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KJPP

Volume 28, Supplement 1, October 2024

The Korean Journal of
Physiology &
Pharmacology

October 31 (Thu) - November 1 (Fri), 2024
고려대학교 의과대학

Program Book

초록집 다운로드

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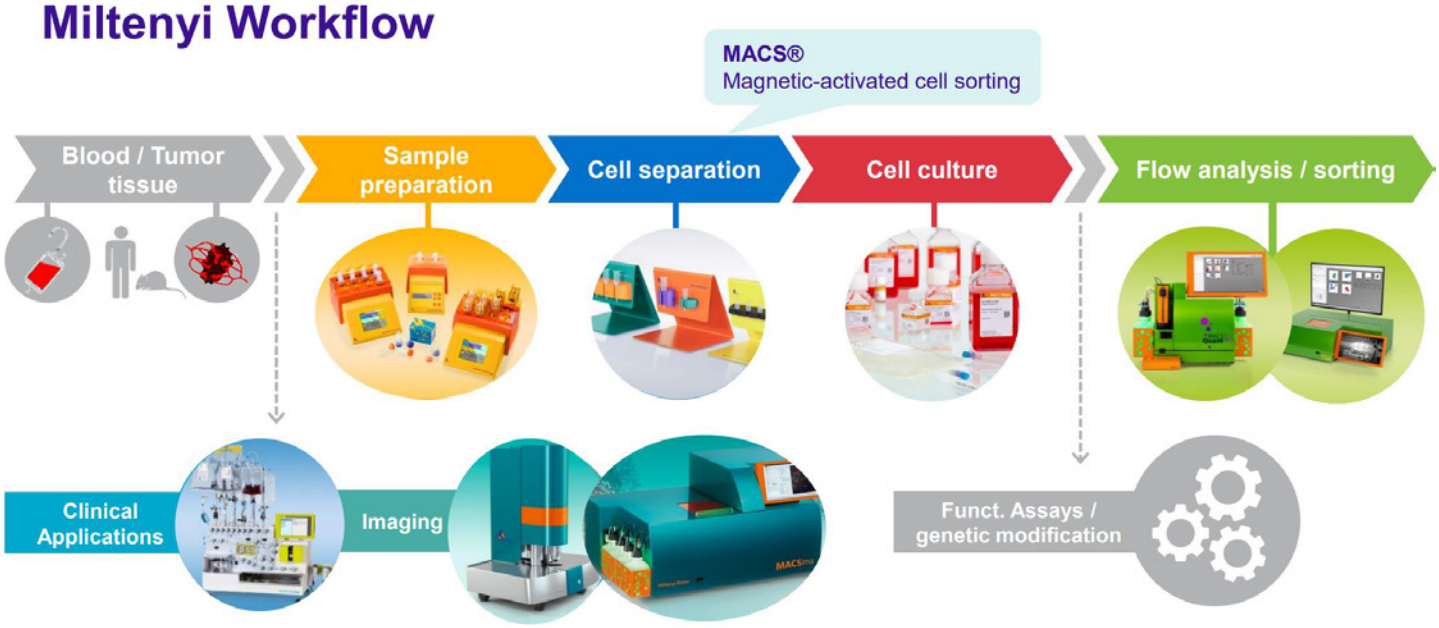
Miltenyi Biotec

Miltenyi Workflow



DoGenBio

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Cell viability, proliferation, cytotoxicity를 측정하는 kit

Oxidative Stress Assay Kit

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04 EZ-Hydrogen Peroxide/Peroxidase Assay Kit
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06 EZ-Total Antioxidant Capacity (TAC) Assay Kit
07 EZ-DPPH Antioxidant Assay Kit

Metabolism Assay Kit

01 EZ-Lactate Assay Kit
02 EZ-Acetylcholinesterase Assay Kit
03 EZ-Ascorbic Acid Assay Kit
04 EZ-ATP Assay Kit
05 EZ-Free Fatty Acid Assay Kit
06 EZ-Free Glycerol Assay Kit
07 EZ-Glucose Assay Kit
08 EZ-HDL, LDL/VLDL Assay kit
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Aims and Scope

The Korean Journal of Physiology & Pharmacology (Korean J. Physiol. Pharmacol., KJPP) is the official journal of both the Korean Physiological Society (KPS) and the Korean Society of Pharmacology (KSP). The journal launched in 1997 and is published bi-monthly in English. KJPP publishes original, peer-reviewed, scientific research-based articles that report successful advances in physiology and pharmacology. KJPP welcomes the submission of all original research articles in the field of physiology and pharmacology, especially the new and innovative findings. The scope of researches includes the action mechanism, pharmacological effect, utilization, and interaction of chemicals with biological system as well as the development of new drug targets. Theoretical articles that use computational models for further understanding of the physiological or pharmacological processes are also welcomed. Investigative translational research articles on human disease with an emphasis on physiology or pharmacology are also invited. KJPP does not publish work on the actions of crude biological extracts of either unknown chemical composition (e.g. unpurified and unvalidated) or unknown concentration. Reviews are normally commissioned, but consideration will be given to unsolicited contributions. All papers accepted for publication in KJPP will appear simultaneously in the printed Journal and online.

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Editorial Board

2024 대한생리학회 임원명단

고 문 김광진 김기순 김기환 김명석 김선희 김용근 김 전 김종규 김종환
김중수 나흥식 남숙현 남택상 류판동 문창현 민병일 민영기 박경표
박병림 박양생 박재식 박춘식 박형진 방효원 배선호 백은주 서덕준
서창국 신형철 신홍기 양일석 엄대용 엄융의 연동수 윤평진 이상호
이석강 이승일 이영만 이원정 이윤열 이종은 이종흔 이중우 이진옥
이호섭 임중우 조경우 조양혁 한희철 호원경 홍성근 홍승길

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기획위원 강다원 고은아 고재홍
김경미 김나리 김형규
박소영 배영민 이은희
전주홍 진영호 차승규
최윤희 황선욱

학술이사 배재성

학술위원 강다원 김경미 김기우 김병주
김선광 김성준 김현우 김형규
김희정 남주현 박규상 박정환
배영민 서보암 손종우 오병철
우주한 이규필 이용석 이준용
임승순 임현호 최윤희 허준영
홍재우 황선욱

이 사 강다원 강대길 강동묵 강봉균 공인덕 곽지연 구용숙 권성춘 김경년
김나리 김동욱 김명준 김민선 김병주 김보경 김상정 김성주 김성준
김세훈 김수미 김영미 김용운 김원재 김의용 김재호 김정훈 김종연
김현진 김형규 나창수 민선식 박규상 박소라 박소영 박우현 박원선
박종성 박중진 박지호 박진봉 박철규 배영민 배재성 배재훈 배혜란
서상원 서인석 송대규 신동민 안덕선 안도환 안동국 안승철 염재범
오석배 우선희 우재석 우현구 윤신희 윤영욱 이 광 이덕주 이동현
이무열 이문영 이민구 이배환 이상진 이석호 이성중 이수환 이영호
이용석 이은희 이장헌 이정범 이지희 임승순 임인자 임채헌 장성호
장은화 전병화 전양숙 전제열 정성우 정승수 정승준 정한성 조영욱
조하나 진영호 차승규 천상우 최윤희 최한석 한 진 한승호 한인옥
한재희 한호재

감 사 이용석 고재홍

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범문사

바이오솔릭스

Contents

Welcome Message

대한생리학회 회원여러분,

안녕하십니까?

올해에도 여러 많은 어려움이 있었고, 또 유난히 긴 장마와 무더위를 견디며 오늘에 이르렀습니다. 이제 결실의 좋은 계절에 회원여러분을 직접 뵙고 제76회 대한생리학회 학술대회를 고려대학교 의과대학 (서울, 안암동)에서 10월 31일(목)~11월 1일(금) 양일간 개최하게 되어 무엇보다 기쁘게 생각합니다.

이번 제76회 대한생리학회 학술대회에서는 두 개의 Plenary Lecture, 18개의 심포지엄과 Young Faculty Presentation, 그리고 다수의 포스터 발표가 진행될 예정입니다. 생명의 이치를 탐구하는 학문인 생리학은 여전히 새로운 도전의 영역을 찾아가며 놀랄만한 과학적 성과를 내고 있으며 이번 학술대회 또한 이를 위한 교류의 장이 될 것입니다.

지난해 성공적인 FAOPS 개최의 힘을 이어 앞으로도 대한생리학회의 지속적인 저변 확대를 기대합니다. 생리학 학문 후속세대가 충분히 그리고 활발히 양성되는 데에도 우리 학회의 역할이 크다고 생각하고 있습니다. 함께 탐구하고 꿈꾸며 발견하는 학문적 성과의 공유가 이번 학술대회에서도 빛을 바라길 소망합니다.

제76회 대한생리학회 주관교를 맡아 수고해주신 고려대학교 의과대학 생리학교실 교수님들, 성공적인 학술대회를 위해서 보다 더 나은 프로그램 준비로 애써주신 대한생리학회 학술이사 및 학술위원 여러분, 그 밖의 여러 도움을 주신 손길들에게 깊이 감사드립니다. 그럼 멋진 10월의 마지막 날에 학회에서 뵙기를 고대합니다. 고맙습니다.

대한생리학회 회 장 **공인덕**

Welcome Message

제76회 대한생리학회 정기학술대회를 저희 고려대학교 의과대학교 생리학교실에서 주관하게 되어 영광입니다. 학술대회를 준비해주신 학회 회장님과 이사님께 깊이 감사드리며, 학술대회에 참가하는 모든 회원분들을 환영합니다.

1928년 민족에 의해서, 민족을 위하여 설립된 저희 고려대학교 의과대학은 이제 미래의학을 선도하기 위해 창의적인 의과학자 양성에 힘쓰고 있습니다. 저희 생리학교실은 임상 진료를 함께 하는 생리학, 장애인 재활체육으로 사회적 약자를 위한 생리학, 등 생리학의 지평을 넓히려 노력하고 있습니다.

