-D-052

Common and distinct functions of mouse Dot1l in the regulation of endothelial transcriptome

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Epigenetic mechanisms play a crucial role in the development of endothelial cells, particularly lymphangioblasts, during cardiovascular development. Among these mechanisms, Dot1l-mediated gene transcription in mice is essential for the development and proper functioning of lymphatic endothelial cells (LECs). However, the role of Dot1l in the development and function of blood endothelial cells (BECs) was not fully understood. To explore this, RNA-seq datasets from Dot1l-depleted or -overexpressing BECs and LECs were utilized to conduct a comprehensive analysis of the regulatory networks involved in gene transcription and associated pathways. The study revealed that Dot1l depletion in BECs resulted in significant changes in the expression of genes associated with cell-to-cell adhesion and immunity-related biological processes. On the other hand, Dot1l overexpression led to modifications in the expression of genes related to various forms of cell-to-cell adhesion and angiogenesis-related biological processes. Furthermore, genes involved in specific tissue development-related pathways were found to be altered in both Dot1l-depleted BECs and LECs. Interestingly, Dot1l overexpression in BECs altered the expression of genes linked to ion transportation, while in LECs, it affected genes involved in immune response regulation. One of the most significant findings was that Dot1l overexpression in BECs induced the expression of genes associated with angiogenesis. Additionally, an increased expression of MAPK signaling pathways was observed in both Dot1l-overexpressing BECs and LECs. These results highlight the distinct transcriptomic programs of endothelial cells and underscore the differential roles of Dot1l in regulating gene transcription in BECs and LECs. Therefore, our transcriptomic analyses of Dot1l-depleted and Dot1l-overexpressing endothelial cells provide a unique insight into the regulatory functions of Dot1l. This study is the first to delineate the specific epigenetic regulatory functions of Dot1l in two different types of endothelial cells, thereby contributing significantly to our understanding of endothelial cell biology and epigenetic regulation.

***Corresponding author :** Kwonho Hong

***Keywords :** Blood endothelial cell, Lymphatic endothelial cell, Epigenetics, DOT1L, Transcriptional regulation

PS-D-053

Dynamic change of R-Loop implicates in the regulation of zygotic genome activation in mouse

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In mice, zygotic genome activation (ZGA) occurs in two steps: minor ZGA at the one–cell stage and major ZGA at the two–cell stage. Regarding the regulation of gene transcription, minor ZGA is known to have unique features, including a transcriptionally permissive state of chromatin and insufficient splicing processes. The molecular characteristics may originate from extremely open chromatin states in the one–cell stage zygotes, yet the precise underlying mechanism has not been well studied. Recently, the R-loop, a triple–stranded nucleic acid structure of the DNA/RNA hybrid, has been implicated in gene transcription and DNA replication. Therefore, in this study, we examined the changes in R-loop dynamics during mouse zygotic development, and its roles in zygotic transcription or DNA replication. Our analysis revealed that R-loops persist in the genome of metaphase II oocytes and preimplantation embryos from the zygote to the blastocyst stage. In particular, zygotic R-loop levels dynamically change as development proceeds, showing that R-loop levels decrease as pronucleus maturation occurs. Mechanistically, R-loop dynamics are likely linked to ZGA, as inhibition of either DNA replication or transcription at the time of minor ZGA decreases R-loop levels in the pronuclei of zygotes. However, the induction of DNA damage by treatment with anticancer agents, including cisplatin or doxorubicin, does not elicit genome-wide changes in zygotic R-loop levels. Therefore, our study suggests that R-loop formation is mechanistically associated with the regulation of mouse ZGA, especially minor ZGA, by modulating gene transcription and DNA replication.

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***Keywords :** R-loop, Zygotic genome activation, Transcription, DNA replication

PS-D-054

RNA helicase DEAD-box-5 is involved in R-loop dynamics of preimplantation embryos

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R-loops are DNA:RNA triplex hybrids, and their metabolism is tightly regulated by transcriptional regulation, DNA damage response, and chromatin structure dynamics. R-loop homeostasis is dynamically regulated and closely associated with gene transcription in mouse zygotes. However, the factors responsible for regulating these dynamic changes in the R-loops of fertilized mouse eggs have not yet been investigated. This study examined the functions of candidate factors that interact with R-loops during zygotic gene activation. In this study, we used publicly available next-generation sequencing datasets, including low-input ribosome profiling analysis and polymerase II chromatin immunoprecipitation-sequencing (ChIP-seq), to identify potential regulators of R-loop dynamics in zygotes. These datasets were downloaded, reanalyzed, and compared with mass spectrometry data to identify candidate factors involved in regulating R-loop dynamics. To validate the functions of these candidate factors, we treated mouse zygotes with chemical inhibitors using in vitro fertilization. Immunofluorescence with an anti-R-loop antibody was then performed to quantify changes in R-loop metabolism. We identified DEAD-box-5 (DDX5) and histone deacetylase-2 (HDAC2) as candidates that potentially regulate R-loop metabolism in oocytes, zygotes and two-cell embryos based on change of their gene translation. Our analysis revealed that the DDX5 inhibition of activity led to decreased R-loop accumulation in pronuclei, indicating its involvement in regulating R-loop dynamics. However, the inhibition of histone deacetylase-2 activity did not significantly affect R-loop levels in pronuclei. These findings suggest that dynamic changes in R-loops during mouse zygote development are likely regulated by RNA helicases, particularly DDX5, in conjunction with transcriptional processes. Our study provides compelling evidence for the involvement of these factors in regulating R-loop dynamics during early embryonic development.

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***Keywords :** DEAD-box-5, Gene transcription, R-loop, Zygote

PS-D-055

Development of a novel humanized knock-in mouse model of retinitis pigmentosa with RP9 and RP1L1 mutations

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Retinitis Pigmentosa (RP) is a progressive retinal disease that can cause vision loss without a current treatment option. Therefore, it is crucial to develop animal models with RP features to develop new treatment options. RP has over 150 known genetic causes, with inheritance patterns including autosomal dominant (AD), autosomal recessive (AR), and X-linked recessive (XR). While AD inheritance is rare, it often leads to rapid retinal degeneration and poor visual prognosis compared to other genetic patterns. This study aimed to induce mutations in RP-related genes RP9 and RP1L1 using CRISPR-Cas9 gene editing to create such models. Genetic abnormalities identified in humans were introduced into mice by replacing nucleotides with single-stranded oligodeoxynucleotides (ssODNs). Mice were monitored and analyzed through imaging and tests up to 4 and 12 months to evaluate retinal degeneration progression. The RP9 and RP1L1 mutant mice showed no significant differences compared to wild-type controls. Despite the introduction of targeted mutations, the anticipated retinal degeneration and vascular thinning were not observed in these mouse models. The retinal phenotype of mutant mice remained similar to that of wild-type mice, raising intriguing questions about the role of RP9 and RP1L1 mutations in inducing retinal degeneration. In conclusion, the RP9 and RP1L1 mouse models did not exhibit the expected changes in retinal degeneration. This difference in phenotype could stem from interspecies variations between humans and mice or the possibility that genetic abnormalities diagnosed in humans may have different effects from those caused by other genetic conditions. The results of this study underscore the need for further research to draw conclusive findings.

***Corresponding author :** Joo Yong Lee

***Keywords :** CRISPR-Cas9, RP9, RP1L1, Retinitis Pigmentosa

PS-D-056

Investigating immunomodulatory properties of porcine peripheral blood-derived mesenchymal stem cells: a comparative study with bone marrow-derived MSCs

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Porcine mesenchymal stem cells (MSCs) have become an important tool for overcoming immune rejection in the study of immune rejection. Specifically, bone marrow-derived mesenchymal stem cells (BM-MSCs) have demonstrated significant immunomodulatory capabilities. Although harvesting BM-MSCs is difficult, peripheral blood-derived mesenchymal stem cells (PB-MSCs) are easy to harvest at any time and the procedure is much less invasive. However, the immunomodulatory effects of PB-MSCs are poorly understood. In this study, cells with round, fibroblast-like, and elongated morphologies, previously reported as MSCs, were obtained from Porcine peripheral blood mononuclear cells (PBMC) and characterized by MSC bio-markers. The characterization of this isolated PB-MSCs was confirmed by MSC surface markers CD44, CD73, CD90, and CD105, and were negative for CD11b and CD45. The results show that PB-MSCs have similar properties to BM-MSCs. To assess the immunomodulatory potential of the BM-MSC and PB-MSC, we examined inflammation-related cytokine expression in Human monocyte (THP-1) cells treated with phorbol-12-myristate-13-acetate (PMA) and Lipopolysaccharide (LPS), and then indirectly co-cultured with MSCs. As a result, pro-inflammatory markers TNF-α, IL-1β, and IL-6 are decreased and anti-inflammatory markers IL-10 and TGF-β are increased. Therefore, it has been confirmed that PB-MSCs have the same immunomodulatory function as BM-MSCs. Additionally, functional evaluation of PB-MSCs, such as immunomodulation, will be studied with a focus on in-vitro studies of cytokine secretion and immune cell interaction mechanisms to better understand their therapeutic potential.

***Corresponding author :** Jinsoo Lee, Jeong Ho Hwang

***Keywords :** Peripheral Blood-Derived Mesenchymal Stem Cells (PB-MSCs), Bone Marrow-Derived Mesenchymal Stem Cells (BM-MSCs), Immune-modulation, Cytokines, Cytotoxicity

PS-D-057

Effect of atherogenic diets on lesion phenotype in LDLR knockout mouse

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Background: Cardiovascular diseases, particularly atherosclerosis, are major health concerns globally, primarily driven by hypercholesterolemia and high-fat diets. The Western diet, high in fat and cholesterol, is closely linked to increased cardiovascular risk. In experimental models, cocoa butter, rich in saturated fats, induces hypercholesterolemia. Additionally, the bile acid sodium cholate enhances intestinal absorption of cholesterol and fats while also inducing inflammation, thereby promoting atherosclerosis formation. This study investigates how these dietary components differentially affect atherosclerosis progression, focusing on lesion size and phenotype.
Methods: LDLR KO mice transplanted with wild type bone marrow were assigned to three dietary groups: (1) 15.8% fat(half from cocoa butter) and 1.25% cholesterol diet, (2) 15.8% fat(half from cocoa butter), 1.25% cholesterol and 0.5% sodium cholate, (3) a Western diet (Research Diets, #D12079B). After 15 weeks on these diets, the size and phenotype of atherosclerotic lesions were assessed using Oil Red O staining and immune fluorescence staining.
Conclusion: Our findings indicate that specific dietary components have a significant impact on the progression and phenotype of atherosclerotic lesions in LDLR KO mice. The Western Diet group exhibited minimal lesion formation, whereas the sodium cholate-enriched diet resulted in the most severe atherosclerotic changes, suggesting a synergistic effect on lipid absorption and lesion development. These results enhance our understanding of the mechanistic pathways through which dietary fats and bile acids influence atherosclerosis and also provides a guidance on the selection of appropriate atherogenic diets.

***Corresponding author :** Jae-Hoon Choi

***Keywords :** Atherosclerosis, Atherogenetic diets, Cocoa butter, Sodium cholate

PS-D-058

Creating promoters for specific expression in porcine vascular endothelial cells using transcriptome analysis

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Background / Aim: The primary targets of xenograft rejection are the endothelial cells that line the blood vessels of transplanted porcine organs. Developing promoters that induce gene expression specifically in endothelial cells could potentially improve graft survival and reduce rejection mechanisms. The aim of this study was to develop promoters that could specifically induce potent gene expression in porcine vascular endothelial cells.
Methods: Total RNA was extracted from porcine aortic endothelial cells (PAECs) and ear skin fibroblasts (PEFs) obtained from alpha 1,3-galactosyltransferase knockout (GTKO) pigs. RNA sequencing was performed, and the expression profiles were used for differentially expressed genes (DEGs) analysis. The Human Protein Atlas database was employed as a reference for transcriptome comparative analysis. Real-time PCR analysis was conducted on tissues including the aorta and cells.
Results: We identified 34 genes unique to GTKO PAECs through transcriptome comparative analysis of 243 DEGs. *ESAM* exhibited the most significant relative fold change (approximately 1700-fold) in expression in the GTKO PAECs, with *PEAR1* following at approximately 400-fold. Blood-vessel-rich lung tissue exhibited a high level of *ESAM* expression. The expression of *ESAM* was moderate in the aorta and high in the heart and kidney. The expression of *PEAR1* was non-specific in all tissues, including the vascularized lung tissue. We selected *ESAM* and *PEAR1* to create endothelium-specific promoters due to their significant expression in GTKO PAECs. Finally, the ESAM1.0, ESAM1.5, PEAR1.0, PEAR1.5, and PEAR2.0 promoters were developed.
Conclusions: ESAM and PEAR1, which are unique to porcine vascular endothelial cells, were identified through transcriptome analysis. Consequently, we developed five promoters based on the *ESAM* and *PEAR1* genes: ESAM1.0, ESAM1.5, PEAR1.0, PEAR1.5, and PEAR2.0. The transcriptional activity of these promoters will be validated through further investigation.

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***Keywords :** Xenotransplantation, Porcine Vascular Endothelial Cells, Transcriptome Analysis, ESAM, PEAR1

PS-D-059

Comparative transcriptome analysis of PBMCs in cats diagnosed with and recovered from feline infectious peritonitis virus

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Feline infectious peritonitis (FIP) is a viral disease caused by feline coronavirus (FCoV), which is an enveloped virus with a single-stranded RNA genome approximately 30 kb in length. While FCoV generally causes mild symptoms, approximately 5% of cases progress to death in cats worldwide. Biologically, FCoV shares some virological features with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, suggesting common therapeutic strategies may be applicable. GS-441524, the parent drug of Remdesivir and a competitive inhibitor of nucleoside triphosphates (NTPs) in viral RNA synthesis, is well-known for treating FIP. However, comparative transcriptome and gene ontology (GO) analyses between FIP-diseased (FIPD) and FIP-recovered (FIPR) cats have not yet been reported. In this study, mRNA expression profiles between peripheral blood mononuclear cells (PBMCs) of healthy, FIPD, and FIPR cats were compared to identify immunological changes. As a result, 2591 (FIPD/healthy) and 2363 (FIPR/FIPD) differentially expressed genes (DEGs) ($p < 0.05$, $|\log2 \text{ fold change}| \geq 1$) were found. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Ingenuity Pathway Analysis (IPA) indicated that the patterns of canonical pathways related to inflammation and immune response were clearly opposite between FIPR/FIPD and FIPD/healthy. Furthermore, KLF6 and NF-kB functioned as key regulatory transcription factors in the canonical pathways. In conclusion, FIP induces functional changes in PBMCs through the activation of KLF6 and NF-kB, but GS-441524 inhibits FCoV RNA synthesis, leading to the suppression of signaling activation.

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***Keywords :** Feline infectious peritonitis, GS-441524, RNA sequencing

PS-D-060

The modulation of pro-inflammatory chemokines and cytokines in monocytes and macrophages under the influence of shear stress

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Loss of endothelial cells beneath arterial surfaces is linked to the accumulation of monocytes or macrophages, which are sensitive to mechanical stimuli like shear stress. However, the impact of mechanical stimulation on monocytes hasn't been fully explored. To assess this, we examined how shear stress influences the expression of inflammatory molecules and surface proteins in human THP-1 cells. Shear stress increased the inflammatory chemokine CCL2, amplifying the transcriptional and protein-level changes of monocytes along with tumor necrosis factor (TNF)-α and interleukin (IL)-1β. We found elevated surface levels of heat shock protein 70 (HSP70), HSP90, and HSP105 through mass spectrometry-based proteomics, confirmed through western blot analysis, flow cytometry, and immunofluorescence. Blocking HSP70/HSP105 and HSP90 inhibited CCL2 expression, secretion, and monocytic cell migration, indicating a link between HSPs and inflammatory responses. Additionally, we observed increased HSP90 immunoreactivity and coexistence with CD68-positive cells in atherosclerotic plaques of ApoE-deficient mice fed a high-fat diet and human femoral artery endarterectomy samples. These findings suggest that shear stress-induced polarization of monocytes/macrophages towards a pro-inflammatory state is associated with increased surface protein levels, particularly HSPs. Targeting the regulation of these HSPs on monocytes/macrophages could present a novel therapeutic approach for shear stress-induced inflammation.

***Corresponding author :** Dongjun Lee

***Keywords :** Shear stress, Monocyte, Macrophage, Cytokine, Heat shock protein

PS-D-061

Macrophage derived non-canonical WNT promotes pancreatic cancer progression through direct inhibition on T cell proliferation

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The Wnt signaling pathway plays a crucial role in the transition of pancreatic acinar cells to pancreatic ductal adenocarcinoma (PDA) precursor lesion. However, the cellular sources of WNT, particularly from the tumor stromal area, have been understudied. Considering the importance of the tumor microenvironment (TME) in cancer, this study aims to elucidate the contribution of Wnt signaling from myeloid cells, rather than cancer cells. Reanalysis of single-cell RNA sequencing (scRNA-seq) data from pancreatic cancer patients (n = 16) identified myeloid cells as the most abundant constituent in the TME. Next, we generated myeloid cell-specific *Porcn* knockout mice (*Csf1r;Porcn*$^{fl/fl}$), in which Csf1r^{+} myeloid cells do not secret any WNT isoforms. In the orthotopic KPC tumor model, *Csf1r;Porcn*$^{fl/fl}$ mice showed significantly reduced tumor growth compared to wild-type (WT) mice. Flow cytometry revealed significantly higher infiltration of CD8^{+} T cells in tumors from *Csf1r;Porcn*$^{fl/fl}$ mice. To investigate the direct effect of macrophage-derived WNT on T cell, culture supernatant from WT bone marrow-derived macrophages (BMDMs) was added to isolated T cells, resulting in inhibited CD8^{+} T cell proliferation. In contrast, no such effect was observed with BMDMs from *Csf1r;Porcn*$^{fl/fl}$ mice. Interestingly, WT BMDM culture medium did not activate the canonical Wnt signaling pathway, as shown by TOP/FOP flash assay, suggesting the possible action of non-canonical WNT from macrophages. Further, scRNA-seq on PDA tumors from *Csf1r;Porcn*$^{fl/fl}$ and WT mice showed high expression of *Wnt5a* in tumor-associated macrophages (TAMs). This was validated in human PDA tissue by confirming co-localization of *WNT5A* gene expression in CD68+ macrophages using in situ hybridization. Consistent with flow cytometry results, CD8^{+} T cells were increased in *Csf1r;Porcn*$^{fl/fl}$ tumors, with high expression of *ROR1*, a non-canonical WNT receptor. These results indicate the possibility of non-canonical Wnt signaling in CD8^{+} T cells. In summary, this study demonstrates that TAMs-derived WNT promotes pancreatic cancer development by suppressing CD8^{+} T cell proliferation independently of canonical Wnt signaling pathway. These findings underscore the need to consider diverse cellular WNT sources, and the role of non-canonical WNT when developing cancer therapies targeting WNT.

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***Keywords :** Pancreatic ductal adenocarcinoma, Wnt signaling pathway, Tumor associated macrophage, Tumor microenvironment, CD8+ T cell

PS-D-062

The ablation of NAD(P)H: quinone oxidoreductase 1 alleviates the pathogenesis of primary sclerosing cholangitis in animal models

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Primary sclerosing cholangitis (PSC) is a liver disease characterized by chronic inflammation and severe fibrosis. In this study, we explored the impact of NQO1 ablation to understand its involvement in the progression of PSC pathogenesis. NQO1 wild-type (WT) and knockout (KO) mice were subjected with either a DDC-containing diet or a control diet for one week. Various pathogenic characteristics, including blood biomarkers, inflammation, and fibrosis, were evaluated. Differential gene expression affected by NQO1 ablation in PSC condition was determined through RNA sequencing of liver tissues. In the PSC-mimetic animal model, mRNA and protein levels of NQO1 were notably elevated, particularly in hepatocytes near the portal vein. The expressions of antioxidant genes in response to DDC were diminished in the liver of NQO1 KO mice compared to WT mice, resulting in decreased lipid peroxidation stained with 4-HNE in the liver of NQO1 KO mice, irrespective of NAD, porphyrin, and total bile acid. NQO1 KO mice exhibited lower levels of AST, ALT, and total bilirubin, albeit not ALP, than WT mice. Histological data further indicated that deficiency of the *Nqo1* gene improved cell death and fibrosis, as evidenced by reduced TUNEL-positive hepatocytes and collagen accumulation in the liver. RNA sequencing data revealed a negative correlation with epithelial mesenchymal transition, G2M checkpoint, or TNF-a signaling via NFkB in gene set enrichment analysis (GSEA). Additionally, GSEA analysis suggested that NQO1 KO mice exhibited a positive association with bile acid metabolism, oxidative phosphorylation, or xenobiotic metabolism. Consistent with RNA sequencing, a similar pattern of genes related to fibrosis was observed in the results using quantitative real-time polymerase chain reaction. This study unveils a novel role of NQO1 in the pathogenesis of PSC, suggesting that NQO1 contributes to lipid peroxidation, the progression of hepatocyte cell death, and fibrosis in PSC-mimetic animal models.

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***Keywords :** NAD(P)H: quinone oxidoreductase 1 (NQO1), Primary sclerosing cholangitis (PSC), Inflammation, Fibrosis, Cholestasis

PS-D-063

Effects of Humulus japonicus aqueous extract on cognitive function in aging

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Cognitive aging is the age-related change in cognitive function that typically occurs as people age. Along with the aging population, the incidence of various age-related neurodegenerative diseases is increasing. Research is needed to delay or prevent cognitive decline associated with aging and promote healthy aging. The use of natural extracts has been considered as an environmentally friendly alternative. *Humulus japonicus* (HJ) is a perennial herb found in East Asian countries such as Korea, China and Japan. Anti-oxidative and anti inflammatory effects of HJ have been reported. The extract of HJ has demonstrated a neuroprotective effect by preventing midbrain dopaminergic neuronal death in a mouse model of Parkinson's disease. In addition, the extract of HJ ameliorated the progression of Alzheimer's disease (AD) by inhibition of neuroinflammation in the brain of animal model of AD. However, the effect of HJ on the age-related cognitive decline has not been demonstrated. In this study, to investigate the effects of HJ aqueous extract on age-related cognitive decline, the HJ aqueous extract was administrated in 18-month-old female mice. General locomotor activity, learning, and memory of aged mice were assessed using behavioral tests. In addition, it was investigated whether changes in the brain due to aging were influenced by HJ in aged mice.

***Corresponding author :** Chul-Ho Lee, Kyoung-Shim Kim

***Keywords :** Humulus japonicus, Natural extract, Brain, Coginitive aging

PS-D-064

Adipocyte specific deficiency of A20 enhances energy homeostasis and lipid metabolism in diet-induced obesity

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Backgrounds: Many studies on ubiquitin editing enzyme A20 have been extensively centered on its roles in inflammation and immune diseases; less understood are in vivo functions of A20 in other physiological/pathophysiological contexts, particularly metabolism. Adipose tissue is defined by the presence of specialized lipid processes that function in storing energy for maintaining energy homeostasis. Moreover, unhealthy adipose tissue is highly related to metabolic maladaptation such as obesity, cardiovascular and metabolic diseases. Which is why regulating adipose tissue lipid metabolism takes center stage in maintaining whole-body conditioning.
Methods: For in vivo experiments, we have generated adipose tissue specific A20 knock-out mice(Adipoq-Cre; A20fl/fl (A20FATKO)) mice by interbreeding Adipoq-Cre and A20 floxed mice. With A20FATKO mice, we fed a high-fat diet (HFD) for up to 14 weeks and sacrificed them for further investigation. For in vitro experiments, we have generated immortalized preadipocytes wherein loss of A20 by CRISPR/Cas9 vector systems.
Results: conditionally deleting A20 in pan-adipocytes protects mice from the high-fat diet-induced metabolic disease at least in part through preventing adipose tissue hypertrophy and hepatic steatosis. Gene expression profiling of Subcutaneous White Adipose Tissue (SAT) reveals inhibiting adipocyte A20 reduces adipose tissue inflammation and reprograms SAT lipid metabolism to favor catabolism. Such reprogramming may associate with our in vitro results using immortalized preadipocytes wherein loss of A20 by CRISPR/Cas9 promotes b-adrenergic signaling-induced lipid oxidation and thermogenesis. Our findings provide unexpected roles for A20 in adipose tissue's lipid handling and systemic energy homeostasis.
Conclusions: Conditional knockout of A20 in pan-adipocyte protects mice from high-fat diet-induced weight gain with alleviated metabolic disorders. A20 deletion in subcutaneous white adipose tissue (SAT) reprograms lipid metabolism catabolically like beige fat, such that reprogramming may be due to increased expression of beta-adrenoreceptor (β-AR) signaling target genes which encode oxidative metabolism.

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***Keywords :** Adipose Tissue, Diet-induced Obesity, Transgenic Mouse, Lipid Metabolism

PS-D-065

Effects of dipeptidyl peptidase-4 inhibitor, sitagliptin, on dyskinesia induced by L-dopa in a Parkinson's disease mouse model

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Parkinson's disease (PD) is one of the neurodegenerative diseases, and is characterized by movement disorders such as postural instability, tremors, and bradykinesia. These symptoms are associated with progressive degeneration of dopaminergic neurons in the midbrain. L-dopa-induced dyskinesia (LID) is an incapacitating complication of L-dopa therapy that affects most patients due to its long-term use in Parkinson's disease. Epidemiological studies have suggested that diabetes mellitus has the potential to accelerate PD onset and progression. In addition, insulin resistance, mitochondrial dysfunction, chronic inflammation, and intestinal microbiota imbalance in patients with diabetes are raising the possibility of progression to PD. As a treatment for, dipeptidyl peptidase 4 (DPP-4) and sodium glucose co-transporter 2 inhibitors, are often used as secondary drugs in combination with metformin. It is reported that diabetic patients treated with DPP-4 inhibitors have a significantly reduced incidence of PD, prevent nigrostriatal dopamine degeneration, and improve motor abnormalities. Additionally, DPP-4 inhibitor treatment in PD has been reported to modulate the effects of L-dopa and inhibit the development of LID. Sitagliptin, a selective inhibitor of DPP-4, is a treatment for type 2 diabetes and has the effect of increasing glycemic levels by inhibiting glucagon-like peptide-1. In this study, to investigate the effects of sitagliptin on dyskinesia induced by L-dopa, unilaterally 6-OHDA-lesioned mice were injected with L-dopa for 11 days. Abnormal involuntary movements were conducted on 5th and 10th days of L-dopa administration. Proteomic analysis using the tandem mass tag labeling was performed to determine the changes in proteins caused by sitagliptin cotreatment with L-dopa in the dopamine-depleted striatum of mice.

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***Keywords :** Proteomics, Abnormal involuntary movement, Ndufb2, Arc, Striatum

PS-D-066

Generation of a mouse model expressing Naa10 235 isoform

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Naa10 is a subunit of N-terminal protein acetyltransferase that plays a role in many biological process, such as cell division, proliferation, and tumorigenesis. It is known that Naa10 has several isoforms, each with distinct cellular functions, and it is divided into $Naa10^{225}$ and $Naa10^{235}$ based on the number of amino acids. In human, only the $NAA10^{235}$ is expressed, while in mice, both the $Naa10^{225}$ and $Naa10^{235}$ orthologues are present by alternative splicing at exon 8. Since it has been reported that $Naa10^{225}$ and $Naa10^{235}$ have opposite roles in development of tumors, it is important to investigate their functions in mouse in vivo. The purpose of our study is to generate a mouse model that only expresses $Naa10^{235}$ by introducing a mutation at alternative splicing site which blocks $Naa10^{225}$ expression in order to reveal the function of each isoforms in vivo. Here, we generated expressing only $Naa10^{235}$ using CRISPR/Cas system. It was designed that the mutation at c.471,2 AG>TC (intron 7 splice acceptor site) of Naa10 prevents splicing for $Naa10^{225}$, resulting in $Naa10^{235}$. Cas9, sgRNA targeting splicing site of $Naa10^{225}$ and ssODN were introduced to zygote by electroporation, followed by transfer to pseudo-pregnant female ICR mouse at the 2-cell stage. Out of 12 F0 pups, 1 mouse with 18% HDR efficiency have been produced, and germline transmission is being confirmed by mating the F0 mouse carrying the desired mutation with C57BL/6N male mouse. We expect that this novel mouse model would be useful for studying the function of Naa10 isoforms.

***Corresponding author :** Mi-Ni Lee

***Keywords :** Naa10 isoform, CRISPR/Cas9, HDR, Alternative splice

PS-D-067

Generation of Il1rap knock-out mice and phenotype analysis for schizophrenia-related traits

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Schizophrenia is a hereditary mental disorder that affects approximately 1% of the world population. Hallucination, delusions, disorganized speech, and lack of initiative are major symptoms of schizophrenia. The cause of schizophrenia is known to result from the interaction between genetic and environmental factors, but it has not yet been clearly identified. A recent report suggested that an interleukin 1 receptor accessory protein (*IL1RAP*) c.1324C>T (R442*) nonsense mutation has been identified in a Chinese family with. Overexpression of IL1RAP R442* mutant suppressed the neuronal cell growth, reducing the phosphorylation of JNK and decreasing NF-κB nuclear translocation in cultured cortical neurons. Building upon the previous report, we aimed to investigate whether Il1rap mutations can be associated with mental disorders such as schizophrenia in mice. A mouse model with a knock-out of exon 9, where Il1rap R442* is located, was produced using the CRISPR-Cas9 system. For comparison, an exon 1 knock-out mouse model was also produced. Phenotypes associated with schizophrenia were investigated. A lower willingness to explore and higher levels of anxiety were observed in Il1rap exon 1 knock-out mice but not in exon 9 knock-out mice. Histopathological analyses of mouse brains were also performed, but no recognizable differences were found. Decreases in the phosphorylation of JNK and NF-κB were confirmed in the brains of both types of knock-out mice. In particular, notable reductions in the phosphorylation of JNK and NF-κB were observed in Il1rap exon 1 knock-out mice. These results suggest that the absence of Il1rap induces significant impacts on the phosphorylation of JNK and NF-κB, potentially leading to mental abnormalities in mice.