이번 학술대회가 한국의 생리학이 한단계 더 성장하는 계기가 되기를 바라며 최선을 다해 준비하겠습니다. 학술대회를 통해 뜻깊은 연구주제가 발표되고, 동료 연구자들과 함께 토론되어 올바른 방향이 찾아지기를 기원합니다. 학회를 통해 소중한 연구결과를 발표하시는 모든 연구자에게 경의를 표하며, 함께 연구주제에 질문과 토론해 주시는 모든 회원들에게 감사드립니다. 21세기 의학과 의료의 변화에 의미있는 방향을 제시하는 대한생리학회가 되기를 기원합니다.

고려대학교 의과대학 생리학교실 주임교수 **이 민 구**

Schedule (일정표)

▶ 10월 31일 목요일

Time	Room A	Room B	Room C
	유광사홀	320호 최덕경	418호 윤주홍
08:00 ~ 09:00	등록 및 포스터게시		
09:00 ~ 09:20	개회식		
09:20 ~ 09:30	Coffee Break		
09:30 ~ 11:00	**S1**	**S2**	**S3**
	Hypothalamic Regulation of Body Energy Homeostasis	Progress, Challenges and Prospects in Gene Editing	Innovative New Drug Development
11:00 ~ 13:00	Lunch		
			11:30–12:20 **Lunchon Seminar** SILK Longevity Co., Ltd
13:00 ~ 13:50	**PL1**		
13:50 ~ 14:00	Coffee Break		
14:00 ~ 15:30	**S4**	**S5**	**S6**
	Channels in Action: Advances in Mechanosensitive Ion Channel Research & Clinical Implications	Cutting-edge Academic Session by the Korean Journal of Physiol Pharmacol	Brain and Cognitive Aging
15:30 ~ 16:00	Coffee Break		
16:00 ~ 17:30	**S7**	**S8**	**S9**
	Neural Mechanism underlying Learning and Memory	The Present and Future of Digestive Pathophysiology in Korean Medicine	Joint Symposium with Korean Society of Pharmacology
17:40 ~ 18:00	**Special Session with NRF**		
	National strategic R&D program about K-Brain project and Biomedical Engineering		

▶ 11월 1일 금요일

Time	Room A	Room B	Room C
	유광사홀	320호 최덕경	418호 윤주홍
9:00 ~ 10:30	**S10**	**S11**	**S12**
	Exploring Glial Functions in CNS	Tissue-Specific Immunity: Exploring the Physiological Landscapes Across Different Organs	Novel Therapeutic Strategies for Cardiovascular diseases – Stem cell, miRNA, Mitochondria and beyond
10:30 ~ 10:40	Coffee Break		
10:40 ~ 12:00	**Young Investigator Oral Presentation**		
12:00 ~ 13:00	Lunch		
			12:00–12:50 **Lunchon Seminar** Tomocube, Inc.,
13:00 ~ 13:50	**PL2**		
13:50 ~ 14:00	Coffee Break		
14:00 ~ 15:30	**Young Faculty Presentation**		
	S13	**S14**	**S15**
	Neuroscience	Cancer and Metabolism	Infection and Immunology
15:30 ~ 15:40	Coffee Break		
15:40 ~ 17:10	**S16**	**S17**	**S18**
	Aging and Inflammation	Exploring Novel Pain Circuits from the Periphery to the Brain	Revealing Underlying Mechanism of Metabophyiology through Multi-omics Analysis
17:30 ~	시상, 생리학회 총회 및 폐회사		

Venue Guide (학술대회장 안내)

층별 안내(Floor Plan) / 의과대학

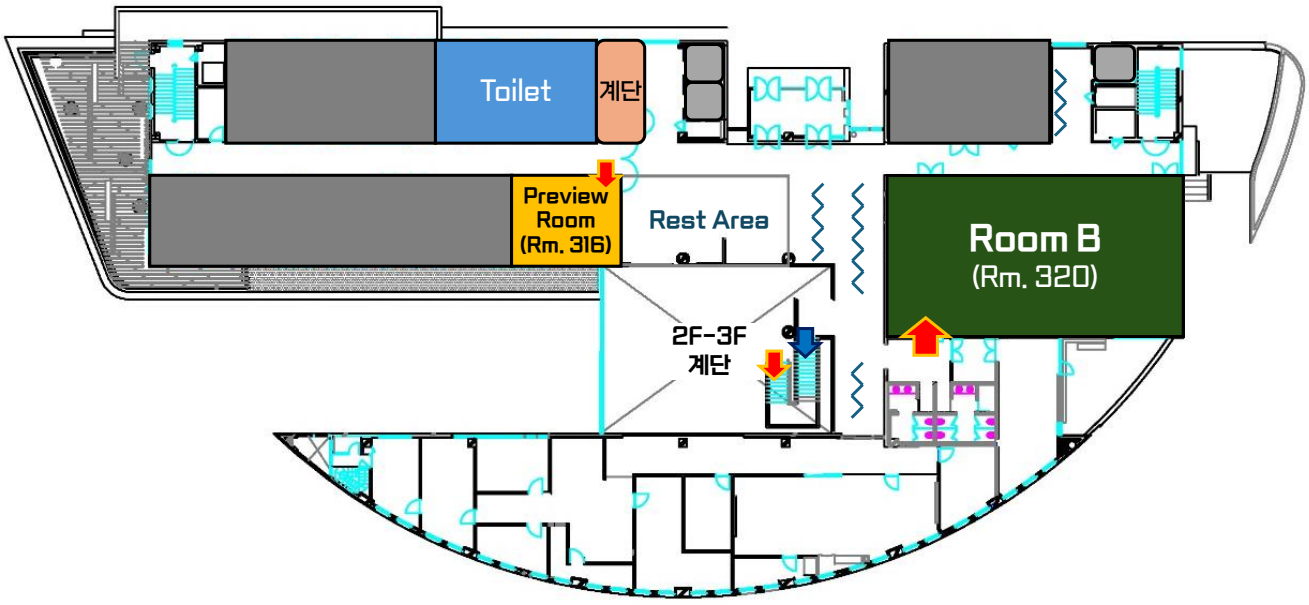
4F	Room C (Rm. 418)	Poster Exhibition (Corridor)		
3F	Room B (Rm. 320)	Poster Exhibition (Lobby)	Preview Room & VIP Room (Rm. 316)	
2F	Registration	Room A (유광사 홀)	Sponsorship Booths	주 출입구(외부 현관)

행사 장소 안내

등록데스크
엘리베이터
계단실
전시부스(10개소)
커피부스(1개소)
포스터 판넬(총 68편)

4F

3F


Toilet
계단
Preview Room (Rm. 316)
Rest Area
Room B (Rm. 320)
2F-3F 계단

2F


Room A (유광사 홀)
계단
Toilet
C
1
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3
8
4
7
2F → 3F
10
5
6
주 출입구
직원식당

• Plenary Lecture

Plenary Lecture 1 (October 31, Thursday, 13:00 ~ 13:50)

Chair: Hyoweon Bang (Chung Ang Univ.)

S 27 PL-1 Oxygen and acid sensing by arterial chemoreceptors
Donghee Kim
Chicago Medical School/RFUMS, USA

Plenary Lecture 2 (November 1, Friday, 13:00 ~ 13:50)

Organizer: Jae-sung Bae (Kyungpook National Univ.), Chair: Chae Hun Im (Ulsan Univ.)

S 27 PL-2 Impairment of homeostasis in neurodegenerative diseases: from bench to clinical trials
Seung Hyun Kim
Hanyang Unviersity Hospital, Republic of Korea

Special Session with NRF (October 31, Thursday, 17:40 ~ 18:00)

Chair : Jae-sung Bae (Kyungpook National Univ.)

National strategic R&D program about K-Brain project and Biomedical Engineering
Sung Hyun Kim
Program Manager: Division of Neuroscience and Advanced Medical Technology

• Symposium (October 31, Thursday)

S01. Hypothalamic regulation of body energy homeostasis (09:30 ~ 11:00)

Organizer and Chair: Ki Woo Kim (Yonsei Univ.), Co-Chair: Sung Hyun Kim (Kyung Hee Univ.)
Co-Organized by Research center for autonomic nervous system and bone homeostasis

S 28 S-1-1 Hypothalamic function of IRX3 and IRX5, genetic determinants of human obesity
Joe Eun Son
School of Food Science and Biotechnology, Kyungpook National University

S 28 S-1-2 Novel hypothalamic mechanisms for orexin-induced feeding
Jong-Woo Sohn
Department of Biological Sciences, KAIST, Korea

S 28 S-1-3 Hypothalamic neural stem cells in aging
Min Soo Kim
Brain Science Institute, KIST, Korea

S02. Progress, Challenges and Prospects in Gene Editing (09:30 ~ 11:00)

Organizer and Chair: Kyoungmi Kim (Korea Univ.), Co-Chair: Hyunji Lee (Korea Univ.)