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***Keywords :** Il1rap, Schizophrenia, CRISPR-Cas9, JNK signaling, NF-κB signaling

PS-D-068

Insight into noncanonical small noncoding RNAs in influenza A virus infection

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Influenza A virus (IAV) induces acute respiratory infections in birds and various mammals, including humans, and presents a significant global public health concern, with considerable economic consequences. Recently, researchers have shown keen interest in noncanonical small noncoding RNAs (sncRNAs) as carriers of epigenetic information, including tRNA-derived small RNAs (tsRNAs), rRNA-derived small RNA (rsRNAs), and Y RNA-derived small RNAs (ysRNAs). Particularly, tsRNAs and rsRNAs are detected in diverse species and demonstrate evolutionary conservation. We analyzed sncRNAs sequencing data in the pulmonary tissue of two genetically distinct mouse strains, C57BL/6J and DBA/2J, to explore strain-specific variations of sncRNAs in response to IAV infection. We systematically compiled information on noncanonical sncRNAs in these two strains and investigated the tsRNAs/rsRNAs/ysRNAs profiles influenced by IAV infection. Specifically, four noncanonical sncRNA families, including rsRNA-12S, GtsRNA-Arg-CCT, GtsRNA-Arg-TCT, and GtsRNA-Lys-TTT, exhibited upregulation upon IAV infection. Notably, DBA/2J mice showed earlier systemic dysregulation of noncanonical sncRNAs after IAV infection compared to C57BL/6J mice, suggesting higher susceptibility to IAV infection in DBA/2J mice. Additionally, strain-specific dysregulation and co-expression patterns of mitochondrial tsRNAs were observed between C57BL/6J and DBA/2J mice. Our study provides a novel insight into noncanonical sncRNAs and their implications in IAV pathology and mouse strain specificity.

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***Keywords :** Small noncoding RNAs, Influenza A virus, TsRNAs, RsRNAs, YsRNAs

PS-D-069

Toxicological effects of 6PPD in Caenorhabditis elegans

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N-(1,3-Dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD) is a synthetic antioxidant commonly used in rubber-based products, such as tires. The release of 6PPD into the environment during tire wear has been shown to pose a threat to wild salmon populations. However, its underlying action mechanism is poorly understood. Here, we evaluated the potential toxicity and targets of 6PPD using the nematode C. elegans as an in vivo model. Exposure to 0.5 mM 6PPD in C. elegans resulted in various adverse effects, including delayed development, decreased body growth, and reduced reproduction. Furthermore, 6PPD exposure negatively impacted healthspan parameters, such as body motility and stress tolerance, ultimately leading to a shortened lifespan. Notably, 6PPD-exposed C. elegans exhibited disrupted mitochondrial function, characterized by reduced mitochondrial membrane potential, lower oxygen consumption, diminished ATP levels, and decreased reactive oxygen species (ROS). 6PPD exposure influences the activity of SKN-1/Nrf2, a key transcription factor involved in stress response and longevity. Loss of SKN-1 attenuated the reductions in lifespan and tolerance against paraquat, but not mitochondrial disturbance suggesting the involvement of SKN-1/Nrf2 in mediating the toxic effects of 6PPD. Taken together, our findings suggested the detrimental impact of 6PPD on developmental processes, overall health, and aging in vivo. Furthermore, our study identifies mitochondria as a key target organelle affected by 6PPD exposure. The association with conserved SKN-1/Nrf signaling highlights a potential molecular mechanism underlying the toxic effects of 6PPD.

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***Keywords :** 6PPD, C. elegans, SKN-1/Nrf2, ROS

PS-D-070

Progesterone receptor membrane component 1 increases the Smad2-dependent signaling through TGF-β R II expression

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The hepatocyte death is a mainly pathogenetic event in chronic liver diseases. When the hepatocytes were persistently dead due to various factors, they were replaced with extracellular matrix from hepatic stellate cells without hepatocyte regeneration. These well-established facts emphasize the importance of hepatic stellate cells as the ultimate driver of liver fibrosis and the development of liver cirrhosis. In hepatic stellate cells, transforming growth factor β (Tgf-β) plays a key role in the fibrotic response via the Smad pathway. As a non-canonical progesterone receptor, progesterone receptor membrane component 1 (Pgrmc1) is associated with diverse molecular regulation of genes and is highly expressed in the liver. To investigate the role of Pgrmc1 in liver fibrosis, we introduced Pgrmc1 knockout mice and injected CCl4 into mice to induce hepatic fibrosis. As a result, the fibrosis and ER stress contents were significantly lower in the Pgrmc1 KO mice compared to wild-type mice. Furthermore, we found that Tgf-β receptor II expression decreased with decreasing Pgrmc1 in Lx-2 cells as hepatic stellate cells. Our results reveal that Pgrmc1 plays a significant role in liver fibrosis disease progression via increasing Tgf-β-mediated smad2 signaling. Therefore, Pgrmc1 deficiency in hepatic stellate cells hinders fibrosis, which could delay complications like liver cirrhosis, leading to the preventive treatment of liver fibrosis.

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***Keywords :** Liver Fibrosis, Progesterone receptor membrane component 1, TGF-beta

PS-E-001

Improving reproducibility in preclinical research through precision evaluation of clinical chemistry tests

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This study conducted a survey to investigate the current status of quality control in analytical equipment within the field of laboratory animals. The survey results revealed that only 20% of institutions performed internal quality control more than once a year, and a mere 10% had experience with external quality control. Among the participating institutions, 80% responded that they were completely unaware of internal quality control, and 90% were unfamiliar with external quality control. To address these issues and enhance the quality of preclinical research and trust in science, this study conducted a precision evaluation of clinical chemistry test items. Fourteen clinical chemistry test items frequently used in the field of laboratory animals were selected, and their precision was evaluated according to the Clinical and Laboratory Standards Institute (CLSI) guideline EP05-A3. The evaluation results were expressed in terms of within-run, between-run, between-day, and total precision using standard deviation (SD) and coefficient of variation (CV). Out of the 14 test items, 12 demonstrated stable precision. However, the CV for AST was relatively high at 8.95, and HDL was also high at 7.50. This study is expected to improve the reproducibility of test results in the sample analysis of preclinical research, enhance the understanding of precision evaluation, alleviate the reproducibility crisis in science, and significantly impact various medical diagnoses and treatments.

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***Keywords :** Reproducibility, Quality control, Precision, Clinical chemistry

PS-E-002

Evaluation of implantable medical devices for dental and periodontal tissue recovery using animal models

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Daegu-Gyeongbuk Medical Innovation Foundation (K-MEDI hub) is a public institution established to support the improvement and diffusion of medical industry research achievements. In this presentation, we would like to introduce specialized animal models and studies to support the domestic and international approval of dental medical devices. For the evaluation of dental medical devices in the mandible of beagles, premolars were extracted and then beagles were spontaneously healed for about 12 weeks. Depending on the kinds of medical devices, other types of tooth extraction and application surgeries were performed. The effectiveness of the dental medical devices was confirmed through qualitative and quantitative evaluation of biocompatibility, reconstruction function of defective tissue, osteogenesis/osteoinduction /osseointegration ability, and foreign body reaction using computed tomography (CT) scan, micro-CT analysis, and histopathological analysis. As a result, a comparative evaluation of the equivalence and superiority of development materials with approved products was possible. Our established preclinical evaluation methods for dental medical devices are expected to contribute to dental medical device research and development, as well as to shorten the product development time and overseas expansion of related domestic companies.

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***Keywords :** Dental medical device, Preclinical research, Dental implant, Bone graft

PS-E-003

Barley beta glucan increase osteoblast differentiation via p38/ERK and Smad1/5/9 phosphorylation

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Bone is highly dynamic tissue whose structure relies on the balance between bone deposition and resorption. Various signaling pathways regulate the differentiation of osteoblast that give rise to the skeleton are regulated by osteogenic genes. reported that barley beta glucan (BBG) is a polysaccharide that is a fiber found in oats or barley, BBG is effective to report biological actions such as modulation of immunological, anti-inflammatory, and anti-cancer. Furthermore, BBG used modern medicine and traditional oriental therapies, and dietary substance. The mitogen-activated protein kinases were revealed as key players in skeletal development and bone homeostasis, (MAPKs) signaling pathway was regulated in apoptosis, differentiation, cell survival, proliferation, development, and stress response. However, it is a role and molecular function in osteoblast differentiation remains unclear. Thus, we investigate that the effect of BBG on osteoblast differentiation in a pre-osteoblast cell line and mouse calvaria primary cells. The study objective is to identify the mechanism by which BBG induces osteoblast differentiation. BBG increase by distal-less homeobox 5 (Dlx5), runt-related transcription factor 2 (Runx2) genes expressions. The staining levels of Alkaline phosphate (ALP) increased by BBG. BBG increases p38/ERK and p-Smad1/5/9 protein levels in MC3T3-E1 cells. Additionally, BBG increases the bone regeneration of the zebrafish tail significantly. Taken together, BBG increased osteoblast differentiation via p38/ERK and Smad1/5/9 phosphorylation. These results demonstrate that BBG enhances osteogenic differentiation via p38/ERK mediated Smad1/5/9 phosphorylation.

***Corresponding author :** Won Gu Jang, Sang-Hyun An

***Keywords :** Barley beta glucan, P38, ERK, Smad1/5/9, Osteoblast differentiation

PS-E-004

Preliminary investigation into long-term stress by isolated captivity-related changes of reproduction hormones in Cynomolgus monkey

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Stress profoundly affects physical and emotional well-being, extending its physiological influence to the female menstrual cycle, impeding the hypothalamus–pituitary–gonadal (HPG) axis, and affecting fertility by suppressing sex-stimulating hormones. The preliminary findings indicated lower-than-normal levels of cortisol, follicle-stimulating hormone (FSH), and estradiol. Anovulatory bleeding occurred in one monkey, which could be linked to stress. In contrast to cortisol, alkaline phosphatase (ALP), which is correlated to cortisol levels, was consistently elevated in menstruating monkeys, suggesting its potential as a stress indicator. The non-menstruating group exhibited stress-related weight loss, emphasizing the observed ALP trends. The preliminary findings indicated lower-than-normal levels of cortisol, follicle-stimulating hormone (FSH), and estradiol. Anovulatory bleeding occurred in one monkey, which could be linked to stress. In contrast to cortisol, alkaline phosphatase (ALP), which is correlated to cortisol levels, was consistently elevated in menstruating monkeys, suggesting its potential as a stress indicator. The non-menstruating group exhibited stress-related weight loss, emphasizing the observed ALP trends. For thousands of years, the human–primate interface has existed in natural environments. However, at the laboratory level, this interface can pose threats to their welfare owing to limited space and the specific purposes of research. Researchers introduce methods such as positive reinforcement training and food preference tests to enhance the welfare of NHPs during the research process, and welfare-enhancing practices related to husbandry management, such as social housing and playgrounds, are utilized. Our research suggests that understanding the menstrual cycle of female Cynomolgus monkeys is a potential approach to enhancing their welfare at the laboratory level.

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***Keywords :** Cotisol, Menstrucation, Reproductive hormone, Stress

PS-E-005

Primate resources center (PRC) supports non-human primate infrastructure for biomedical and bioscience research

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Future bio-industry is emerging as an alternative to solve population, aging, food, environmental and energy problem. In particular, bio-industry, which is the core of the fourth industrial revolution, is a field that will lead human health and economic prosperity. Primates that are essential for preclinical studies for the bio-health industry are national strategic resources, and biotechnology leading countries (US, Germany, Japan, etc.) have already established / studied facilities for primate research since the early 1960s. In 2005, Korea government established Korea National Primate Research Center (NPRC) in Korea Research Institute of Bioscience and Biotechnology (KRIBB). The government build the Primate Resources Center (PRC) in 2015 in order to respond to the globalization trend such as the weaponization of primate resources and the restriction of imports, and it was completed in 2018. PRC is the largest non-human primate infrastructure in Korea. Non-human primates in PRC are extensively quality-controlled by means of microbiological monitoring (e.g., infectious viruses and bacteria) in order to maintain specific pathogen free (SPF) non-human primate resources. In addition, PRC make an efforts to construct collaborative networks and to support industry, academia, institute for non-human primate research, including for neurodegenerative disease models, regenerative medicine, and new-drug discovery related to incurable diseases. Therefore, PRC would like to help researchers to share SPF monkey resources for research purpose, could get various national monkey infra services.

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***Keywords :** SPF animal, Macaque, Biomedical infrastructure, Non-human primate(NHP)

PS-E-006

Potential food inclination of cynomolgus monkey in laboratory environments: enhancing positive reinforcement training and health optimization

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Positive reinforcement and training for health optimization are pivotal for successful studies with monkeys. Potential food inclination is important for studies on cynomolgus monkey in laboratory environments, but evaluations remain scarce. We explored cynomolgus monkey's potential food inclination to establish a reward system for future behavioral assessments. Twelve male and three female monkeys underwent a food inclination assessment in which they were offered four food categories—fruits, vegetables, proteins, and nuts. The monkeys exhibited a higher inclination for plant-based foods, particularly fruits and vegetables, over animal-based proteins like chicken and tuna ($p < 0.0001$), with a notable inclination for nuts (eaten/provided = 100%). Additionally, the consistency of potential food inclination after repeated offerings was investigated, revealing a time-dependent increase in inclination for protein items. Food consumption ratios correlated positively with caloric intake ($r = 0.59$, $p = 0.02$), implying that individuals with a regular high caloric intake and increased body weight are more likely to accept food during positive reinforcement training. Our findings suggest fruits, vegetables, protein-rich foods, and nuts can help with health optimization. However, animal-based protein-rich foods initially had a low preference, which may increase over time. Our study can provide guidelines for positive reinforcement training and health optimization. Future research incorporating natural foraging behaviors and testing the applicability of observed potential food inclinations in practical scenarios would provide additional insights into promoting the overall welfare and health of cynomolgus monkey.

***Corresponding author :** Woori Jo

***Keywords :** Cynomolgus monkey, Positive reinforcement training, Welfare, Dietary choice, Non-humam primate

PS-E-007

The accuracy of estrus prediction in Hanwoo improved by the ruminoreticular biocapsule sensors

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Background: After standing to be mounted by an estrus cow, the recommended time to conduct artificial insemination is the estrus time. However, visual observations are mostly inaccurate; only 50%–60% of the predictions can be confirmed when estrus is detected at night, when many cattle are breeding and behavioral features are less visible. Recently, a bio-capsule sensor-based ICT system (bolus system) has developed a technology that can detect changes in ruminoreticular temperature in real-time through the ICT equipment by inserting and settling it in the rumen of cows. This equipment has been used to conduct various research investigations, such as investigating the changes in the concentration of milk production in cows, ruminoreticular pH, feed intake rate, etc.
Purpose: This study observed the changes in ruminoreticular temperatures and body activities using ruminoreticular biosensors and aimed to compare the accuracy of estrus observation detection.
Results: When the ruminoreticular biosensors were used, estrus was correctly detected in 45 of the 51 predicted cows (88.2%) after the first insemination, and 6 (11.8%) were significantly determined to be non-estrous. The conception rate in the group of cows with the ruminoreticular biosensor (42/61, 68.9%) was 9.2% higher than in the control group (50/64, 78.1%).
Conclusions: Using ruminoreticular biosensors can increase the estrus detection rate on farms and reduce labor costs for estrus observation. However, estrus detection systems must be improved with more precise prediction techniques, as the rate of misprediction by the ruminoreticular biosensor group was 11.8%. Therefore, these findings can be used as primary data for enhancing the accuracy of AI systems for estrus prediction.

***Corresponding author :** Myoung Ok Kim

***Keywords :** Hanwoo, Estrus observation, Ruminoreticular temperature

PS-E-008

LOOK: advanced training program for laboratory animal veterinarians of KCLAM

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The laboratory animal veterinarians (LAVs) play a significant role as unique link between the humane use of laboratory animals and advancement of scientific and medical knowledge in biomedical research. For these reasons, the social need for qualified LAVs in biomedical research has increased steadily over the past years. The Korean College of Laboratory Animal Medicine (KCLAM) recently developed a new educational program for LAVs which is called LOOK: Laboratory animal veterinarian On-the-job training Of KCLAM. The LOOK 2022 & 2023 that is firstly conducted are running a hybrid format combination of remote and in-person meeting. Each program consists of seven courses based on The Guide (NRC 2011) for entry level veterinarians and detailed subjects are included IACUC, veterinary care, and facility management. KCLAM has prepared the practice-oriented learning: LOOK 2024. This program is designed to provide the practical application using the survey and Q&A session related to specific topics such as LAV role & responsibility, facility management and effective prevention and control of rodent diseases. Together, LOOK program is expected to contribute on closing the gap between theoretical content and practice by providing the up-to date information and discussing the work-related issues. KCLAM is trying to provide the continuing education and training for the qualified veterinarians in laboratory animal science to conduct ethical and scientific animal research.

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***Keywords :** LOOK, KCLAM, On the job training, Laboratory animal veterinarian, Education

PS-E-009

Intrathecal administration and analysis of Lidocaine in CSF of Cynomolgus monkeys

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In recent years, the utilization of CNS therapeutics such as gene therapy, monoclonal antibody therapy, cell therapy, and other novel pharmacological interventions has been increasing. This highlights the growing importance of nonclinical evaluations in biological drug development. Effective drug development requires methods to deliver drugs directly to the cerebrospinal fluid (CSF) and to overcome the Blood-brain barrier (BBB). Intrathecal injection (IT) is widely recognized as the most effective procedure for delivering drugs to the CNS. However, in South Korea, there is a shortage of proficient laboratory animal technicians with the skills and methodologies for precise IT administration. Keyprime Research has refined this crucial method to achieve more successful IT administration in nonclinical assessments, particularly in cynomolgus monkeys (Macaca fascicularis), which closely mimic human physiology and immunology. Through the exploration of suitable equipment for direct injection of test substances into the spinal cord of cynomolgus monkeys (n=300) and analysis of lidocaine concentration in the CSF (n=17) to validate indicators of successful IT administration, our study demonstrates that (1) the most suitable and specialized spinal needle for IT injection was from manufacturer Gertie Marx® Needle (IMD, USA), (2) the prone position was identified as the most appropriate posture for stable administration compared to lateral recumbency, accompanied by tail flick responses due to nerve stimulation upon needle insertion, and (3) successful administration via temporary lower limb paralysis using the local anesthetic (2% lidocaine, Daihan, South Korea) proved more functionally effective than confirmation through saline injection. Furthermore, through the analysis of lidocaine concentrations in cynomolgus monkeys' CSF, we were able to confirm the duration and time-point concentration trends in the CSF. The results of this study are expected to enhance the technical proficiency of experimental animal technicians preparing for IT injections and are anticipated to facilitate the successful development of new drugs evaluated in nonhuman primates through precise administration techniques involving complex methodologies.

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***Keywords :** Non-humane primate (NHP), Cynomolgus monkey, Intrathecal (IT) injection, Lidocaine, CSF

PS-E-010

Confirmation of Bactericidal effect using Hypochlorous acid water in the NHP (Non-human Primate) animal room

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The Keyprime Research (KPR), established in 2022, is the largest non-human primate CRO (contracted research organization) for preclinical studies in Korea. The facility has a capacity to house a total of 1,142 animals at any given time and can conduct 36 studies simultaneously. In order to maintain the cleanliness of the non-human primate animal rooms and protect the animals from contamination, the facility has 30 animal rooms that are cleaned daily by staff. Chlorine-based disinfection methods are known to be effective in disinfecting, and hypochlorous acid water is widely used for this purpose. Therefore, KPR employs hypochlorous acid water for cleaning processes in the animal room. The hypochlorous acid water is used to clean the floors and cages of the animal rooms, followed by a final rinse with tap water. The hypochlorous acid solution used in the animal rooms is generated on-site using a hypochlorous acid water generator installed at KPR. In order to evaluate the bactericidal effect of hypochlorous acid water, we applied it to two regulatory bacteria commonly found in non-human primate animal rooms: *Salmonella Abony* and *Pseudomonas aeruginosa*. The results showed that hypochlorous acid water was highly effective in inhibiting the growth of these bacteria. However, when we compared the bactericidal effect of undiluted hypochlorous acid water with that of 10-fold and 2-fold diluted solutions, we found that the inhibitory effect of the diluted solutions was lower than that of the undiluted solution. We also evaluated the bactericidal effect of hypochlorous acid water in the non-human primate animal rooms before and after cleaning. The results showed that the growth of *Salmonella Abony* and *Pseudomonas aeruginosa* was inhibited for at least two hours after cleaning with hypochlorous acid water. Based on these findings, we conclude that hypochlorous acid water is an effective disinfectant for use in cleaning non-human primate animal rooms to prevent contamination, and we will optimize our cleaning protocols accordingly.

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***Keywords :** Non-Human Primate, Toxicity, Quarantine, CRO

PS-E-011

Derivatives of ferulic acid preserve intestinal barrier tight junctions by suppressing inflammatory responses in a mouse model of dextran sulfate sodium-induced inflammatory bowel disease

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Inflammatory bowel disease (IBD), a chronic disorder affecting the colon and rectum, involves the overproduction of pro-inflammatory cytokines causing damage to tight junctions (TJ) in the intestinal epithelial cells and chronic inflammation. The current mainstay of treatment, sulfasalazine, often causes adverse effects, thereby necessitating the exploration of alternative herbal medicines with fewer side effects. *Portulaca oleracea* L. (*P. oleracea*), a traditional medicinal herb, contains feruloyl amide compounds and has demonstrated beneficial effects on various diseases. Ferulic acid (FA), which is abundant in *P. oleracea*, has been reported to have therapeutic potential for IBD. Therefore, we synthesized new compounds by conjugating FA with (±)-octopamine. Our study focused on novel FA derivatives that demonstrate protective effects against the intestinal epithelial barrier and inflammatory responses. In lipopolysaccharide-induced macrophages, C1 and C1a inhibited the production of inflammatory mediators. In a mouse model of dextran sulfate sodium-induced IBD, a treatment with these compounds ameliorated features including a body weight reduction, colon shortening, an increased disease activity index, and histopathological changes. In Caco-2 intestinal epithelial cells, these compounds maintained the TJ protein expression, thereby demonstrating their protective effects on the epithelial barrier. Furthermore, C1a demonstrated greater efficacy than C1 at the same concentration. These findings suggest that the novel FA derivative (C1a) effectively alleviates clinical signs and inflammatory mediators in IBD, making these compounds potential candidates as natural medicines for the treatment of IBD.

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***Keywords :** Inflammatory bowel disease, Dextran sulfate sodium, Ferulic acid, Portulaca oleracea L.

PS-E-012

Development of ethical animal experiment education

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According to the annual animal experiment survey data released by the Korea Animal and Plant Quarantine Agency, the number of animal use in 2023 was 4.58 million, up 10% on average every year since 2017. Among them, the number of animals used for education or training reached 43,000 which is an average increase of 20%. In this situation, we are developing the mouse and rat simulator with the aim of reducing the number of animals used in education and training. We are going to use these simulators to train researchers who are starting animal research for the first time. After learning basic handling and restraint, oral, subcutaneous, intraperitoneal and intravenous injection, after than they will be able to experiment with living animals. Several simulators have already been developed, but we are developing an improved model that feel more like handling real animals. And we plan to develop another simulator to conduct dissection training so that researchers can learn the shape, location and basic structure of the thoracic and abdominal organs. Through this, simulators are used instead of live animals used for education and training (Replacement), the number of animals is reduced (Reduction), and the stress on animals during the process is minimized (Refinement).

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***Keywords :** 3R, Simulator, Education, Training

PS-E-013

Estrogen-related receptor-α (ERRα) modulates the populations of hematopoietic stem and progenitor cells in the bone marrow

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Hematopoietic stem cells (HSCs) can self-renew and generate all differentiated lineages. These cells reside in a specialized bone marrow niche comprising various cell types. The bone marrow niche cells preserve the stemness of HSCs through direct interactions or secreted factors. Bone marrow endothelial cells are particularly crucial for maintaining HSC quiescence and self-renewal. Estrogen-related receptor-α (ERRα) is an orphan nuclear receptor involved in mitochondrial biogenesis and metabolic homeostasis, regulating mitochondrial energy metabolism, function, and dynamics. ERRα is abundantly expressed in the intestine and immune cells. Previous studies have shown that ERRα is essential for maintaining intestinal homeostasis and protecting against colitis by promoting the regeneration and differentiation of intestinal epithelial cells. Conversely, ERRα expression is increased in colorectal cancer, where it plays an oncogenic role. In acute myeloid leukemia (AML), ERRα is a key regulator of mitochondrial respiration, metabolism, and oxidative phosphorylation, contributing to disease progression. Recent research has shown that endothelial ERRα regulates genes linked to angiogenesis. However, the role of ERRα in HSCs is not well understood. To explore ERRα's role in HSC regulation, we analyzed the frequency of hematopoietic cells in ERRα knockout (KO) and conditional KO mice. These mice showed an increased number of hematopoietic stem and progenitor cells (HSPCs) in the bone marrow, suggesting that ERRα is significant in regulating the HSPC pool and may influence HSC self-renewal and stemness in the bone marrow.

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***Keywords :** Hematopoietic stem cell (HSC), ERRa

PS-E-014

Rapamycin and ganetespib suppress inflammatory response induced by 27-hydroxycholesterol

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Atherosclerosis is characterized by the deposition and accumulation of extracellular cholesterol and inflammatory cells within the walls of arterial blood vessels. Among the cholesterol metabolites prevalent in atherosclerosis, 27-hydroxycholesterol (27HC) is the most abundant. This metabolite is a bioactive immune oxysterol known to trigger inflammatory responses, including the activation of immune cells and the secretion of chemokines. Despite its significant role, the detailed molecular mechanisms of 27HC-induced inflammation remain insufficiently understood. In this study, we explored the roles of the mechanistic target of rapamycin (mTOR) and heat shock protein 90 (Hsp90) in the context of 27HC-induced inflammation by utilizing rapamycin and ganetespib, respectively. Our findings revealed that treating THP-1 monocytic cells with rapamycin effectively reduced the expression of CCL2, which is typically increased by 27HC. Additionally, rapamycin suppressed the upregulation and phosphorylation of S6 and 4EBP1 induced by 27HC, although it did not affect AKT. On the other hand, treatment with ganetespib not only decreased the production of CCL2 but also inhibited the expression and phosphorylation of S6, 4EBP1, and AKT, all of which were elevated by 27HC. These results collectively suggest that 27HC promotes inflammation by activating the HSP90/AKT/mTOR signaling pathway. Consequently, both rapamycin and ganetespib show potential as therapeutic agents for treating inflammatory diseases associated with 27HC. This study underscores the significance of targeting the HSP90/AKT/mTOR pathway to mitigate inflammation induced by cholesterol metabolites like 27HC, providing a clearer understanding of the molecular interactions at play and highlighting possible avenues for clinical intervention in atherosclerosis- related inflammation.

***Corresponding author :** Dongjun Lee

***Keywords :** 27-hydroxycholesterol (27HC), Mechanistic target of rapamycin (mTOR), Heat shock protein 90 (Hsp90)

PS-E-015

Protective role of methanol extract of Microsorum membranaceum (D. Don Ching) against Dex-induced muscle atrophy in C2C12 cells and C57BL/6 mice

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Microsorum membranaceum (D. Don Ching) have been used in very limited traditional treatments including fever, but there are no scientific evidences on their efficacy until now. To investigate this potential, we conducted a study where we treated a methanol extract of *M. membranaceum* (D. Don) Ching (MEM) to Dexamethasone (Dex)-induced C2C12 cells and C57BL/6 mice. Firstly, the MEM showed high inhibitory activity against DPPH radicals and the IC50 value was determined to be 7.00972 μg/mL, respectively. A significant dose-dependent decrease in the number of dichlorofluorescein (DCF)-stained cells representing intracellular ROS was detected in the three MEM+Dex treated groups when compared with the Vehicle+Dex treated group. The transcription levels of MuRF1 and Atrogin-1 gene for protein degradation were significantly decreased with dose-dependent manner in Dex-induced atrophy cells after treatment of MEM. However, the diameter of myotube was remarkably increased in the Dex+MEM treated C2C12 cells. Furthermore, the PI3K/Akt/mTOR signaling pathway for protein synthesis was activated after MEM treatment, while the expressions of LC3B and Beclin-1 proteins for protein degradation were inhibited by MEM treatment. In addition, these effects of MEM in Dex treated C2C12 cells will be verified in Dex induced atrophy animal model through analyses for exercise ability, muscle weight, cross section area, myosin heavy chain transition and biomarker proteins expression. Therefore, these results suggest that MEM may have a great therapeutic potential against muscle atrophy.

***Corresponding author :** Dae Youn Hwang

***Keywords :** M. membranaceum, Muscle atrophy, Dexamethasone, Myotube

PS-E-016

Proposal for the harmonization of health monitoring between common marmoset colonies in South Korea

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The increasing development of biopharmaceuticals and the emergence of infectious diseases (e.g., COVID-19) have led to a growing demand for non-human primates (NHPs). The Health Monitoring of NHPs plays a crucial role in enhancing the accuracy and reproducibility of animal experiment results. Moreover, most microbial contamination pose significant threats to the health of both humans and animals. Common marmoset, small new world monkey, are emerging as a valuable animal model in various research fields, including aging research, neuroscience, and infection studies. Many researchers in South Korea are also actively pursuing various studies using common marmoset. Despite this research expansion, there are no discussions for the harmonization of health monitoring between colonies. In this study, we endeavored to establish harmonized standard suitable for the domestic situation through an investigation of relevant laws, literature reviews, and consultations with domestic experts. By discussing with the other common marmoset colony (SNUH), we have derived the draft for the harmonization of health monitoring. These include mandatory items such as bacteria (4) and parasites (3), as well as optional items that institutions may choose to monitor, such as viruses (1) and bacteria (4). Moving forward, our research team plans to establish standards for sample collection, diagnostic techniques, and diagnostic frequency. These outcomes are expected to significantly contribute to the expansion and reliability of common marmoset research in South Korea.