S 28 S-2-1 A novel approach using CRISPR-ribonucleoprotein packaged in virus-like particles to generate genetically engineered mouse models
Kyoungmi Kim
Korea University College of Medicine, Republic of Korea

S 29 S-2-2 Mitochondrial genome editing
Hyunji Lee
Korea University College of Medicine, Republic of Korea

S 29 S-2-3 A functional genomics approach to map extracellular interactions
Hunsang Lee
Korea University

S 29 S-2-4 Controlling and Visualizing Molecualr and Cellular Behavior in Living Cells and Animals
Won Do Heo
KAIST, Republic of Korea

S03. Innovative new drug development : Basic infrastructural technologies for successful drug development and application of latest technologies in drug screening provided by K-MEDI hub (09:30 ~ 11:00)

Organizer and Chair: Se Jin Jung (K-MEDI hub), Co-Chair: Hyung Gee Kim (Korea Univ.)
Co-Organized by KMEDIhub

S 30 S-3-1 Small molecules, big discoveries: accelerating drug development with DNA-encoded library screening
Hyewon Seo
K-MEDI Hub, Republic of Korea

S 30 S-3-2 Development of human pluripotent stem cell-derived organoids for preclinical studies
Bae Jun Oh
K-MEDI hub, Republic of Korea

S 30 S-3-3 Introduction of research and efficacy evalution technique using in-vivo bioimaging
Hoesu Jung
K-MEDI hub, Republic of Korea

S 31 S-3-4 Development of single-molecule-based, next-generation drug screening technology
Mi-Kyung Lee
Korea Research Institute of Bioscience and Biotechnology (KRIBB), Republic of Korea

S04. Channels in Action: Advances in Mechanosensitive Ion Channel Research & Clinical Implications (14:00 ~ 15:30)

Organizer and Chair: Dawon Kang (Gyeongsang National Univ.), Donghee Kim (Rosalind Franklin Univ.)
Co-Organized by Metabolic dysfunction liver disease Research Center

S 31 S-4-1 Structural prediction of tentonin 3,
a mechanosensitive channel
Uhtaek Oh
Brain Science Institute, KIST, Republic of Korea

S 31 S-4-2 Tracking back TREK-2 K^+ channels; PIP2, mechanosensitivity and the C-terminal charged residues
Sung Joon Kim
Seoul National University College of Medicine, Dept. Biomedical Sciences/Physiology, Republic of Korea

S 31 S-4-3 Signal transduction of Merkel cells in response to mechanical stimuli
Young Min Bae
Konkuk University, Republic of Korea

S 32 S-4-4 Mechanosensitive TREK channels: their role in neuroinflammation
Dawon Kang
Gyeongsang National University, Republic of Korea

S05. Cutting-edge academic session by the Korean J Physiol Pharmacol (14:00 ~ 15:30)

Organizer and Chair: Sun-Hee Woo (Chungnam National Univ.),
Co-Chair: Seung-Kuy Cha (Yonsei University Wonju), Sang-Min Park (Chungnam National Univ.)
Sponsored by Korea Instech Co., LTD, Co-Organized by Organelle Medicine Research Center

S 32 S-5-1 Altered inhibitory circuit of the medial prefrontal cortexin a mouse model of neuropathic pain
Sang Jeong Kim
Seoul National University College of Medicine, Republic of Korea

S 32 S-5-2 Overcoming chemo-resistance of cancer via drug repurposing or natural medicine
Sang-Pil Yoon
Jeju National University College of Medicine, Republic of Korea

S 33 S-5-3 The alpha-helical domain of Gα, a new regulator of the heterotrimeric G protein signaling
Ka Young Chung
Sungkyunkwan University, Republic of Korea

S 33 S-5-4 Academic writing in the generative AI era
Sangzin Ahn
Inje University College of Medicine, Republic of Korea

S06. Brain and cognitive aging (14:00 ~ 15:30)

Organizer and Chair: Joong-Jean Park (Korea Univ.)
Co-Organized by Center for Myokine Convergence Research

S 33 S-6-1 The role of neurons and glial cells in controlling age-related memory impairment
Joong-Jean Park
Korea University College of Medicine, Republic of Korea

S 33 S-6-2 Unraveling pathomechanisms underlying ALS:
a multiomics-based approach empowered by *Drosophila* genetics
Sung Bae Lee
Department of Brain Sciences, DGIST, Korea

S 34 S-6-3 Protective influence of the APOE Christchurch variant (R136S) against Alzheimer's disease pathology linked to APOE4
Jinsoo Seo
DGIST, Republic of Korea

S 34 S-6-4 Increased risk of Alzheimer's disease affected by weight changes but not by body mass index
Jee Hoon Roh
Korea University College of Medicine, Republic of Korea

S07. Neural mechanism underlying learning and memory (16:00 ~ 17:30)

Organizer and Chair: Alan Jung Park (Seoul National Univ.)

S 34 S-7-1 Anterior cingulate-amygdala-cerebellum network codes stimulus contingency and task context of trace eyeblink conditioning
Jangjin Kim
Kyungpook National University, Daegu, Republic of Korea

S 34 S-7-2 Circuit mechanism underlying social memory in mice
Yong-Seok Lee
Seoul National University, Republic of Korea

S 35 S-7-3 Cellular learning rules for structural knowledge-based decision flexibility
Jung Ho Hyun
DGIST, Republic of Korea

S 25 S-7-4 Role of mesolimbic dopaminergic circuit in social decision-making
Ja Wook Koo
Korea Brain Research Institute, Republic of Korea

S 35 S-7-5 Flexibility and stability: multifaceted role of the posterior parietal cortex in reversal learning
Seung-Hee Lee
KAIST Department of Biological Sciences/IBS Center for Synaptic Brain Dysfunction, Republic of Korea

S08. The Present and Future of Digestive Pathophysiology in Korean Medicine (16:00 ~ 17:30)

Organizer and Chair: Byung Joo Kim (Pusan National Univ.), Chair: Chang-Gue Son (Dae Jeon Univ.)

S 35 S-8-1 Herbal drug candidate for the antioxidant properties and their metabolism
Young Woo Kim
Dongguk University, Republic of Korea

S 36 S-8-2 *Atractylodes macrocephala* Koidz Alleviates Symptoms in Zymosan-Induced Irritable Bowel Syndrome Mouse Model through TRPV1, NaV1.5, and NaV1.7 Channel Modulation
Byungjoo Kim
Pusan National University, School of Korean Medicine, Republic of Korea

S 36 S-8-3 Identifying novel subtypes of functional gastrointestinal disorder by analyzing nonlinear structure in integrative biopsychosocial questionnaire data
Chang-Eop Kim
Gachon Univesrity, Republic of Korea

S 36 S-8-4 Pathophysiology of Stress-Induced Liver Injury and Its Underlying Role
Chang-Gue Son
Korean Medicine Hospital of Dejeon University, Liver-Immunology Research Center, Republic of Korea

S09. Joint Symposium with Korean Society of Pharmacology (16:00 ~ 17:30)

Organizer and Chair: Jae-sung Bae (Kyungpook National Univ.),
Chair: Chi Dae Kim (Pusan National Univ.), Sung Jun Kim (Seoul National Univ.)
Co-Organized by Senotherapy-based Metabolic Disease Control Research Center

S 36 S-9-1 Dynamic regulation of mitochondria in cellular senescence
Eun Kyung Lee
The Catholic University of Korea, College of Medicine, Republic of Korea

S 37 S-9-2 Finding the equilibrium for the uric acid dynamics
Sung Kweon Cho
Ajou University School of Medicine, Republic of Korea

S 37 S-9-3 Senotherapeutic intervention as a treatment of metabolic diseases
So-Young Park
College of Medicine, Yeungnam University, Republic of Korea

S 37 S-9-4 Therapeutic strategies against age-related fibrotic diseases
Kyu Sang Park
Wonju Yonsei University, College of Medicine, Republic of Korea

• Symposium (November 1, Friday)

S10. Exploring Glial Functions in CNS: Understanding Neuron-Glia Interactions (09:00 ~ 10:30)

Organizer and Chair: Hee Jung Kim (Dankook Univ.), Chair: Dong Woon Kim (Kyung Hee Univ.)

S 37 S-10-1 Rejuvenating aged microglia increases amyloid-β clearance
Dong Woon Kim
Department of Oral Anatomy & Developmental Biology, Kyung Hee University College of Dentistry, Seoul, Republic of Korea

S 38 S-10-2 Conductivity and nano-topography of nanotube platforms modulate astrocyte functions
Bo-Eun Yoon
Department of biomedical Science, College of Bio-convergence, Dankook University, Cheonan, Republic of Korea

S 38 S-10-3 The role of Tweety-homolog (TTYH) family in astrocyte volume regulation
Soo-Jin Oh
Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul, Republic of Korea

S 38 S-10-4 Tracking oligodendroglial development through advanced imaging techniques
Kyung-Ok Cho
Department of Pharmacology, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

S11. Tissue-Specific Immunity: Exploring the Physiological Landscapes Across Different Organs (09:00 ~ 10:30)

Organizer and Chair: June-Yong Lee (Yonsei Univ.), Chair: You Jeong Lee (Seoul National Univ.)
Co-Organized by Innate Immune-Mediated Chronic Inflammatory Disease Medical Research Center

S 39 S-11-1 Human MAIT cells undergo clonal selection and expansion during thymic maturation and aging
You Jeong Lee
Seoul National University, Republic of Korea

S 39 S-11-2 Inflammatory Niche in Lung tissue regeneration and pathogenesis
Jinwook Choi
Gwangju Institute of Science and Technology, Republic of Korea

S 39 S-11-3 Portal immune system: key guardians against gut-derived toxins
Yong-Hyun Han
College of Pharmacy, Kangwon National University, Republic of Korea

S12. Novel therapeutic strategies for cardiovascular diseases - stem cell, miRNA, mitochondria and beyond (09:00 ~ 10:30)

Organizer and Chair: Yin Hua Zhang (Seoul National Univ.)

S 39 S-12-1 Heart regeneration - making breakthroughs & renewed optimism
Hun-Jun Park
The Catholic University of Korea, Republic of Korea

S 40 S-12-2 Estrogen through GPER mitigates stress-induced cardiac inflammation and metabolic disorders
Hong Sun
Department of Physiology, Xuzhou Medical University

S 40 S-12-3 Mitochondrial transplantation for ischemic related cardiovascular diseases
Yin Hua Zhang
Seoul National University College of Medicine, Chinese

S13. Young Faculty Presentation Part 1. Neuroscience (14:00 ~ 15:30)

Organizer and Chair: Jun Young Heo (Chung Nam National Univ.), Chair: Sang Jeong Kim (Seoul National Univ.)
Co-Organized by System Network Inflammation Control Research Center

S 40 S-13-1 AI in neurobiology: from neuron classification to reinforcement learning models
Hyusu Lee
School of Medicine, Pusan National University, Republic of Korea

S 40 S-13-2 Identifying a biomarker for cognitive performance
Alan Jung Park
Seoul National University College of Medicine, Republic of Korea

S 41 S-13-3 Functional significance of *NRGN*, a schizophrenia risk gene, in regulating synaptic plasticity and calcium channel activity
Hongik Hwang
Department of Life Science, University of Seoul, Republic of Korea

S 41 S-13-4 Pathologic α-Synuclein-NOD2 interaction and RIPK2 activation drives microglia-induced neuroinflammation in Parkinson's disease
Bo Am Seo
Yonsei University Wonju College of Medicine, Republic of Korea

S14. Young Faculty Presentation Part 2. Cancer and Metabolism (14:00 ~ 15:30)

Organizer and Chair: Jun Young Heo (Chung Nam National Univ.), Chair: Dae Kyu Song (Keimyung Univ.)
Co-Organized by System Network Inflammation Control Research Center

S 41 S-14-1 Unveiling the role of SON-mediated RNA splicing in genetic diseases and tumorigenesis
Jung-Hyun Kim
National Cancer Center, Republic of Korea

S 41 S-14-2 Tumor-targeted therapy using engineered mesenchymal stem cells remodels tumor microenvironment
Joonbeom Bae
Korea University, Republic of Korea

S 42 S-14-3 In vivo mapping of subcellular proteomes in mice
Kwang-eun Kim
Department of Convergence Medicine, Yonsei University Wonju College of Medicine, Republic of Korea

S 42 S-14-4 Exercise-induced-lactate promotes fatty acid oxidation by the TCA cycle and mitochondrial respiration in muscles of obese mice
Jin-Ho Koh
Yonsei University Wonju College of Medicine, Republic of Korea

S15. Young Faculty Presentation Part 3. Infection and Immunology (14:00 ~ 15:30)

Organizer and Chair: Jun Young Heo (Chung Nam National Univ.), Chair: Jihee Lee (Ewha Womans Univ.)
Co-Organized by System Network Inflammation Control Research Center

S 42 S-15-1 Sesamin enhances apoptosis of activated T cells by physically interacting with MCL-1 and shows therapeutic effect on allergic dermatitis
Hyunsu Lee
Department of Physiology, Daegu Catholic University School of Medicine, Republic of Korea

S 42 S-15-2 Tofacitinib Uptake by patient-derived intestinal organoids predicts individual clinical responsiveness
Kyung Ku Jang
Yeonsei University College of Medicine, Republic of Korea

S 43 S-15-3 Principles and applications of atomic force microscopy in studying virus entry mechanism
Jinsung Yang
Gyeongsang National University, Republic of Korea

S 43 S-15-4 In vivo imaging of invasive aspergillosis with 18F-fluorodeoxysorbitol positron emission tomography in small animals
Dong-Yeon Kim
College of Pharmacy, Gyeongsang National University, Republic of Korea

S16. Inflammation and aging (15:40 ~ 17:10)

Organizer and Chair: Youn-Hee Choi (Ewha Womans Univ.)
Co-Organized by Inflammation-Cancer Microenvironment Research Center

S 43 S-16-1 Role of interaction between cancer-associated fibroblasts and apoptotic cancer cells in lung cancer suppression
Jihee Lee
Ewha Womans Univ., Republic of Korea

S 43 S-16-2 Novel target for antiaging intervention in the elderly:from the aspect of mid old cells
Tae Jun Park
Ajou University School of Medicine, Republic of Korea

S 44 S-16-3 Supramolecular Senolytics via Intracellular Oligomerization of Peptides
Ja-Hyoung Ryu
Ulsan National Institute of Science and Technology (UNIST), Republic of Korea

S 44 S-16-4 Senescent microglia: a universal target in brain aging and neurodegenerative diseases
Min-Soo Kwon
CHA University, Republic of Korea

S17. Exploring novel pain circuits from the periphery to the brain (15:40 ~ 17:10)

Organizer and Chair: Sun Kwang Kim (Kyung Hee Univ.)

S 44 S-17-1 Translational neurophotonics for visualizing and manipulating the nervous system
Euiheon Chung
Gwangju Institute of Science and Technology (GIST), Republic of Korea

S 44 S-17-2 Neuroimmunity in Pain: Role of Natural Killer Cells
Seog Bae Oh
Seoul National University, Republic of Korea

S 45 S-17-3 Nocifensive behavior-associated activation of cerebellar Bergmann glia modulate chronic neuropathic pain
Sang Jeong Kim
Seoul National University College of Medicine, Republic of Korea

S 45 S-17-4 Metabotropic glutamate receptors in the brain show characteristic patterns in neuropathic pain state
Geehoon Chung
Neurogrin, Republic of Korea

S18. Revealing underlying mechanism of metabophyiology through Multi-omics analysis (15:40 ~ 17:10)

Organizer and Chair: Seung-Soon Im (Keimyung Univ.), KyeongJin Kim (Inha Univ.)

S 45 S-18-1 The role of NAD+ recycling at the nexus of glucose and lipid metabolism
Wondong Kim
Hanyang University, Republic of Korea

S 45 S-18-2 Fibrotic tumor microenvironment promotes metastatic tumor growth in fatty liver
Yoon Mee Yang
College of Pharmacy, Kangwon National University, Republic of Korea

S 46 S-18-3 Nearby nutrients dictate metabolism and maintain open chromatin landscape to support cancer growth
Min-Sik Lee
POSTECH, Republic of Korea

S 46 S-18-4 Host and microbial compensation in a model of leucine breakdown deficienty
Yong-Uk Lee
Dankook University, Republic of Korea

• Young Investigator Oral Presentation (November 1, Friday, 10:40 ~ 12:00)

S 47 Y-01

Nuclear aggregation of profilin-1 impairs the phagocytic function of DNA damage-induced senescent microglia

Chan Rim[1], Soyoung Sung[1], Hui-Ju Kim[1], Seung Hyun Kim[4,5], Minyeop Nahm[3]*, Min-Soo Kwon[1,2]*
[1]Department of Pharmacology, Research Institute for Basic Medical Science, School of Medicine, CHA University, Seongnam, Korea, [2]Brainimmunex Inc. Seongnam, Korea, [3]Dementia Research Group, Korea Brain Research Institute, Daegu, Korea, [4]Department of Neurology, College of Medicine, Hanyang University, Seoul, Korea, [5]Cell Therapy Center, Hanyang University Hospital, Seoul, Korea

S 47 Y-02

POMC neuron-specific mitochondrial methionyl-tRNA formyltransferase deficiency improves energy metabolism through enhanced sympathetic activity

Carlos Noriega Polo[1,2,3], Cheol-Sang Hwang[4], Kyu-Sang Park[1,2,3]
[1]Department of Physiology, [2]Mitohormesis Research Center, [3]Department of Global Medical Science, Yonsei University Wonju College of Medicine, Wonju, Korea, [4]Department of Life Science, Korea University, Seoul, Korea

S 47 Y-03

Astrocytic FoxO1 in the hypothalamus regulates metabolic homeostasis

KhanhVan Doan[1,2]*, Sang Hee Lyoo[1]*, Thu ThiAnhHa[1], Le TrungTran[1,2], Dong JooYang[1], ThiDang Mai[1], SeulKi Kim[1,2], Ronald A. DePinho[3], Dong-Min Shin[1], Yun-Hee Choi[1] and Ki Woo Kim[1,2]
[1]Division of Physiology, Department of Oral Biology, Yonsei University College of Dentistry, Seoul, Korea, [2]Department of Applied Life Science, BK21 FOUR, Yonsei University College of Dentistry, Seoul, Korea, [3]Department of Cancer Biology, University of Texas MD Anderson Cancer Center, Houston, Texas, USA

S 47 Y-04

Neurophysiological mechanisms of synaptic and cognitive dysfunction in phenylketonuria

Woo Seok Song[1], Jae-min Lim[1], Young Sook Kim[1], Young-Soo Bae[1], Sang Ho Yoon[1], Myoung-Hwan Kim[1,2]
[1]Department of Physiology and Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [2]Seoul National University Bundang Hospital, Seongnam, Gyeonggi, Korea

S 48 Y-05

Distinct modulation of calcium-activated chloride channel TMEM16A by a novel drug-binding site

Jae Won Roh[1,2], Heon Yung Gee[2], Wook Lee[3], Joo Hyun Nam[1]
[1]Departments of Physiology Dongguk University College of Medicine, Gyeongju, Korea, [2]Department of Pharmacology, Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, Korea, [3]Department of Biochemistry, Kangwon National University, Chuncheon, Korea

S 48 Y-06

Roles of CALHM channels: Exploring ATP release hemichannel vs. Electrical gap junction, or both?