***Corresponding author :** Kyoung Sun Lee

***Keywords :** Harmonization of Health Monitoring, Common Marmoset

PS-E-017

Discovery of stress-specific biomarkers through correlation analysis of stress and stress-related protein changes in beagle dogs

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Stress is the changing of the psychological state to protect the body against external, as well as non-specific biological reactions occurring in response to various injuries and stimuli applied to the body. The body secretes more cortisol and corticosterone under stressed conditions. It is known that elevated serum cortisol and corticosterone levels significantly correlate with the symptoms of various diseases. Also, analysis of proteins in the blood can determine the prognosis of various diseases and predict new treatments. The objective of this study is to examine the association between stress and changes in serum and to explore biomarker changes by stress. To evaluate changes in serum caused by stress, the healthy 10 beagles were selected, which varied in age and clinical status. To induce stress in animal models, an Elizabethan collar (E-collar) was worn on their necks and put in the cage from 3:00 pm to 6:00 pm three times a week during the experiment period. After 3 hours, the blood was collected from 10 beagles. Enzyme-linked immunosorbent assay (ELISA) method was performed to quantify the cortisol and corticosterone levels in serum. As a result, cortisol, and corticosterone were significantly increased according to a period of induced stress. Additionally, to confirm the correlation between stress and proteins in serum, LC-MS/MS was performed to analyze stress-specific biomarkers in serum. As a result, its significant related secretion (50%), cellular stress response (16.67%), angiogenesis (20%), cell differentiation (7.14%), cell migration (11.11%), extracellular matrix (15.38%), immune response (7.32%), inflammatory response (11.11%) and neurogenesis (11.11%). Stress was changed to specific proteins, such as TIMP1, TREM2, RAB8A, KRT9, PPBP, THBS, and HSPB1 in serum. In conclusion, sustained stress exposure changes the blood concentration, and it can cause various diseases. Furthermore, by identifying and analyzing the characteristics of proteins expressed due to stress, the cause of the disease can be identified, and new treatments can be proposed accordingly.

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***Keywords :** Stress, Stress-specific biomarker, Serum protein, LC-MS/MS, Canine

PS-E-018

Enhancing animal research training: TALK course

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In 2022, the Animal and Plant Quarantine Agency reported over 4.99 million laboratory animals used for scientific purposes in Korea across 517 facilities, including rodents, rabbits, dogs, pigs, non-human primates, birds, fishes, reptiles, and amphibians. The Korea Mouse Phenotyping Center (KMPC) and the Korean College of Laboratory Animal Medicine (KCLAM) developed the "TALK: Training of Animal Research Level-up course" in response to the 2023 "Development of Standard Educational Contents for Animal Facility User" survey that reflected limitations of existing educational programs such as lack of practical applicability and diversity. The course is for a range of stakeholders, including investigators dealing with animals in research, managers, operators, IACUC members, and attending veterinarians. There are 70 micro learning modules in 8 categories that cover legislation, IACUC, maintenance and operation of facility, quality control of laboratory animals, animal welfare and the 3Rs, humane animal experiment, and occupational health & safety of personnel. The course consists of basic, introductory training for new users, mandatory training for facility managers & operators, and IACUC members in compliance with the Laboratory Animal Act and Animal Protection Act, presented through MP4 videos with PPT slides and voice narrations. Future directions involve offering more advanced courses on anesthesia, necropsy, and additional educational contents, specifically aimed at foreign researchers. The TALK course, developed by KMPC and KCLAM, addresses the major needs for standardized and diverse educational contents in the field of laboratory animal research, aiming to enhance the competence and compliance of individuals engaged in animal experimentation in Korea.

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***Keywords :** Animal experiment, Laboratory animal, Laboratory animal user training, User training

PS-E-019

Flow cytometric xenocrossmatching and clinical outcomes in porcine islet xenotransplanted non-human primates: a comparative analysis

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Introduction: Monitoring humoral immunity in xenotransplant recipients is important for successful transplantation. We analyzed the results of flowcytometric xenocrossmatching in non-human primates (NHPs) after porcine islet xenotransplantation and compared them to clinical outcomes.
Methods: Sera were collected 4-9 times over 20 weeks from five NHPs after islet xenotransplantation. Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized whole blood of donor Pigs (QKO; GGTA1, CMAH, β4galNT2, iGb3s quadruple genes knock-out). 2.5x10^5 porcine PBMC and 50 µl NHP serum were incubated with fluorochrome-conjugated anti-porcine CD3 epsilon, CD21 and anti-human IgG, IgM antibodies. Acquisition and analysis were performed on a Cytek spectral flowcytometer. Median fluorescent index (MFI) ratios (MFI after islet transplantation/ MFI before islet transplantation) were monitored and compared with clinical data, including ATG induction, infection and graft failure.
Results: All five NHPs received anti-thymoglobulin (ATG) induction therapy and showed an increase in T-cell IgG MFI ratios (4.83-1.04) at postoperative day (POD) 0, followed by attenuation by POD14. For NHPs (#1, #2), the T/B cell IgG MFI ratio gradually increased until graft failure (NHP 1: 3.44/1.97 at POD63, NHP 2: 24.3/11.19 at POD56). IgM results showed a similar trend, but were not as pronounced as IgG. NHPs (#3, #5), which remained stable, the T/B cell IgG/IgM MFI ratio stayed below 3 until POD140. NHP (#4) had a low MFI ratio due to excessive immunosuppression and a fungal infection.
Conclusion: The flowcytometric xenocrossmatching results can be used as a monitoring tool to predict clinical outcomes after islet xenotransplantion.

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***Keywords :** Xenotransplantation, Xenocrossmatching

PS-E-020

Effective expansion of primate NK(natural killer) cell by Interleukin-15(IL-15)

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Non-human primates(NHP) are in the spotlight as important experimental animals because they have similar characteristics to humans. In particular, immune system of NHP is very similar to humans, unlike the murine model, it can establish disease models such as human acquired immune deficiency syndrome(AIDS) and hepatitis. So, NHP can provide useful information for the development of treatments and vaccines that human infectious disease. Natural killer (NK) cells are a type of innate immune cell that removes abnormal or infected cells through perforin and granzyme. They are important cells that are involved in the acquired immune system through NK cell memory. Conventional primate NK cell extensions were mostly performed by IL-2. However, primate NK cells exhibited insufficient activation at low concentrations of recombinant human interleukin IL-2(rhIL-2), so we confirmed recombinant human interleukin 15 (hrhIL-15) to determine whether other stimuli can expand primate NK cells. IL-15 receptor has structural features that identically possess IL-2 receptor and γc and IL-2/IL-15Rβ(CD122) and activates the JAK and STAT signaling pathways. Therefore, we expected that rhIL-15 could replace and complement rhIL-2, which was primarily used to culture of primate NK cells. Consequently, we confirmed that rhIL-15 is an effective option for primate NK cell expansion, which we expect to establish an effective basis for future follow-up studies using primate NK cell.

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***Keywords :** Non-human primate(NHP), Natural killer(NK) cell, Cytokine, Interleukin-2, Interleukin-15

PS-E-021

SP-8356 attenuates LPS-induced acute lung Injury by Inhibiting inflammatory cytokines and immune cell infiltration

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This study investigated SP-8356, a synthetic derivative of (1S)-(-)-verbenone, for its anti-inflammatory and protective properties in a mouse model of lipopolysaccharide (LPS)-induced acute lung injury (ALI). ALI, characterized by excessive inflammation and compromised lung function, is a critical condition often seen in various pulmonary diseases. SP-8356 was examined for its potential to mitigate these deleterious effects by targeting intracellular signaling pathways and inflammatory responses. The study found that SP-8356 effectively inhibited the activation of key signaling molecules, including NF-κB and Akt, which are pivotal in orchestrating the inflammatory cascade. This inhibition led to a significant reduction in the expression of inflammatory cytokines in different cellular components of the lung. By dampening the cytokine storm associated with ALI, SP-8356 demonstrated its capacity to attenuate the inflammatory response, thereby potentially limiting tissue damage and maintaining pulmonary function. Moreover, SP-8356 treatment preserved the structural integrity of both epithelial and endothelial barriers within the lung. These barriers play crucial roles in maintaining tissue homeostasis and preventing fluid leakage into the airspaces, which is a hallmark of ALI progression. Additionally, SP-8356 exhibited a notable reduction in immune cell infiltration into the inflamed lung tissue. This effect underscores its ability to mitigate immune-mediated damage and further supports its protective role in ALI. Overall, the findings highlight SP-8356 as a promising therapeutic candidate for pulmonary inflammatory diseases that culminate in ALI. Its multifaceted actions in suppressing inflammation, preserving lung structure, and reducing immune cell infiltration suggest that SP-8356 could potentially offer a comprehensive approach to managing acute lung injury associated with severe pulmonary inflammation. Further research and clinical trials are warranted to fully elucidate its therapeutic potential and safety profile in human applications.

***Corresponding author :** Jong-Ik Hwang

***Keywords :** SP-8356, Acute lung injury, Inflammatory cytokines

PS-E-022

Neurokinin-2 receptor negatively modulates substance P responses by forming complex with Neurokinin-1 receptor

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Tachykinins and their cognate receptors, neurokinin receptors (NKs) including NK1, NK2, and NK3 play vital roles in regulating various physiological processes including neurotransmission, nociception, inflammation, smooth muscle contractility, and stimulation of endocrine and exocrine gland secretion. Their abnormal expression has been reported to be associated with neurological disorders, inflammation, and cancer. Even though NKs are expressed in the same cells with their expression being inversely correlated in some conditions, there is no direct evidence to prove their interaction. Understanding the functional crosstalk between NKs in mediated downstream signaling and cellular responses may elucidate the roles of each receptor in pathophysiology. In this study, I showed that NKs were co-expressed in some cells. However, different from NK3, which only forms homodimerization, I demonstrated a direct interaction between NK1 and NK2 at the protein level using co-immunoprecipitation and NanoBiT-based protein interaction analysis. Through heterodimerization, NK2 downregulated substance P-stimulated NK1 signals, such as intracellular Ca^{2+} mobilization and ERK phosphorylation, by enhancing β-arrestin recruitment, even at the ligand concentration that could not activate NK2 itself or in the presence of NK1 specific antagonist, Aprepitant. In A549 cells with receptors deleted and reconstituted, NK2 exerted a negative effect on substance P/NK1-mediated cell migration. This study has provided the first direct evidence of an interaction between NK1 and NK2, which highlights the functional relevance of their heterodimerization in cellular responses. I demonstrated that through dimerization, NK2 exerts negative effects on downstream signaling and cellular response mediated by NK1.

***Corresponding author :** Jong Ik Hwang

***Keywords :** Neurokinin receptors, Substance P, Receptor dimerization, NanoBiT assay, Cellular signaling

PS-E-023

Current status of animal experimentation and committee operations in domestic animal experimentation institutions in 2023

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This study aims to analyze the composition and operational aspects of Institutional Animal Care and Use Committees (IACUCs) established in animal experimentation institutions, as mandated by Article 51 of the Animal Protection Act. The analysis is based on the performance reports of the IACUCs and is intended to serve as foundational data for enhancing the welfare of laboratory animals in the future. In 2023, a total of 550 institutions reported the establishment of IACUCs to the Animal and Plant Quarantine Agency. These institutions included industries (301), universities (130), public institutions (82), and hospitals and health institutions (37). The IACUCs comprised a total of 3,182 members, with an average of 5.79 members per committee. Annually, the committees reviewed a total of 42,098 animal experimentation plans, of which 5.4% were either revised and resubmitted or disapproved. The main reasons for non-approval included insufficient justification for the number of animals requested, inappropriate animal experimentation methods, and inadequate assessment of animal pain and stress. A total of 4,581,798 animals were used in experiments, with 76.1% (3,484,636 animals) being used in legally regulated tests (38.8%) and basic research (37.3%). The findings of this study will be used as foundational data for the continuous development of policies aimed at improving laboratory animal welfare. Additionally, the results will inform the development of training programs for committee members, reflecting the current state of animal experimentation and the continuing education system for committee members.

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***Keywords :** IACUC, Animal Experimentation, Animal Protection, Animal Welfare, Laboratory animal

PS-E-024

Phlorotannis prevent vocal fld fibrosis via aerosol inhalation in laser-induced firosis model

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Vocal fold fibrosis is an abnormal condition characterized by unfavorable changes in the organization of the extracellular matrix in vocal fold lamina propria. To prevent and treat vocal fold fibrosis, a number of synthetic drugs, such as mitomycin C and the glucocorticoid family, are used after surgery, but these are known to have some side effects. Therefore, using both in vitro and in vivo studies, this study investigated whether phlorotannins extracted from *Ecklonia cava* have the potential to prevent vocal fold fibrosis with minimal side effects. The results show that phlorotannins suppressed both the expression of the fibrotic phenotypic marker and cell migration by inhibiting the activation of the mitogen-activated protein kinase (MAPK) and Smad2/3 signaling pathways in human vocal fold fibroblasts stimulated by transforming growth factor-β. Additionally, phlorotannins exhibited antifibrotic efficacy without an excessive inflammatory response in a laser-induced fibrosis rabbit model when delivered as an aerosol via inhalation. Based on these results, phlorotannins should be considered a promising candidate for use in the prevention of vocal fold fibrosis.

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***Keywords :** Ecklonia cava, Inhalation, Phlorotannins, Vocal fold fibrosis

PS-E-025

Introduction of Ajou MBD T2B Center

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The Efficacy Test Center for Mental & Behavioral Disorders at Ajou University Hospital (Ajou MBD T2B Center) is a specialized center that supports the success of clinical trials and the commercialization of medical products. We offer clinical utility analysis for product development, non-clinical evaluation based on global standards for mental and behavioral disorders, validity evaluation considering regulatory approval, and exploratory clinical support utilizing patient cohorts. Major non-clinical services. In vitro efficacy test: Cytotoxicity evaluation, cell-based new target screening, protein expression and activity evaluation, biomarker evaluation, antioxidant efficacy evaluation, image analysis (expression and distribution analysis of cell organelles and proteins), fluorescence immunological evaluation, and multi-omics evaluation, etc. In vivo efficacy test: Behavioral evaluation, clinical pathological evaluation, histopathological evaluation, radiological evaluation, pharmacological evaluation, immunological evaluation, and preliminary toxicity evaluation (non-GLP), etc. Customized services: We provide non-clinical (in vivo/in vitro) trial design and consultation, clinical trial design and consultation, consignment testing, and approval consultation for drugs, medical devices, and digital therapeutics. Additionally, we design and perform exploratory clinical trials for digital therapeutics, offer patient specimen and sample utilization services, and deliver result reports at the level of an international common technical document (CTD). Target diseases: Mental and behavioral disorders include dementia, depression, sleep disorders, ADHD, anxiety, behavioral disorders, addiction, schizophrenia, bipolar disorder, obsessive-compulsive disorder, cognitive impairment, autism, anorexia, and others. How to apply: Apply for service via email (kjs0829@ajou.ac.kr), phone (031-219-7920), or website (http://www.mbdt2b.re.kr)

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***Corresponding author :** Sang-Rae Lee

***Keywords :** Mental & behavioral disorders, In vitro & in vivo Efficacy Service , Non-clinical research

PS-E-026

Altering SURF4 expression levels enhances tumorigenic MEK-ERK pathway activation in solid cancers

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SURF4 codes for a conserved ER integral membrane protein characterized by multiple predicted transmembrane domains. As a cargo receptor, SURF4 facilitates protein secretion, transport, and export from the ER. Research has shown that SURF4 is crucial for preserving the integrity of the ER-Golgi intermediate compartment (ERGIC) and the Golgi apparatus, as well as regulating store-operated calcium entry (SOCE). Additionally, SURF4 has been implicated in viral replication. In a previous study, SURF4 was identified through in silico analysis of Kaplan-Meier survival curves in patients with various cancers. Our findings indicate that altering SURF4 expression levels can transform normal cells into tumor cells and influence cell migration in vitro. Moreover, SURF4 supports tumorigenic transformation in vivo. In this study, we further explored the oncogenic role and function of SURF4 in human cancer cell lines. We discovered that SURF4 overexpression modulates MEK or ERK activation across multiple solid tumor cell lines, including those from breast, prostate, ovarian, and colorectal cancers. These findings provide new insights into the molecular mechanisms by which SURF4 acts as a positive regulator of MEK-ERK signaling in solid tumors.