Young Keul Jeon[1,2,3], Jae Won Kwon[1,2], Sung Joon Kim[1,2,3]
[1]Department of Physiology, [2]Department of Biomedical Sciences, [3]Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, Seoul, Korea

S 48 Y-07

Inhibition of Lactate Dehydrogenase A stimulates lipid catabolism and thermogenesis via AMPK and NADH in mouse brown adipose tissue

Soo Kyung Lee[1,2,3], Aye Hsu Lae[1,2,3], Jaetaek Kim[4], Chanbae Park[5]*, Kyu-Sang Park[1,2,3]*
[1]Department of Physiology, [2]Organelle Medicine Research Center, [3]Department of Global Medical Science, Yonsei University Wonju College of Medicine, Wonju, [4]Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Chung Ang University, Seoul, [5]Department of Physiology, Department of Biomedical Sciences, Ajou University, Suwon, Korea

S 49 Y-08

Cancer cells induce lipolysis by secreting cytokine CCL to obtain free fatty acids from fat tissue for cancer proliferation and migration

Jeong-Eun Yun[1,3], Jieun Seo[4,5], Yeseon Son[1,3], Do-Won Jeong[6] , Yang-Sook Chun [2,3]
[1]Department of Biomedical Sciences, [2]Ischemic/Hypoxic Disease Institute, [3]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [4]Faculty of Engineering, Yokohama National University, [5]Kanagawa Institute of Industrial Science and Technology, Kawasaki, Japan, [6]Department of Cell Biology, Harvard Medical School, Boston, MA, USA

S 49 Y-09

Gaussian filter-based image denoising detects hidden sweat glands and enhances accuracy of active sweat gland density (ASGD) measurements

Seung-hyun Lee[1], Tae-hwan Park[1], Sim-sung Kim[2], Seung-hyun Na[2], You-jeong Nam[2], Eon-ah Choo[1], Jong-in Park[3], Yi-rang Lim[3], Mun-jeong Kim[3], Da-jeong Bae[3], Jin Kim[1], Young-hyun Jung[1] and Jeong-beom Lee[1,2,3]*
[1]Department of Physiology, College of Medicine, Soonchunhyang University, Cheonan, [2]Department of Healthcare Business, the Graduate School, Soonchunhyang University, Asan, [3]Department of Medical Sciences, Graduate School, Soonchunhyang University, Asan, Korea

S 50 Y-10

Compartment-specific protein expression and function of neuronal mitochondria

Dong Cheol Jang[1†], Su Yeon Kim[1,2†], Won Seok Kim[1†], Hyunsu Jung[1], Yongcheol Cho[3]*, Seok-Kyu Kwon[1,4]*
[1]Brain Science Institute, Korea Institute of Science and Technology (KIST), [2]Department of Neuroscience, College of Medicine, Korea University, [3]Department of Brain Sciences, Daegu Gyeongbuk Institute of Science & Technology (DGIST), [4]Division of Bio-Medical Science & Technology, KIST School, Korea University of Science & Technology (UST)

S 50 Y-11

Non-invasive neuromodulation of cerebrospinal fluid flow

Seunghwan Choi[1], Sun Kwang Kim[1,2]
[1]Department of East-West Medicine, Graduate School, Kyung Hee University, Seoul, Korea, [2]Department of Physiology, College of Korean Medicine, Kyung Hee University, Seoul, Korea

S 50 Y-12

Comparison of modulation efficiency with electrical stimulation between normal and degenerated primate retina

Seongkwang Cha[1], Yongseok Yoo[2], Yong Sook Goo[1,3]*
[1]Department of Physiology, College of Medicine, Chungbuk National University, Cheongju, Korea, [2]School of Computer Science and Engineering, Soongsil University, Seoul, Korea, [3]Biomedical Research Institute, Chungbuk National University Hospital, Cheongju, Korea

S 51 Y-13
Role of the STING-IRF3 pathway in ambient GABA homeostasis and cognitive function
Ramesh Sharma[1,2], Chiranjivi Neupane[1,2], Fei Fei Gao[3], Thuy Linh Pham[2], Yoo Sung Kim[4], Bo-Eun Yoon[4], Eun-Kyeong Jo[5], Kyung-Cheol Sohn[6], Gang Min Hur[6], Guang-Ho Cha[3], Sun Seek Min[7], Cuk-Seong Kim[2], and Jin Bong Park[1]*
[1]Laboratory of Veterinary Pharmacology, College of Veterinary Medicine and Research Institute for Veterinary Science, Seoul National University, Seoul, Korea, [2]Department of Physiology, [3]Infectious Biology & Medical Science, Chungnam National University, Daejeon, Korea, [4]Department of Molecular Biology, Dankook University, Cheonan, Korea, [5]Department of Microbiology, [6]Pharmacology & Medical Science, Chungnam National University, Daejeon, Korea, [7]Department of Physiology, Eulji University School of Medicine, Daejeon, Korea

S 51 Y-14
GLP-1 and its Derived Peptides Mediate Pain Relief Through Direct TRPV1 Inhibition Without Affecting Thermoregulation
Eun Jin Go[1], Sung-Min Hwang[1], Hyunjung Jo[1], Md. Mahbubur Rahman[1], Jaeik Park[1], Ji Yeon Lee[2], Youn Yi Jo[2], Byung-Gil Lee[3], YunJae Jung[3], Temugin Berta[4], Yong Ho Kim[1]*, Chul-Kyu Park[1]*
[1]Gachon Pain Center and Department of Physiology, College of Medicine, Gachon University, Incheon, Korea, [2]Department of Anesthesiology and Pain Medicine, Gil Medical Center, Gachon University, Incheon, Korea, [3]Lee Gil Ya Cancer and Diabetes Institute Gachon University, Incheon, Korea, [4]Pain Research Center, Department of Anesthesiology, University of Cincinnati Medical Center, Cincinnati, OH, USA

S 51 Y-15
Impaired mitophagy flux and mitochondrial dysfunction in pulmonary arterial hypertensive smooth muscle and their recovery by KV7.4 activator URO-K10
Seung Beom Oh[1], Suhan Cho[3], Young Keul Jeon[1], Sung Joon Kim[1,2]
[1]Department of Biomedical Sciences, [2]Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, [3]Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, MD, USA

S 51 Y-16
Effects of caffeine ingestion and thermotherapy on blood orexin circulation in humans
Tae Hwan Park[1], Hye Jin Lee[1], In Ho Lee[2], Seung Jea Lee[3], Jong In Park[1], Eon Ah Choo[1], Jeong Beom Lee[1]*
[1]Department of Physiology, College of Medicine, Soonchunhyang University, [2]Department of Occupational and Environmental Medicine, Soonchunhyang University Cheonan Hospital, [3]Department of Medical Sciences, Soonchunhyang University, Korea

S 52 Y-17
Anti-inflammatory effects of fermented and aged mountain-cultivated ginseng sprouts via suppression of MAPK-NF-κB pathway in lipopolysaccharide-stimulated RAW264.7 macrophages
Dang Long Cao[1,2], Min-Seok Woo[1,3], Eun-Jin Kim[1,3], Byeonggyu Ahn[1,2], Anjas Happy Prayoga[1,2], Sang Soo Kang[2,4], Kye Man Cho[5], Dawon Kang[1,2,3]*
[1]Department of Physiology, College of Medicine, Gyeongsang National University, Jinju, Korea, [2]Department of Convergence Medical Science, Gyeongsang National University, Jinju, Korea, [3]Institute of Medical Sciences, Gyeongsang National University, Jinju, Korea, [4]Department of Anatomy, College of Medicine, Gyeongsang National University, Jinju, Korea, [5]Department of GreenBio Science and Agri-Food Bio Convergence Institute, Gyeongsang National University, Jinju, Korea

S 52 Y-18
Effects of thermotherapy on irisin and lipid metabolism in middle aged obese woman
Seung-hyun Na[1,2], Kang-soo Cho[1,2], Sun-jin Kim[1,2], You-jeong Nam[2], Sim-sung Kim[2], Jin Kim[1], Young-hyun Jung[1], Jeong-beom Lee[1,2]*
[1]Department of Physiology, College of Medicine, Soonchunhyang University, Cheonan, [2]Department of Healthcare Business, the Graduate School, Soonchunhyang University, Asan, Korea

Poster Presentation (October 31, Thursday)

P01: Basic Neuroscience

S 53 A01-01
Calcium dynamics of cerebellar Purkinje neurons encode social interaction state
Suin Lim[1,2,4], McLean Bolton[4], Yong-Seok Lee[1,2,3]*, Sang Jeong Kim[1,2,3]*
[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Memory Network Medical Research Center, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University College of Medicine, Seoul, Korea, [4]Max Planck Florida Institute for Neuroscience, Jupiter, Florida, United States

S 53 A01-02
Genome-wide sequencing of isolated glial cells suggests age-related changes in oxidative phosphorylation in *Drosophila melanogaster*
Yun-Ho Cho[1], Gwang-Ic Son[1], Gye-Heung Kim[2], Joong-Jean Park[1]
[1]Department of Physiology, College of Medicine, Korea University, Seoul, Korea, [2]ReadyCure Inc., Seoul, Korea

S 53 A01-03
Bergmann glia inhibit Purkinje cell activity through interneuron
Jaegeon Lee[1,2], Seung Ha Kim[1,2], Yong-Seok Lee[1,2,3], Sang Jeong Kim[1,2,3]*
Department of [1]Physiology and [2]Biomedical Sciences, Seoul National University College of Medicine, [3]Memory Network Medical Research Center, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University College of Medicine, Seoul, Korea

S 53 A01-04
Chemogenetic modulation of the prelimbic cortex to the nucleus accumbens core circuit reduces cocaine-induced increase of risk choice behavior
Joonyep Han[1], Myungji Kwak[1], Wha Young Kim[2], Jeong-Hoon Kim[1,2]
Departments of [1]Medical Science and [2]Physiology, Yonsei University College of Medicine, Seoul, Korea

S 54 A01-05

Association of α-CaMKII hypoactivity with male-specific auditory sensory processing impairments in a mouse model of Noonan syndrome

Soobin Kim[1], Sohyeon Park[2], Hung M. Vu[3], Yujin Kim[4], In Gyeong Koh[4], Gaeun Park[1], Minkyung Kang[1], Sang Jeong Kim[1], Joon Yong An[4], Min-Sik Kim[3], Moo Kyun Park[5], Yong-Seok Lee[1]

[1]Department of Biomedical Sciences, Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University College of Medicine, Seoul, Korea, [3]Department of New Biology, DGIST, Daegu, Korea, [4]Department of Integrated Biomedical and Life Science, Korea University, Seoul, Korea, [5]Interdisciplinary Program in Neuroscience, Seoul National University College of Natural Sciences, Seoul, Korea

S 54 A01-06

Increased mGluR5 in somatostatin-positive interneurons mediates mPFC deactivation in a mouse model of neuropathic pain

Mirae Jang[1,2], Jaegeon Lee[1,2], Seung Ha Kim[1,2], Sang Ho Yoon[1,2,3], Myoung-Hwan Kim[1,2,3], Yong-seok Lee[1,2,3], Sun Kwang Kim[4], Geehoon Chung[4]*, Sang Jeong Kim[1,2,3]*

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Memory Network Medical Research Center, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University College of Medicine, Seoul, Korea, [4]Department of Physiology, College of Korean Medicine, Kyung Hee University, Seoul, Korea

S 54 A01-07

Activation of a hypothalamus-habenula circuit suppresses cocaine-induced locomotion via presynaptic release of glutamate and orexin.

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S 55 A01-08

A mechanism of sexual dimorphism in social recognition following resocialization after social isolation

Tae-woo Kim[1,2], Gaeun Park[1,2], Yong-Seok Lee[1,2]

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S 55 A01-09

Synergistic inhibition of TRPC channels and calcium dysregulation to combat ROS-mediated excitotoxicity in neurodegeneration

Chansik Hong

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S 55 A01-10

Regulation of Kv2.1 channels by phosphatidylinositol 4,5-bisphosphate (PIP2) in neurons

Ah Reum Lee[1], Isabella Salzer[3], Jae-Won Yang[3], Kang-Sik Park[1,2]

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S 56 A01-11

Mechanisms of Kv2.1 in the interaction between neurons and astrocytes. Regulation of Kv2. 1 in the interaction between neurons and astrocytes

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[1]Departments of Biomedical Science, Graduate school, Kyung Hee University, Seoul, Korea, [2]Departments of Physiology, College of Medicine, Kyung Hee University, Seoul, Korea

S 56 A01-12

A parabrachial-lateral hypothalamic pathway mediating long-term cold hyperalgesia

Juping Xing, DanBi Ahn, Hyung Kyu Kim, Baoji Lu, Eun Ah Jo, Jing Ma, Bonggi Kim, Hee Young Kim*

Department of Physiology, Yonsei University College of Medicine, Seoul, Korea

S 56 A01-13

Physiological profiling of cannabidiol reveals profound inhibition of sensory neurons

Joo Hyun Nam[1], Gracesenia Chahyadinata[2], Ashleya Battenberg[2], Brian J. Wainger[2]

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S 56 A01-14

Effects of phosphodiesterase 5 inhibitor, AR1001, on traumatic brain injury-induced neuron death

Min Kyu Park[1], Hyun Wook Yang[1], Seo Young Woo[1], Hyun Ho Jung[1], Bo Young Choi[2,3], Sang Won Suh[1]*

[1]Department of Physiology, Hallym University, College of Medicine, Chuncheon, Korea, [2]Institute of Sport Science, Hallym University, Chuncheon, Korea, [3]Department of Physical Education, Hallym University, Chuncheon, Korea

S 57 A01-15

L-theanine ameliorates traumatic-brain-injury-induced hippocampal neuronal death in rats

Min Kyu Park[1], Bo Young Choi[2,3], A Ra Kho[4,5], Song Hee Lee[1], Dae Ki Hong[1,6], Beom Seok Kang[1], Chang Jun Lee[1], Hyun Wook Yang[1], Seo Young Woo[1], Se Wan Park[1], Dong Yeon Kim[1], Hyun Ho Jung[1], Won il Yang[2,3,7], Sang Won Suh[1]*

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S 57 A01-16

Algorithmic Targeting of Pathological Subclusters in the Nervous System for Pain Modulation

Miri Kim, Songhyeon Kim, Minseok Kim, Chaeeun Kim, Yebeen Kim, Ji Yeon Lim, Minji Jeon, Sun Wook Hwang

Department of Biomedical Sciences, Korea University College of Medicine, Seoul, Korea

P02: Neuronal Pathophysiology

S 57 B01-01

Altered Glutamatergic Signaling and Neuroinflammation in an ADHD Model

GwangSeok Lee[1,2], JaeSoo Kim[1,2], Ji-Hyun Park[1,2], Mi-Hye Kim[1,2], Bo-Eun Yoon[3], Hee Jung Kim[1]*

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S 58 B01-02

Obesity augments seizure severity and neuroinflammatory responses in status epilepticus

GwangSeok Lee[1,2], Su Bin Lee[1,2], Myung Ju Kim[3]*, Hee Jung Kim[1]*

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S 58 B01-03

Therapeutic potential of near-infrared low-level laser therapy in a diabetic neuropathy model

Hyung Chan Kim[1,2], Min Ji Kim[1,2], Jae Soo Kim[1,2], Dong Woon Kim[3], Sehwan Kim[4], Hee Jung Kim[1]*

[1]Department of Physiology, College of Medicine, Dankook University, Cheonan, Korea, [2]Department of Medical Laser, Graduate School, Dankook University, Cheonan, Korea, [3]Department of Oral Anatomy & Developmental Biology, Kyung Hee University College of Dentistry, Seoul, Korea, [4]Department of Biomedical Engineering, College of Medicine, Dankook University, Cheonan, Korea

S 58 B01-04

The neurotoxicity of SSRI antidepressant by TRPC5 hyperactivation aggravates the motor function of Parkinson's disease

Byeongseok Jeong[1,2], Insuk So[2], Chansik Hong[1]*

[1]Department of Physiology, Chosun University College of Medicine, Gwangju, Korea, [2]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea

S 59 B01-05

Cirtical Role of DRD2 in Dopaminergic Neuron Survival and Alpha-Synuclein-Driven Caspase-3 Activation

Lee Ya Kim[1†], Eun Ji Kang[1†], Dae Ki Hong[2], Eun Ji Kang[1], Sowon Lee[1], Eun Hee Ahn[1,3]*

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S 59 B01-06

Analgesic effects of transcutaneous auricular vagus nerve stimulation (taVNS) in neuropathic pain

Hyunjin Shin[1], Geehoon Chung[1,2], Sun Kwang Kim[1,2]

[1]Department of Science in Korean Medicine, Graduate School, Kyung Hee University, Korea, [2]Department of Physiology, College of Korean Medicine, Kyung Hee University, Korea

P03: Electrophysiology and Ion channel

S 59 C01-01

Rectification profile alterations in TREK channel mutants

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Department of Physiology, College of Medicine and Institute of Medical Sciences, Gyeongsang National University, Jinju, Korea

S 60 C01-02

Reduced expression of TWIK-related K+ channels in the retina exacerbates retinal pathological changes in a painful diabetic peripheral neuropathy mouse model

Seungmin Shin[1,2†], Eun-Jin Kim[1,4†], Dawon Kang[1,3,4*]

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S 60 C01-03

Interventricular Differences in Inotropic Responses Induced by Isoproterenol in Rat Cardiomyocyte

Ryeon Heo, Young-Keul Jeon, Sung Joon Kim

Department of Physiology and Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea

S 60 C01-04

Citronellol modulates inhibitory neurotransmission in substantia gelatinosa neurons of the trigeminal subnucleus caudalis in mice

Thi Quy Nguyen, Seon-Hui Jang, Soo-Joung Park, Seon-Ah Park, Seong-Kyu Han*

Department of Oral Physiology, School of Dentistry & Institute of Oral Bioscience, Jeonbuk National University, Jeonju, Jeonbuk, Korea

S 60 C01-05

Modulation of nociceptive properties by beta-ionone in substantia gelatinosa neurons of trigeminal subnucleus caudalis in juvenile mice

Thi Quynh Nhu Tran[1], Seon-Ah Park[1], Soo-Joung Park[1], Won Jung[2,3], Seong-Kyu Han[1]*

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S 61 C01-06

The Impact of Non-Competitive NMDA Receptor Antagonist MK-801 on Kv3.1 Channels: Insights into Schizophrenia

Jin Ryeol An[1], Mi Seon Seo[1], Tae Jun Park[1], Hye Ryeong Lee[1], Solah Park[1], Yeji Lee[1], Sang Woong Park[2], Young Min Bae[1]

[1]Department of Physiology, KU Open Innovation Center, Research Institute of Medical Science, Konkuk University School of Medicine, Chungju, Korea, [2]Department of Emergency Medical Services, Eulji University, Seongnam, Korea

S 61 C01-07

STIM1 Deficiency Protects Against RAAS-Mediated Podocyte Dysfunction and Proteinuria in Adenine-Induced Kidney Injury

Kyu-Hee Hwang[1,2,3], Seoyun Jun[4], Rahyun Won[4], Sunhee Park[4], Hayeon Oh[4], So Jeong Park[4], Seung-Kuy Cha[1,2,3¶], Ji-Hee Kim[4¶]

Department of [1]Physiology, [2]Department of Global Medical Science, and [3]Organelle Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea, [4]Department of Occupational Therapy, Soonchunhyang University, Asan, Korea

S 61 C01-08
Pannexin-mediated ATP release induces enhancement of ventricular Ca^{2+} transients under shear stress via P2Y1 purinoceptor signaling
Phuong Kim Luong, Hieu Trong Huynh, Tran N. Trinh, Sun-Hee Woo*
College of Pharmacy, Chungnam National University, Daejeon, Korea

S 62 C01-09
Differential regulation of current kinetics by beta subunits in N-type calcium channel
Jin-Nyeong Woo, Byung-Chang Suh
Department of Brain Sciences, DGIST, Daegu, Korea