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***Keywords :** SURF4, Oncogene

PS-E-027

Stilbenoid derivatives: Potent inhibitors of HIF-1α-centric metabolism under hypoxia

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Under hypoxic microenvironment, hypoxia inducible factor (HIF)-1α is critical transcription factor that regulates gene expression required for angiogenesis, proliferation, metastasis, invasion, and drug resistance promoting cancer malignancy. In addition, HIF-1α increases the expression of genes associated to cancer metabolism. Most of cancer exhibit enhanced not only glycolytic metabolism but also mitochondrial respiration even in hypoxic condition. Owing to its function in cancer, HIF-1α is thought to be a highly effective anticancer therapeutic approach in the hypoxic microenvironment. In this study, stilbenoid derivatives were designed, synthesized and assessed for their capacity to inhibit HIF-1α centric cancer metabolism and evaluated for inhibition of cancer cell viability and HIF activation. Through the structure-activity relationship studies, compound 28e was identified as the most effective derivative. More specifically, 28e suppressed the accumulation of HIF-1α protein and the expression of its target genes including GLUT1 and PDK1 without affecting HIF-1α mRNA expression. Moreover, 28e inhibited glucose uptake, glycolytic metabolism, and mitochondrial respiration of cancer cells, decreasing cellular ATP production under hypoxic conditions. Furthermore, 28e exert significant anti-tumor effects without weight loss and effectively reduced the accumulation of HIF-1α protein in tumor tissue in vivo xenograft mouse model. Taken together, this study suggests that stilbenoid derivatives exert anticancer activity by targeting HIF-1α centered cancer metabolism under hypoxic conditions.

***Corresponding author :** Hyun Seung Ban

***Keywords :** Stilbenoids, Hypoxic cancer, HIF-1α, Cancer metabolism

PS-E-028

Improved tumor ablation with square waveforms in radiofrequency ablation: a comparative study

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Purpose: Radiofrequency ablation (RFA) is a localized treatment for primary liver cancers, including hepatocellular carcinoma and intrahepatic cholangiocarcinoma. Despite various adjustments to the input parameters of RF generators, the limited ablation range remains a significant obstacle. This study aimed to compare the ablation range and efficacy of sine and square electrical waveforms in a mouse tumor model.
Methods and Materials: An RF generator capable of adjusting electrical waveforms was developed. The ablation ranges of sine and square waveforms were compared in porcine liver tissue. In vivo efficacy was evaluated using 45 BALB/c nude mice. Post-RFA, the mean tumor volumes and survival rates of mice subjected to both waveforms were measured. Additionally, cellular coagulative necrosis, inflammatory cell infiltration, HSP 70 expression, TUNEL assays, and TNF-α deposition were assessed to determine the inflammatory and apoptotic responses.
Results: The ablation range of the square electrical waveform was significantly larger than that of the sine waveform in porcine liver tissue (all $p<0.001$). In the in vivo mouse model, the mean tumor volume in the square waveform group was significantly lower than in the sine waveform group ($p<0.001$), which correlated with a higher survival rate (60%). The square waveform also induced significantly greater cellular coagulative necrosis, inflammatory cell infiltration, HSP 70 expression, TUNEL-positive cells, and TNF-α deposition compared to the sine waveform (all $p<0.05$).
Conclusion: RFA using square electrical waveforms demonstrated enhanced therapeutic potential for tumor management due to its larger ablation range and more effective tumor reduction compared to sine waveforms. These findings suggest that square waveforms could be a more effective option for improving the outcomes of RFA in clinical settings.

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***Keywords :** Radiofrequency ablation, Local heat treatment, Electrical waveforms, Ablation ranges, Tumor ablation

PS-E-029

Enhanced antimicrobial efficacy of Zn/AgNP dual-layer coated catheters in reducing CAUTIs: an in vitro and in vivo study

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Purpose: Catheter-associated urinary tract infections (CAUTIs) are commonly caused by prolonged catheterization, leading to bacterial colonization and biofilm formation. While commercial catheters coated with silver nanoparticles (AgNP) inhibit bacterial growth, their long-term efficacy diminishes due to reduced silver ion release. Dual-coating strategies combining antimicrobial and antiseptic actions have emerged as potential solutions. This study aims to assess the safety and efficacy of Zn/AgNP coatings both in vitro and in vivo.
Methods and Materials: A commercially available silicone catheter (8 Fr, 20 cm) was sequentially coated with polydopamine, AgNP, and Zn using RF sputtering, resulting in uncoated, AgNP-coated, and Zn/AgNP-coated catheter samples. Surface analysis was conducted using FESEM-EDS and FIB-EDS. Additional assessments included contact angle measurements, tensile properties, ion release profiles, and antimicrobial efficacy. In vivo studies involved dividing rabbits into groups receiving each catheter type, followed by a 4-week period after which urine samples, cystoscopic evaluations, and surface analyses were performed. Histological analyses (H&E, MT, and TUNEL) assessed inflammation, epithelial integrity, collagen deposition, and apoptosis.
Results: Both AgNP-coated and Zn/AgNP-coated catheters were successfully fabricated, exhibiting distinct surface characteristics as observed in FESEM images. The dual-layer coating strategy achieved effective bactericidal action while reducing cytotoxicity through sustained and controlled release of AgNPs and Zn ions. Catheter placement in rabbits was completed without complications, and all animals survived the study period. Urethroscopic examination revealed significant differences in sludge formation between groups ($p<0.001$). Microscopic analysis indicated significant variations in biofilm presence among groups ($p<0.001$). Histopathological evaluations showed significant differences in inflammatory cell infiltration, epithelial layer thickness, and TUNEL-positive cell deposition ($p<0.001$).
Conclusion: The Zn/AgNP dual-layer coating enhances the clinical management of urinary catheterizations by effectively reducing CAUTIs and substantially lowering the risk of complications associated with prolonged catheter use.

***Corresponding author :** Jung-Hoon Park

***Keywords :** Antibacterial, Antifouling, Catheter-associated urinary tract infections, Silver nanoparticles, Zinc

PS-E-030

The absence of Sirt1 within the non-hematopoietic bone marrow microenvironment does not impact the functionality of hematopoietic stem cells in adult mice

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SIRT1, a known histone deacetylase, serves diverse functions within biological systems. Recent studies have underscored its relevance in maintaining stem cell homeostasis, impacting processes such as cell proliferation, differentiation, apoptosis, and inflammatory responses. Moreover, SIRT1 has emerged as a pivotal player in delaying aging, prolonging lifespan, and mitigating aging-related effects through its involvement in mitochondrial metabolic regulation. Notably, investigations into Sirt1's role within the hematopoietic stem and progenitor system have revealed its impact on cell population dynamics, particularly under stress conditions. Activation of SIRT1 has been shown to modulate hematopoietic stem and progenitor cells, altering their numbers and functions. Extending this line of inquiry, a recent study explored SIRT1's contribution within the non-hematopoietic bone marrow microenvironment. Surprisingly, ablating Sirt1 within the non-hematopoietic bone marrow microenvironment yielded outcomes akin to controls, with no significant alterations observed in mature blood cell production or the frequencies of hematopoietic stem and progenitor cells. Intriguingly, the absence of SIRT1 did not impair stem cell functionality under stress conditions. These findings collectively suggest that SIRT1 may not be indispensable for regulating pools of hematopoietic stem and progenitor cells in this context.

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***Keywords :** Sirt1, Metabolic regulation, hematopoietic stem

PS-E-031

Meta-analysis of the effects of single versus mixed housing for environmental enrichment of Beagle dogs in toxicity studies

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Environmental enrichment (EE) aims to enhance the quality of life of experimental animals by providing additional, temporary environmental stimuli to improve their psychological and physiological well-being. EE is utilized to improve the environment of animals across various research fields that involve experimental animals. However, there is a lack of research evaluating the impact of environmental enrichment on the results of animal experiments. This study aimed to assess the effects of single and mingled housing on clinical signs, food consumption and body weight gain in Beagle dogs used in toxicity studies conducted at the Korea Institute of Toxicology. In the single-housing group, each dog was housed individually during the experiment, while in the mingled-housing group, two or three dogs were housed together except during administration and measurement. The results of this study revealed whether mingled housing compared to single housing had an effect on physiology of Beagle dogs in a toxicity study. These findings provide valuable information for the design and interpretation of future toxicity studies using Beagle dogs and contribute to the improvement of animal welfare in experimental settings.

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***Keywords :** Environmental enrichment, Beagle dog, Mingle , Food consumption

PS-E-032

National primate infrastructure for biomedical and basic science

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Primates are valuable resources for different research fields including genetics, evolutionary biology, biomedical research, neuroscience, regenerative research, microbiology, vaccine development and pharmacology. Because primates have more biological and behavioral similarities and closer genetic relationship to humans than other animal models. However, primate resources are limited to access for individual researchers. In 2005, Republic of Korea government established National Primate Research Center (NPRC). First purpose of NPRC is production and supply of specific pathogen free (SPF) primate in Republic of Korea. Second purpose is supporting the regenerative medicine (bio organ transplantation, stem cell and gene therapy). The last one is supporting the basic biomedical research and basic science. Recently, NPRC established primate resource bank with various primate samples (Tissue deoxyribose nucleic acid (DNA), Blood DNA, ribose nucleic acid (RNA), cDNA, paraffin blocks (brain), etc) from crab-eating monkey, marmoset monkey, rhesus monkey, African green monkey, and squirrel monkey. And also, we established cutting edge medical imaging technique using 3 Tesla magnetic resonance imaging (3T-MRI), positron emission tomographic-computed tomographic (PET-CT), micro PET-CT, and angiography imaging system. Therefore, researchers who want to access the primate resources and use the imaging analysis with primate for research purpose could get various national primate infra service, easily (http://portal.kribb.re.kr/primate).

***Corresponding author :** Jae-Won Huh

***Keywords :** Basic science, Biomedical, Infrastructure, Monkey, Primate

PS-E-033

Proposal for standardization of GLP equipment validation methods

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According to GLP principles and guidelines (KGLP, OECD), the Test Management and/or Study Director are responsible for preparing and checking procedures for equipment operation, validation and maintenance, including computerized systems used in non-clinical studies. Additionally, equipment used for data generation, measurement, or assessment must have operational procedures by undergoing standardization in testing and calibration of relevant validation parameters, as per KGLP and US FDA guidelines. To ensure the validity and integrity of GLP study data, including computerized systems, it is crucial to validate whether the equipment has the appropriate design and processing capabilities that to match the planned study design (protocol), whether it includes necessary operating parameters, and whether it detects and adjusts for deviations from known measurement national or international standards. GLP regulatory authorities require institutions to establish management levels based on the frequency and purpose of equipment usage, including computerized systems. Currently, domestic GLP test facilities have been managing internal and external regular inspections, maintenance, calibration, and validation by developing standardized operating procedures tailored to their respective realities. However, it cannot be claimed that they possess a completely integrated and globally standardized system for calibration, qualification, and validation that satisfies data integrity. The root causes for this issue can be attributed to the lack of dedicated internal personnel and/or expertise, increased maintenance costs when utilizing external professional companies, and the absence of systematic standardization methods within the country. In this presentation, we propose the practical aspects of standardizing the validation methods for representative equipment in GLP test facilities, such as an autoclave or steam sterilizer. This includes the composition of validation overview, parameters or criteria for installation qualification, operational qualification, performance qualification, and practical case of Korea Institute of Toxicology.

***Corresponding author :** Kyu Hyuk Cho

***Keywords :** Equipment, Autoclave, Steam sterilizer, Validation

PS-E-034

Proposal for animal facility validation standards in GLP test facilities

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GLP animal facilities are required to ensure the facility's appropriateness for conducting a non-clinical study or animal research and to adequately validate the facility's design, construction, and/or environmental conditions for the quality and integrity of the data. In the early days of GLP in Korea, GLP laboratories individually focused on Specific Pathogen-Free (SPF) and environmental conditions of animal rooms. Now, facility/environment validation has been requested globally and by domestic GLP regulatory agencies. However, due to the lack of domestic standards, GLP laboratories in Korea risk missing key elements in validation management and having different validation criteria. The key factors in validation are as follows: (1) GLP facilities should consider cleaning and/or hygiene management, such as managing inert materials on floors, walls, and ceilings of animal facilities and properly placing test-related equipment and supplies. (2) Laboratories for experiments and laboratories for measurements should be physically separated. Further, sterility and particulate testing should be conducted. (3) Facility managers should manage the HVAC system, environmental control, and procedural documents of whether measurements (e.g., temperature, humidity, airflow, etc.) comply with specifications. (4) To prevent cross-contamination or confusion of projects, proper separation in various test activities, materials, and equipment should be ensured, and a sufficient number of animal (or laboratory) rooms or separable spaces should be provided. This presentation will present the key elements, practices, and standards that should be included in facility validation in GLP animal facilities.