S 62 C01-10
Role of TREK-2 (KCNK10) K+ channel in differentiation of human epidermal keratinocyte
Elina Da Sol Chung[1,2#], Young Keul Jeon[1,2], Joong Heon Suh[1,3,4], Dong Hun Lee[3,4], Woo Kyung Kim[5,6], Joo Hyun Nam[5,6], Sung Joon Kim[1,2*]
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S 62 C01-11
Asarinin: A Natural TRPV3 Inhibitor Unveiled by In Silico Screening with Therapeutic Potential for Inflammatory Skin Disorders
Nhung Thi Hong Van[1], Jae Won Roh[1,2], Huyen Dang[1], Joo Hyun Nam[2]
[1]Departments of Physiology Dongguk University College of Medicine, Gyeongju, Korea, [2]Department of Pharmacology, Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, Korea

S 63 C01-12
WNK1 suppresses autophagy by inhibiting TRPML1-mediated peri-lysosomal Ca^{2+} dynamics
Subo Lee[1,2,3], Kyu-Sang Park[1,2,3*], Seung-Kuy Cha[1,2,3*]
[1]Department of Physiology, [2]Department of Global Medical Science and,
[3]Organelle Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea

S 63 C01-13
Unraveling the molecular reason of opposing effects of α-mangostin and norfluoxetine on TREK-2 at the same binding site
Nhung Thi Hong Van[1], Gangrae Kim[2], Wook Lee[2], Joo Hyun Nam[1]
[1]Departments of Physiology Dongguk University College of Medicine, Gyeongju, Korea, [2]Department of Biochemistry, Kangwon National University College of Natural Sciences, Chuncheon, Korea

S 63 C01-14
Diphenyleneiodonium suppresses cardiac Ca^{2+} signaling and contraction
Qui Anh Le[#], Tran Nguyet Trinh[#], Phuong Kim Luong, Vu Thi Van Anh, Ha Nam Tran, Joon-Chul Kim, Sun-Hee Woo*
College of Pharmacy, Chungnam National University, Daejeon, Korea

P04: Muscle Physiology

S 63 D01-01
Immature skeletal myotubes are an effective source for improving the terminal differentiation of skeletal muscle
Seung Yeon Jeong[1,2], Jun Hee Choi[1,2], Paul D. Allen[3], Eun Hui Lee[1,2]
[1]Department of Physiology, College of Medicine, The Catholic University of Korea, Seoul, Korea, [2]Department of Medical Sciences, Graduate School, The Catholic University of Korea, Seoul, Korea, [3]Department of Anesthesiology, University of Tennessee, Graduate School of Medicine, Knoxville, TN, USA

S 64 D01-02
Possible mechanism for difference in Ca^{2+}-frequency response between right and left atrial myocytes
Hieu Trong Huynh, Tran Nguyet Trinh, Phuong Kim Luong, Sang-Yoon Kim, Sang-Min Park, Sun-Hee Woo
College of Pharmacy, Chungnam National University, Daejeon, Korea

S 64 D01-03
Lubiprostone improves distal segment-specific colonic contractions through TRPC4 activation stimulated by EP3 prostanoid receptor
Junhyung Lee[1], Byeongseok Jeong[1,2], Chansik Hong[1*]
[1]Department of Physiology, Chosun University College of Medicine, Gwangju, Korea, [2]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea

S 64 D01-04
Extracts H ameliorate skeletal muscle wasting in High-Fat Diet-induced sarcopenic obesity via activating FNDC5 signaling pathway
Ji-Soo Choi[1], Hyun-Sol Lee[1], Hee-Min Kang[1], Jae-Won Choi[2], Rengasamy Balakrishnan[2], Dong-Kug Choi[1,2*]
[1]Department of Biotechnology, Konkuk University, Chungju, Korea, [2]Department of Biotechnology, College of Biomedical and Health Science, and Research Institute of Inflammatory Disease (RID), Konkuk University, Chungju, Korea

S 65 D01-05
αKlotho Mitigates Doxorubicin-Induced Muscle Atrophy by Regulation of Transcriptional Factors, FOXO3a and Myogenin
Sung-Eun Kim[1], Mi-Young Lee[1,2], Ji-Hee Kim[3]
Department of [1]Medical Biotechnology, [2]Department of Medical Science, [3]Department of Occupational Therapy, Soonchunhyang University, Asan, Korea

S 65 D01-06
The effects of TFAM on Calcium Dynamics in Skeletal Muscle
Vuong Quang Ha[1,3], Kim Han-Byeol[1,2,3], Park Sol-Yi[1,3], K Sreekumaran Nair[4], Jin-Ho Koh[1,2,3*]
Department of [1]Convergence Medicine and [2]Global Medical Science and [3]Mitohormesis Research Center, Yonsei University Wonju College of Medicine,
[4]Division of Endocrinology and Metabolism, Mayo Clinic, Rochester, MN, United States

S 65 D01-07 Compound A enhances PGC-1α in skeletal muscle, modulates kynurenine metabolism, and improves mitochondrial function in chronic kidney disease
Hee-Min Kang[1], Hyun-Sol Lee[1], Ji-Soo Choi[1], Jae-Won Choi[2], Rengasamy Balakrishnan[2], Dong-Kug Choi[1,2*]
[1]Department of Biotechnology, Konkuk University, Chungju, Korea, [2]Department of Biotechnology, College of Biomedical and Health Science, and Research Institute of Inflammatory Disease (RID), Konkuk University, Chungju, Korea

S 66 D01-08 Skeletal muscle-specific DKK3 overexpression exacerbates insulin resistance in obese mice
Su-Yeon Jeong[1,2], Min-Gyeong Shin[1], Hye-Na Cha[1,2], Soyoung Park[1,2], Yu-Kyoung Park[1,2], Su-Ryun Jung[1,2], So-Young Park[1,2]
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P06: Endocrine and Energy Metabolism

S 66 E01-01 Subunit-specific developmental roles of phosphatidylinositol 3-kinase in steroidogenic factor-1- expressing cells
My Khanh Q. Huynh[1,3*], Sang Hee Lyoo[1,2*], Aran Lee[1], Dong Joo Yang[1], Yun-Hee Choi[1#], Ki Woo Kim[1,2]
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S 66 E01-02 Primary Cilia in the Hypothalamic Neurons Mediate Metabolic Effects of Butyrate
Dong Joo Yang[1#], Khanh Van Doan[1#], Aran Lee[1], Sang Hee Lyoo[1,2], Yeseong Hong[1,2], Da Young Kim[1,2], Chanshik Park[1], Yun-Hee Choi[1], Ki Woo Kim[1,2]
[1]Division of Physiology, Department of Oral Biology, Yonsei University College of Dentistry, Seoul, Korea, [2]Department of Applied Biological Scienece, BK21 FOUR, Yonsei University College of Dentistry, Seoul, Korea

S 66 E01-03 Liver receptor homolog-1 regulates methionine cycle via BHMT in liver
Sulagna Mukherjee, Dae-Kyu Song, Jae-Hoon Bae, Seung-Soon Im
Department of Physiology, Keimyung University School of Medicine, Daegu, Korea

S 67 E01-04 Regulatory Mechanism for Aldehyde Dehydrogenase 1B1 by Liver Receptor Homolog-1 in the Liver
Min-Hee Seo, Dae-Kyu Song, Jae-Hoon Bae, Seung-Soon Im
Department of Physiology, Keimyung University School of Medicine, Daegu, Korea

S 67 E01-05 SREBP-1c deficiency ameliorates liver injury and fibrosis in non-alcoholic steatohepatitis via lipocalin-2
Eun-Ho Lee, Dae-Kyu Song, Jae-Hoon Bae, Seung-Soon Im
Department of Physiology, Keimyung University School of Medicine, Daegu, Korea

S 67 E01-06 Regulation of Cystathionine γ-lyase by Liver Receptor Homolog-1 in the Liver
Soo-Young Park, Dae-Kyu Song, Jae-Hoon Bae, Seung-Soon Im
Department of Physiology, Keimyung University School of Medicine, Daegu, Korea

S 67 E01-07 Isocitrate Dehydrogenase 2 Deficiency Impairs Brown Adipocyte Differentiation through Suppression of LncBate10 Expression
Jae-Ho Lee, Dae-Kyu Song, Jae-Hoon Bae, Seung-Soon Im
Department of Physiology, Keimyung University School of Medicine, Daegu, Korea

P08: Inflammation and Immune physiology

S 68 F01-01 Heterozygous Apex1 Deficiency Aggravates LPS-Induced Systemic Inflammatory Response in Mice
Sungmin Kim[1,3], Hee Kyoung Joo[1,3], Eunju Choi[2,3], Ka-Young Lee[2,3], Hao Jin[2,3], Eun-Ok Lee[3], Yu-Ran Lee[3], Cuk-Seong Kim[1,2,3], Byeong Hwa Jeon[1,2,3]
[1]Research Institute of Medical Sciences, [2]Department of Medical Science and [3]Department of Physiology, College of Medicine, Chungnam National University, Daejeon, Korea

S 68 F01-02 Suppression of NF-κB via exosome-based delivery modulates microglia and macrophages to reduce age-related neuroinflammation
Chae-Jeong Lee[1#], Seung Hyun Jang[2#], Jiwoo Lim[1], So-Hee Ahn[3], Soo-Jin Song[4], Jung A Shin[4], Chulhee Choi[3*], Heon Yung Gee[2*], Youn-Hee Choi[1*]
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[3]ILIAS Biologics Inc., Daejeon, Korea,
[4]Department of Anatomy, Ewha Womans University College of Medicine, Seoul, Korea