***Corresponding author :** Kyu Hyuk Cho

***Keywords :** GLP animal facilities, Facility Validation, HVAC system, Health monitoring

PS-E-035

AZD7648, a potential DNA-PK inhibitor, acts as a synergistic radiosensitizer in human sarcoma xenograft mice

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Sarcoma is a type of cancer with a low incidence, and usually occurs in body's soft or connective tissues. It shows favorable reactivity of surgery, chemotherapy, or radiotherapy for stage 1 to 3. However, metastatic sarcomas have low responsiveness for various cancer treatments, so it is quite difficult to treat. Radiosensitizers combined with radiotherapy are a good alternative to enhance radiation response for metastatic sarcomas. Previous researches have reported that AZD7648 combined with radiation confirmed notable antitumor effects in carcinoma and some kinds of soft tissue sarcoma. In this study, we investigated whether AZD7648 had a radiosensitizing effect in human sarcoma xenograft mice at lower concentration of AZD7648 and ionizing radiation (IR) than in previous studies. HT1080 human fibrosarcoma cell line and A673 human rhabdomyosarcoma cell line were injected in to the right thigh of Balb/c-nude mice. The mice were randomly divided into 4 groups: Control, AZD7648, IR, AZD7648+IR. AZD7648 was orally administered at 50 mg/kg daily for 3 days from grouping. The IR and AZD7648+IR were irradiated with single 5 Gy at the day after grouping. To access tumor growth delay, the mice were sacrificed when the average tumor volume in each group reached 2000 ㎣. The tumor growth delay in AZD7648+IR was 14 days longer and prolonged by 2-fold in HT1080 xenograft model, and 5 days longer and prolonged by 1.38-fold in the A673 xenograft model compared to the IR alone. Next, to evaluate tumor growth inhibition, all mice were sacrificed when the average tumor volume in the control reached 2000 ㎣. AZD7648+IR significantly inhibited tumor growth compared to the IR in HT1080 xenograft mice. Moreover, AZD7648+IR strongly inhibited tumor growth compared to IR in radioresistant A673 xenograft mice. Taken together, we demonstrated that low doses of AZD7648 and IR synergistically radiosensitized various human sarcomas xenograft mice.

***Corresponding author :** Youngjoo Kwon, Youn Kyoung Jeong

***Keywords :** AZD7648, Radiosensitizer, Sarcoma, Radiotherapy, Xenograft mice

PS-E-036

Calcineurin inactivation by baicalein reduces neuronal apoptosis caused by prion protein

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Prion diseases are a group of devastating neurodegenerative conditions characterized by neuronal cell death. Calcineurin, also known as protein phosphatase 2B (PP2B), is abundant in the brain. Activation of calcineurin plays a role in prion-induced neurodegeneration, suggesting potential for treatment via phosphatase inhibition. Tacrolimus, formerly known as FK506, is a well-known immunosuppressive drug that binds to the FK506-binding protein. Baicalein is a major flavonoid extracted from the roots of *Scutellaria baicalensis Georgi*, a medicinal herb used in traditional Chinese medicine. Baicalein has demonstrated neuroprotective properties against calcium-dependent neuronal cell death. In this study, we explored the effects of baicalein on prion disease development using neuronal cells. In this study, we focused on whether baicalein could reduce prion peptide-induced neurotoxicity by disrupting intracellular calcium balance, leading to calcineurin inactivation. We observed that baicalein protected cells from prion peptide-induced neuronal cell death. Our results showed baicalein's regulation of calcineurin through activity assays and Western blot analysis. Baicalein treatment inhibited calcineurin activated by PrP (106-126) and calcium production. Furthermore, baicalein upregulated p62 and downregulated LC3-II, indicating suppression of autophagy flux. Baicalein alleviated prion protein-induced neuronal cell death by activating calcineurin and inhibiting autophagy. FK506 suppressed calcineurin activation as well as the neuroprotective effects of baicalein. Thus, these results highlight the protective role of baicalein against prion-induced neuronal cell death, suggesting its potential as a therapeutic agent for neuro-degenerative diseases.

***Corresponding author :** Chan Hee Park

***Keywords :** Prion protein, Baicalein, Calcineurin

PS-E-037

Exploring the functional organization and neural dynamics of the motor cortex using graphene electrodes and wireless recording in rhesus monkeys

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The traditional homunculus model of the motor cortex has come under scrutiny due to individual brain variability and concerns regarding the overstated precision and continuity of the motor map. To investigate the functional organization and dynamic neural responses within the motor cortex, we employed subdural graphene electrodes for simultaneous recording and stimulation in rhesus monkeys (n=2). Graphene electrodes were chosen for their exceptional sensitivity, biocompatibility, and flexibility, making them promising tools for recording and manipulating neuronal activity. This approach was complemented by a wireless recording system, allowing for the capture of neuronal activity during natural behaviors. Our study reveals that clustering of ECoG data into groups of nearby channels indicates a distinct functional organization within the motor cortex. Each cluster corresponds to specific motor control regions, with increased gamma activity associated with vocalization and decreased beta activity linked to movement behavior. Furthermore, significant changes in power and network connection strength were observed mainly in the alpha and beta frequency bands following electrical brain stimulation under normal conditions, indicating that these frequency bands are crucial for the baseline functional connectivity of the motor cortex. These findings enhance our understanding of the motor cortex's functional architecture and its dynamic neural responses, providing a foundation for further research into cortical stimulation and motor control.

Corresponding author **:** Eunha Baeg, Sunggu Yang

Keywords **:** Monkeys, Motor cortex, Graphene electrodes, Brain stimulation, Functional connectivity

PS-E-038

HanDam (Twist) improves wrinkle through activation of TGF-β on UV-B irradiation-Induced skin photoaging in Hairless mice

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The aim of this study was to evaluate the wrinkle improvement of HanDam (Twist) on Ultraviolet B (UV-B) irradiation-induced skin photoaging in hairless mice. Photoaging is one of the aging caused by extrinsic aging, and UV-B is known to be the main cause. Many surgeries have been developed to improve wrinkles induced by photoaging. Face-lifting using PDO thread has been evaluated as a safe and effective surgery. HanDam (Twist) is a lifting thread for wrinkle improvement with a unique morphological feature of a twisted shape. Wrinkles were induced by UV-B irradiation on the backs of female hairless mice for 6 weeks. After inducing wrinkles, Thread was treated and tested for 6 weeks. Our results showed that treatment with HanDam (Twist) effectively ameliorated UV-B irradiation-induced wrinkle formation and wrinkle depth. Histological evaluation of the skon also revealed that HanDam (Twist) significantly increased collagen density. In measuring protein expression related to collagen production, HanDam (Twist) significantly increased Transforming growth factor beta (TGF-β) and collagen type 1 (COL1). In addition, matrix metalloprotease-1 (MMP-1) protein expression was significantly decreased. Our results indicate that HanDam (Twist) ameliorates UV-B irradiation-induced skin aging in hairless mice. These findings suggest that HanDam (Twist) improves the effectiveness of lifting threads for skin care compared to existing products.

Corresponding author **:** Jung Kee Kwon

Keywords **:** Skin aging, Face lift, Transforming growth factor beta , Collagen type 1

PS-E-039

Inhibition of infiltrating monocytes ameliorate neurological and behavioral outcomes of SAH mice model

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Subarachnoid hemorrhage (SAH) is a typeof hemorrhagic stroke that induces asterile inflammation, which cause resident immune cells to activate, andrecruit Ly6C+CD11b+ classical monocytesvia mediationof Chemokine ligand CCL2(MCP-1), and its receptor CCR2.To determineroles of infiltrating monocytes during SAH condition, we used CCR2-/-transgenic mice thatprevents blood monocyte recruitment, andcreated SAH model via Middle cerebral artery (MCA) perforation.Here, we describe changes in immune cell composition within brain parenchymaand meninges during early time points (24hrs, 72hrs) after SAH. Also, wedescribe motor and cognitive changes after SAH induction. Finally, we confirmchanges in cytokine levels of early time points of SAH. Taken together, ourfindings suggest that monocyte may play a crucial role in neuronal cell deaththrough persistent inflammatory reaction, which may be a potential therapeutictarget in reducing SAH burden.

Corresponding author **:** Yi rang Na, Seung Hyeok Seok

Keywords **:** Subarachnoid Hemorrhage (SAH), Myeloid cell, CCR2 knockout, Stroke

PS-E-040

Assessing brain functional changes in a rat model of lipopolysaccharide- induced sepsis-associated encephalopathy using multi-parametric MRI

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Sepsis-associated encephalopathy (SAE) is a severe complication of sepsis that results in widespread brain dysfunction due to systemic inflammation. This study aimed to investigate the functional and metabolic alterations in a rat model of SAE using multi-parametric magnetic resonance imaging (mpMRI). Twenty-one Sprague-Dawley rats were divided into three groups: control (CTRL, n = 7), SAE05 (5 mg/kg LPS, n = 7), and SAE10 (10 mg/kg LPS, n = 7). The mpMRI was performed 24 hours post-LPS injection to obtain apparent diffusion coefficient (ADC), cerebral blood flow (CBF), T1, and T2 maps. The findings revealed significantly elevated ADC and T1 values in the hippocampus of both SAE groups compared to the control group. These elevated ADC values suggest increased water diffusion within the extracellular space, indicative of vasogenic edema may due to blood-brain barrier (BBB) disruption. Additionally, increased T1 values were associated with inflammatory responses, including cell swelling and capillary leakage. The disruption of the BBB, as evidenced by these changes, highlights the severity of neuroinflammation and cellular damage in SAE. The ability of mpMRI to sensitively detect these alterations underscores its potential as a non-invasive diagnostic tool for monitoring the progression and severity of neuro-inflammation in SAE. Future research should include pathological and histological methods to validate these imaging findings and explore potential therapeutic interventions. These insights into the mechanisms of brain damage in SAE may contribute to the development of more effective diagnostic and therapeutic strategies for managing this critical condition.

Corresponding author **:** Do-Wan Lee

Keywords **:** Sepsis-associated encephalopathy, Multi-parametric MRI, Apparent diffusion coefficient, Inflammation, T1 mapping

PS-E-041

Therapeutic effects of muscle regeneration at different melittin concentrations in rabbit atrophied muscle

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Objective: This research aimed to explore the healing impacts of Melittin treatment on gastrocnemius muscle wasting caused by immobilization with a cast in rabbits.
Methods: Twenty-four rabbits were randomly allocated to four groups. The procedures included different injections: 0.2mL of normal saline to Group 1 (G1-NS); 4μg/kg of Melittin to Group 2 (G2-4μg/kg Melittin); 20μg/kg of Melittin to Group 3 (G3-20μg/kg Melittin); and 100μg/kg of Melittin to Group 4 (G4-100μg/kg Melittin). Ultrasound was used to guide the injections into the rabbits' atrophied calf muscles following two weeks of immobilization via casting. Clinical measurements, including the length of the calf, the compound muscle action potential (CMAP) of the tibial nerve, and the gastrocnemius muscle thickness, were assessed. Additionally, cross-sectional slices of gastrocnemius muscle fibers were examined, and immunohistochemistry and Western blot analyses were performed following two weeks of therapy.
Results: The mean regenerative changes, as indicated by clinical parameters, in Group 4 were significantly more pronounced than in the other groups ($p<0.05$). Furthermore, the cross-sectional area of the gastrocnemius muscle fibers and immunohistochemical indicators in Group 4 exceeded those in the remaining groups ($p<0.05$). Western blot analysis also showed a more significant presence of anti-inflammatory and angiogenic cytokines in Group 4 compared to the others ($p< 0.05$).
Conclusion: Melittin therapy at a higher dosage can more efficiently activate regeneration in atrophied gastrocnemius muscle compared to lower doses of Melittin or normal saline.

***Corresponding author* :** Dong Rak Kwon

***Keywords* :** Muscle atrophy, Melittin, Muscle regeneration, Concentration, Rabbit models

2024

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Z

25초 Scan으로 8가지의 정확한 체성분 결과치 얻을 수 있습니다.

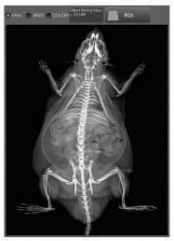
정확성
Micro CT, NMR의 정확성

편의성
DXA의 편의성, 빠른 측정시간

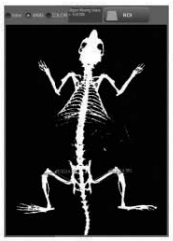
고해상도
DR의 이미지 해상도

BMD / BMC / Bone Area / fat(%)
fat(g) / Lean(g) / Total weight

In Vivo Imaging



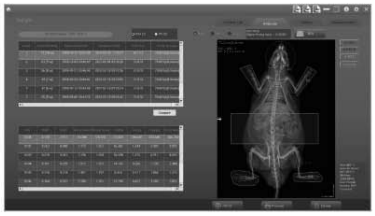
X-Ray Image



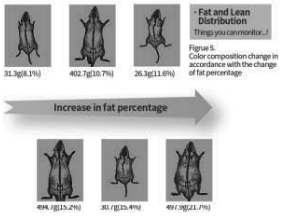
BMD Image

Fat/Lean Color Mapping Image

Longitudinal Measurement In Vivo



Measurement Window for each ROI
약 25초 Scan으로 3가지 Type의 영상과 8가지의 값이 산출됩니다. [BMD, BMC, Bone Area, fat(%), fat(g), Lean(g), Total weight]



History Analysis for Each ROI
iNSiGHT VET DXA는 실험동물의 희생 없이 In-Vivo 상태에서 체성분 및 골밀도 변화의 추적 관찰이 가능하며 다양한 영상을 통해 약물, 운동요법 처치, 기능성 식품 등의 처치 이후 뼈, 연골 부위, 지방분포, 근육 변화를 일단위, 주 단위, 월 단위로 추적 관찰이 가능합니다.

Special Feature

DXA Features	Description
Non-Invasive Analysis	고비용, 에너지 집약적이면 기존 화학적 성분분석 방식이 아닌, 비침습적 분석방식을 통한 비용 및 노동력 절감 효과의 극대화
Longitudianl in-Vivo F/U	실험동물의 희생 없이 In-Vivo 상황에서의 체성분 및 골밀도 변화의 추적관찰이 가능
Accurate Results for Lean/Fat/Bone (< CV 1%, R^2 > 0.99)	Bone 기준, 1% 이내 측정오차 제공 (Precision Error % Accuracy Error in Static Condition) Chemical 성분분석 방식과 비교 시 R^2 0.99 이상의 정밀도
Fast Scan (< 25 Sec.)	피사체를 '긁는' 방식으로 스캔하는 Fan Beam 타입 기술이 아닌, 한 번에 피사체를 포착하는 Cone Beam 타입 기술로, Lab DXA장비 중 최단시간 내 스캔 완료
Quick & Easy Pre-Treatment	실험동물을 해부할 필요 없이, 단순 주사/흐흡 마취만 필요, 전 처리에 소요되는 시간 및 노동력 절감 효과의 극대화
No Radiation for Researcher & Minumum Dose for Animal	캐비닛 형식의 완전 차폐를 통한 연구자의 피폭 완전 차단, Micro CT 대비 동물 피폭선량의 최소화
High Resolution (Pixel Size of 100um)	100um급 a-Si TFT Flat Panel Detector 적용을 통해, 3.5lp/mm 수준의 일반 DR 보다 더 우수한 16lp/mm의 고해상도 이미지 제공 (4 배율 확대 모드 기준)
DR Images for Bone/Cartilage, Fat, Lean Distribution Analysis	고해상도 영상을 통해, 약물 / 운동요법 처치 / 기능성식품 등의 처치 이후 뼈 / 연골 부위, 지방분포, 근육 변화의 일단위, 주 단위, 월 단위 이미지 변화 추적 가능
Wide Scan Area (16.5cm x 25.5cm)	넓은 스캔 영역의 확보를 통해 500g까지의 소형동물 측정 가능

iNSiGHT DXA vs NMR vs Micro CT

Function	iNSiGHT	NMR	Micro CT
3D Image	N/A	N/A	YES
Slice Image	N/A	N/A	YES
2D DR Image	YES	N/A	YES
BMD (g/cm²)	YES	N/A	PARTLY YES (By Gray Scale Mapping, Not by DXA's Material Analaysis. Less Accuarate Than DXA)
BMC (g)	YES	N/A	YES (By Gray Scale Mapping, Not by DXA's Material Analaysis. Less Accuarate Than DXA)
FAT (g)	YES	YES	OPTIONAL (Depends on Device)
LEAN (g)	YES	YES	OPTIONAL (Depends on Device)
FAT (%)	YES	YES	N/A
Bone Area (cm²)	YES	N/A	N/A
Free Body Fluid (Water)	N/A	YES	N/A
Heavy Animal (500g) Measurement	YES	N/A	N/A
Price	LOW	MIDDLE	HIGH

RAONBIO

다시 돌아온 일상의 소중함, 라온바이오㈜가 함께 합니다.

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깨뜨리는 위협에 맞서,
비임상 분야 생명공학 연구가
최일선을 담당하고 있습니다.
라온바이오(주)는 비임상 분야
동물실험의 미래를
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● IVC System

● Lab Animal

● Diet ● Equipment ● Reagent ● Enrichment

RAONBIO

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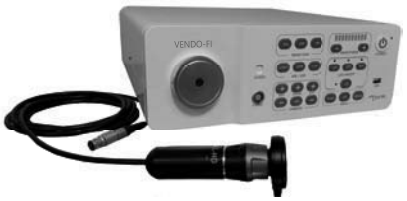
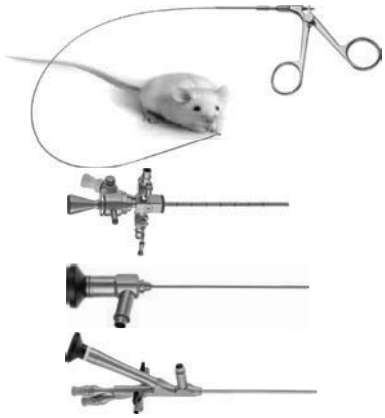
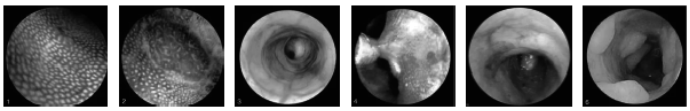
Light, 고용량 LED







blood gas analyzer

Samples: 65 µL
Measuring time: 35 sec

Derived parameters

pH(T)
pCO2(T)
cHCO3-(P)
cBase(B)
cBase(B,ox)
cBase(Ecf)
cBase(Ecf,ox)
cHCO3 - (P,st)
cH+
cH+(T)
ctCO2(P)
ctCO2(B)
pH(st)
pO2(T)
pO2(A)
pO2(A,T)
p50
p50(T)
p50(st)
pO2(A-a)
pO2(A-a,T)
pO2(a/A)
O2(a/A,T)
pO2(a)/FO2(I)
O2(a,T)/FO2(I)
cCa2+(pH=7.40)
Anion Gap(K+)
Anion Gap
DO2
Hct
pO2(x)
pO2(x,T)
ctO2(B)
ctO2(a-v-)
BO2
ctO2(x)
FShunt
FShunt(T)
RI, RI(T)
VO2
mOsm
Qx
Qt
V(B)
sO2
FO2Hb

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비임상에서 실험실 구축으로 서비스 영역 확대

대규모 LAB 컨설팅 구축 경험 및 노하우를 바탕으로 사업영역 확장

각 실험실에 최적화된 Lay-out 설계 노하우 X 맞춤형 장비 공급 및 시공 능력 확보

HLB 바이오스텝(주)

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revvity

Innovative, hands-free, automated ultrasound.
Vega® Pre-clinical Ultrasound System

Get more consistent results with a hands-free system that removes the use of a handheld transducer. Unlike traditional ultrasound systems, the Vega uses a bottom-up approach with the transducers located under the imaging stage. The automated positioning of the transducers can scan coronal, sagittal, and axial orthogonal planes across the whole body producing high-resolution 3D data that looks more like MRI images than traditional ultrasound.

Advantages of this unique design include:

- **Ease of use.**
- **More consistent results.**
- **More accurate data.** By removing physical contact between the transducer and the animal, tissues are not 'distorted' or 'warped' during 3D image acquisition
- **Enables widefield imaging relative to handheld approach.**
- **High speed scanning.** Automated hands-free transducers enable fast and consistent scanning
- **Streamlined imaging workflow.**

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SCAN QR and Download

Figure 3. Automated bottom-up imaging with camera guidance for widefield imaging.

Figure 4. Top-down view of imaging stage showing transducers in middle bay.

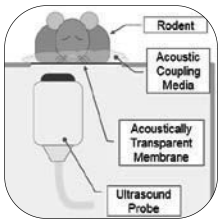

Figure 5. Diagram showing details of bottom-up imaging design.

Vega® Pre-clinical Ultrasound System

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친환경 실험동물실 구축!
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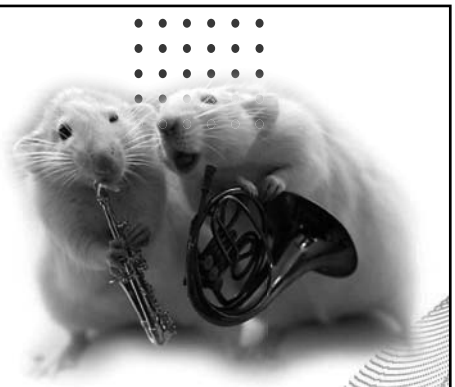
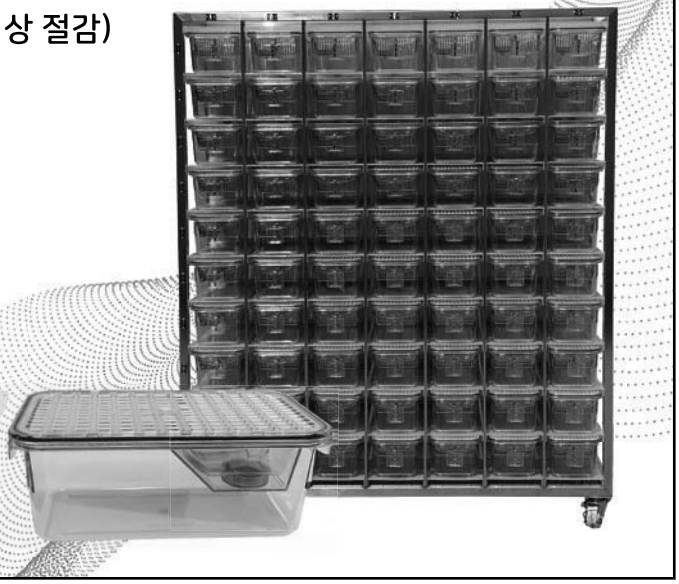


- 실험동물실 면적, 건축비용 절감 (약30%이상 절감)
- 쾌적한 실험동물실 (취기 없음)
- 열에너지(항온항습기 전기료) 70% 절감
- 유지 관리비 90% 절감
- 렉 세척, 배기노즐 세척 인건비 절감 등



기획, 예산 무료 컨설팅 제공

지금은 저성비 시대입니다!

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1
- 기술지원 서비스에서 해당 서비스 클릭
- 담당자 연락처 확인(이메일, 전화, 팩스, 우편으로 서비스 신청)

2
- 기술지원 분야별 담당자 확인
- 이메일, 전화, 팩스, 우편 서비스신청의 경우 확인 메일 발송

3
- 기술지원 분야별 담당자에게 확인

4
- 마우스등 특수한 조건의 서비스인 경우 의뢰자가 직접 수령
- 또는 전문업체에 의뢰(배송비 의뢰자 부담)
- 모니터링 결과 등은 우편 발송(거래명세서, 계산서 포함)

5
- 서비스 결과 수령 후 3주 이내 입금 요망
- 계산서 필요 시 사업자등록증 사본 제출 (이메일 또는 팩스)

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Public Service for Bio-Health industry
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인증 현황

AAALAC - i 인증	우수동물실험시설 인증	전문가 위원회 구성
		

서비스 분야

- 신약·의료기기 후보물질 유효성 평가
- 융·복합 바이오 제품 성능평가
- 인간화 마우스 이용 면역항암제 등 평가
- 마모셋 등 영장류 이용 항체의약품 등 약물동태 평가
- 첨단바이오 이미징 장비를 활용한 비임상 지원
- 독성병리 등 예비 안전성 평가

시설 현황

- 연면적 : 9,832m2(3,000평)
- 주요시설
  - 동물이용 생물안전 3등급
  - 첨단대체시험법 개발 등 업무 확장
  - 高 난이도 수술 등 기술서비스 고도화
  - 차세대 인간화 마우스 연구시설
  - 마모셋 영장류 ABL-3 시설 운영 등

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- 병리분석장비(슬라이드스캐너 등) 13종
- 행동평가장비(Y-MAZE 등) 20종
- 모델제작장비(미세조작시스템 등) 9종

“ 비침습 바이오이미징 평가를 위한 첨단장비 보유 ”

49년 !
품질을 파는 정직한 기업

STEAM Sterilizer
모든 의료용품의 완벽한 멸균 관리는 고도의 의료시술 만큼 매우 중요한 사안입니다.

PLASMA Sterilizer
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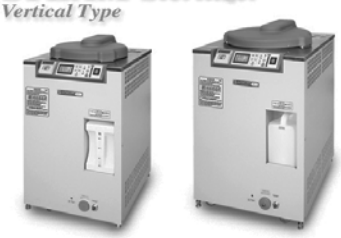
저온 플라즈마 멸균기는 열과 압력, 습기에 민감한 의료용품을 안전하고 신속하게 멸균하는데 사용됩니다.

STEAM Sterilizer
Vertical Type



전동식 자동문, 레토르트제품 전용 사이클로 더욱 편리하고 안전하게 멸균작업을 실행합니다 !

EO Gas Sterilizer
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가스멸균은 높은 온도나 습기에 취약하여 증기멸균 방법을 적용할 수 없는 의료 기자재를 멸균하는데 사용됩니다.

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혈액 및 약품을 2℃~6℃의 냉장실내 온도를 정밀하게 유지하여 보존, 혈액 및 약품이 변질되거나 동결할 위험이 없도록 실시간 온도제어가 이루어지고 있습니다.

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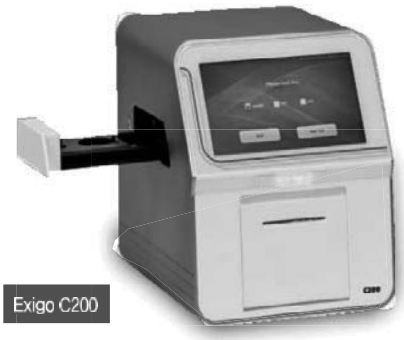
Animal Diagnostic System



Exigo C200

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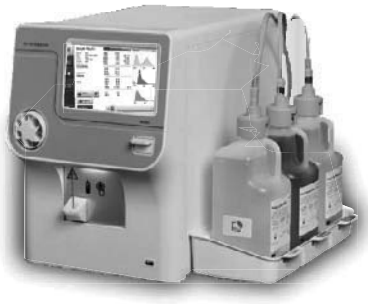
Internal quality control
다양한 샘플 종류 – serum, plasma or whole blood
검체 필요량 : 100μL
14가지 항목을 한 번에 검사 가능
Maintenance free
내장형 프린트 장착
5인치 칼라 터치 스크린
ALB, ALP, ALT, AMY, AST, CK, CREA, GLU, GGT, LDH, Total Bil, Total Chole, TP, UA , UREA , K , Na , Cl , Mg , Phos , CHE , Ca , TG, CK, GLOB , cCRP , TCO2



Exigo H400

HEMATOLOGY

19 parameters including 4–part WBC diff
(LYM, MONO, NEUT, EOS)*
4diff : Exigo eso – dog, horse Exigo H400 – dog, horse, cat
eosinophil granulocytes는 시약을 이용해 직접 측정
검사 시간 : 1분 (4–part WBC diff* : 3분)
샘플량 : 125 μL (MPA : 20μL)
고품질 7–inch color touch–screen
QC program plus automated cleaning
4 reagents (Diluent, System Cleaner, Lyse, EOS)
Built–in mixer
바코드 리더기 제공.

▣ 판매원 : POBANILAB 포스트바이오 금천지사(구 더블유메디텍) 02-2098-9983 / 031-523-2731

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저온멸균기
De-con Pass Room
De-con Pass Box
DRY FOG System
과산화수소 멸균대행

사육장비
ABL3 Marmoset Cage System
Clean Rack
일반사육장비

실험기자재
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2024 KALAS International Symposium

발 행 일 : 2024년 7월 22일

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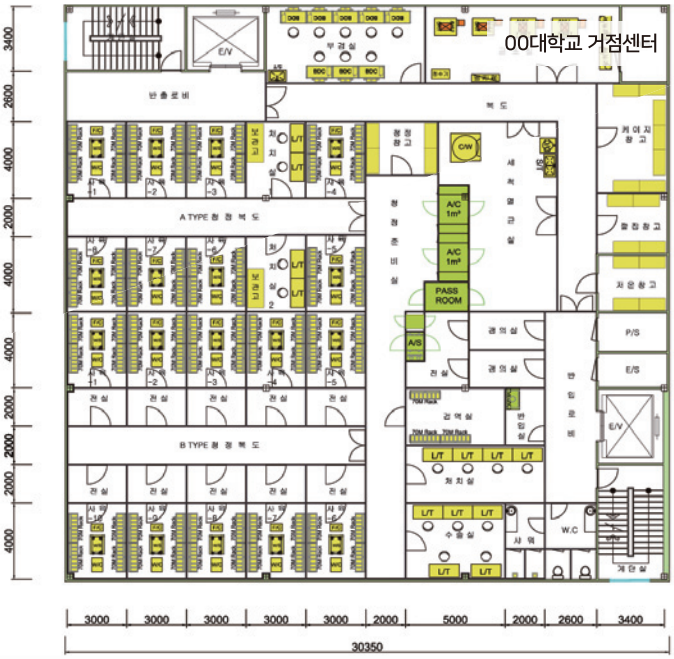
차세대

친환경 실험동물실 구축

지금은 저성비 시대입니다.



시설분야 혜택

01 실험동물실 면적, 건축비용 **약 30% 절감**

02 공조실 면적 비용 **약 50% 절감** 및 공조기 **용량 75% 절감**

03 열에너지(항온항습기 전기료) **70% 절약**

04 취기(냄새)없는 **쾌적한 실험동물실 실현**

05 룸배기구와 룸배기 필터 불필요 **(오염 원인 제거, 유지관리비 절감)**

NISO Rack Cage set 분야 혜택

01 **동양인 체형**의 관리 편리성

02 렉 세척 불필요, 배기노즐 **청소 없음**

03 정전, 고장, 지진으로 인한 정전에도 **밀사 원인 없음**

04 케이지 이동시 별도 **전동 트랜스퍼 불필요**

05 액세서리(캐치, 밸브)없는 심플성, **리크없는 물병**으로 안전 필터 연1회 교환외 소모품 없음

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