S 68 F01-03 Increase in PDGFRα expression in the lipopolysaccharide-induced acute lung injury mouse model
Dang Long Cao[1,2†], Eun-Jin Kim[1†], Byeonggyu Ahn[1,2], Anjas Happy Prayoga[1,2], Jina Ha[1,2], Kee Woong Kwon[3,5], Eun-A Ko[4*], Dawon Kang[1,2,5*]
[1]Department of Physiology, College of Medicine, Gyeongsang National University, Jinju, Korea, [2]Department of Convergence Medical Science, Gyeongsang National University, Jinju, Korea, [3]Department of Microbiology, College of Medicine, Gyeongsang National University, Jinju, Korea, [4]Department of Physiology, Colledge of Medicine, Jeju National University, Jeju, Korea, [5]Institute of Medical Sciences, Gyeongsang National University, Jinju, Korea

S 69 F01-04 Sesamin enhances apoptosis of activated T cells by physically interacting with MCL-1 and shows therapeutic effect on allergic dermatitis
Hee-Suk Park, Hyun-Su Lee
Department of Physiology, Daegu Catholic University School of Medicine, Daegu, Korea

S 669 F01-05 Polypharmacological Effects of Honokiol on Allergic Rhinitis: Modulating TMEM16A, TRPV1, and Calcium Signaling
Nhung Thi Hong Van[1,2], Jintae Kim[1], Yu-Ran Nam[1,2], Huyen Dang Thi[1,2], Hyun Jong Kim[1,2], Woo Kyung Kim[1,3], Joo Hyun Nam[1,2]
[1]Channelopathy Research Center (CRC), Dongguk University College of Medicine, Goyang, Korea, [2]Department of Physiology, Dongguk University College of Medicine, Gyeongju, Korea, [3]Department of Internal Medicine Graduate School of Medicine, Dongguk University, Goyang, Korea

S 69 F01-06 IDH2 Deficiency Triggers Endothelial Inflammation via P66sh-mediated Mitochondrial Oxidative Stress
Sohee Jeon[1,2], Su-jeong Choi[1], Shuyu Piao[1], Harsha Nagar[1], Seonhee Kim[1], Cuk-Seong Kim[1,2]
Department of Medical Science, Chungnam National University, Brain Korea 21 FOUR Project for Medical Science, Chungnam National University

S 70 F01-07 Real-Time Imaging of In Vivo Drug Response Mechanisms within Thymic Tissues
Junyoung Park[1], Hyungjin Kwon, Kubra Akyildiz, Junghyun Ohm, Hyunseok Kim
IVIM Technology, Seoul, Korea

S 69 F01-08 Gas6-induced AIM suppresses acute lung injury by inhibiting NLRP3 inflammasome activation and inducing autophagy in alveolar macrophages
Kyungwon Yang*, Sung-Hee Jung*, Ye-Ji Lee, Jihee Lee Kang
Departments of Physiology, Inflammation-Cancer Microenvironment Research Center, College of Medicine, Ewha Womans University, Seoul, Korea

S 70 F01-09 Astrocytic iNOS upregulation contributes to chronic below-level neuropathic pain after spinal cord injury in rats
Youngkyung Kim[1], Hyunggoo Kang[2], Young Wook Yoon[1]
[1]Departments of Physiology, Korea University College of Medicine, Seoul, Korea, [2]Department of Emergency Medicine, College of Medicine, Hanyang University, Seoul, Korea

P09: Cellular Physiology and Cancer

S 70 G01-01 Identification of potent bioactive compound from Artemisia princeps for breast cancer therapy
Seung-Yeon Ko[1], Hack-Sun Choi[2], Youn-Hee Choi[1]
[1]Department of Physiology, Inflammation-Cancer Microenvironment Research Center, College of Medicine, Ewha Womans University, Seoul, Korea, [2]Department of Biochemistry & Molecular Biology, Yonsei University College of Medicine, Seoul, Korea.

S 71 G01-02 Mitochondrial methionyl-tRNA formyltransferase participates in integrated stress response
Thuy Ngo[1,2,3], Ha Thu Nguyen[1,2,3], Carlos Noriega-Polo[1,2], Cheol-Sang Hwang[4], Kyu-Sang Park[1,2,3]
[1]Department of Physiology, [2]Organelle Medicine Research Center, [3]Department of Global Medical Science, Yonsei University Wonju College of Medicine, Wonju, [4]Department of Life Science, Korea University, Seoul, Korea

S 71 G01-03 *Paeonia japonica* inhibits tumor growth in the mouse CT-26 colon tumor model
Anlin Zhu, Dohyang Kim, Jaewoo Hong*
Department of Physiology, Daegu Catholic University School of Medicine, Daegu, Korea

S 71 G01-04 Treatment of EGFR-mediated tumors via lysosome acidification
Dohyang Kim, Anlin Zhu, Jaewoo Hong*
Department of Physiology, Daegu Catholic University School of Medicine, Daegu, Korea

S 72 G01-05 Mitochondrial Ca^{2+}-regulating gene dynamics as key drivers of the transition from MASLD to MASH
Jiyeon Oh[1,2,3], Boyeong An[4], Taesic Lee[5], Kyu-Hee Hwang[1,2,3], Seung-Kuy Cha[1,2,3]
[1]Department of Physiology, [2]Department of Global Medical Science, [3]Organelle Medicine Research Center, Yonsei University Wonju College of Medicine, Wonju, Korea, [4]Department of Integrative Biology, University of California, Berkeley, USA, [5]Division of Data Mining and Computational Biology, Department of Convergence Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

P14: Environmental Physiology and Thermoregulation

S 72 H01-01 Sweating Patterns on the Dorsal and Palmar Hands under Heat Stress
Maria Stenkina, Joo-Young Lee
College of Human Ecology, Seoul National University, Seoul, Korea

S 72 H01-02 Relationships with morphological variables, cardiovascular fitness during exercise, and thermo-physiological responses under passive heat stress according to Sasang typology
Joo-Young Lee[1], Andrew Gorski[2]
[1]College of Human Ecology, Seoul National University, Seoul, Korea, [2]Department of Philosophy in Korean Medicine, College of Korean Medicine, Kyung Hee University, Seoul, Korea

S 72 H01-03 Neurotoxicity of polystyrene in human induced pluripotent stem cell-derived neuron via *Hes* signaling pathway change
Jin Lee, Yugyeong Kim, Young Hyun Jung, Jeong-beom Lee, Jin Kim
Department of Physiology, College of Medicine, Soonchunhyang University, Cheonan, Korea

S 73 H01-04 Impact of gestational and lactational low-level cadmium exposure on neurodevelopment
Mi-Hye Kim[1,2], Jae Hyuk Shim[1,2], Hee Jung Kim[1]*
[1]Department of Physiology, College of Medicine, [2]Department of Medical Laser, Graduated School, Dankook University, Cheonan, Chungnam, Korea

S 73 H01-05 Assessing Music Therapy's impact in Mental Health Care for Alleviating Depression and Stress among Adolescents with Atopic Dermatitis in Multicultural Families in Republic of Korea
Jong-In Park[1], Seunghyun Lee[1], Young-Hyun Jung[1], Jin Kim[1], Yi-Rang Lim[3], You-Jeong Nam[1,2], Hyo-Jeong kang[3], Jeong-Beom Lee[1,2,3]
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S 73 H01-06 Effects of dance movement therapy on anxiety of juvenile delinquents in a detention center: Role of dopamine and body temperature in anxiety
Eon-ah Choo[1], You-jeong Nam[2], Seung-hyun Lee[1,2], Hyo-jeong Kang[3], Sim-sung Kim[2], Jong-in Park[3], Yi-rang Lim[3], Mun-jeong Kim[3], Da-jeong Bae[1], Jin Kim[1], Young-hyun Jung[1], Jeong-beom Lee[1,2,3]*
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S 74 H01-07 Impact of GIM Guided Imagery and Music using Ambient music on heart rate variability and plasma cortisol
Yi-rang Lim[1,3], You-jeong Nam[2], Sim-sung Kim[2], Jong-in Park[3], Jin Kim[4], Young-hyun Jung[4], Jeong-beom Lee[2,4]*
[1]Korea National University of Arts, Seoul, [2]Department of Healthcare Business, the Graduate School, Soonchunhyang University, Asan, [3]Department of Medical Sciences, Graduate School, Soonchunhyang University, Asan, [4]Department of Physiology, College of Medicine, Soonchunhyang University, Cheonan, Korea

S 74 H01-08 The acclimatization of Haenyeo to a cold environment and occupational characteristics evaluated by fibroblast growth factor 21 levels
Jeong-beom Lee[1,2] , In-ho Lee[1,3], Sang-hee Hong[2], Tae-hwan Park[1], Seung-hyun Lee[1], You-jeong Nam[1], Eon-ah Choo[1], Jong-in Park[1], Yi-rang Lim[2], Mun-jeong Kim[2], Da-jeong Bae[1], Jin Kim[1], Young-hyun Jung[1], Eun-chul Jang[3], Soon-chan Kwon[3], Young-Sun Min[3]
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P15: Others

S 75 I01-01 TRPML3 regulates type III unconventional protein secretion of MIF
Jiwoo Park, Suzi Choi, Hyun Jin Kim
Departments of Physiology, Sungkyunkwan University School of Medicine, Suwon, Korea

S 75 I01-02 The cholesterol-binding protein STARD3NL negatively regulates autophagy through interaction with TRPML3
Sihyun Choi, Suzi Choi, Hyun Jin Kim
Departments of Physiology, Sungkyunkwan University School of Medicine, Suwon, Korea

S 75 I01-03 The scramblase ATG9A regulates TRPML3 activation by PI3P in autophagy
Jee Hye Choi, Sungmin Ahn, So Woon Kim, Hyun Jin Kim
Departments of Physiology, Sungkyunkwan University School of Medicine, Suwon, Korea

S 75 I01-04 Ulinastastin Attenuates Vascular Damage in IDH2-Deficient Endothelial Cells via TGF-β/MMP7/SDS2 signaling pathway
GiangHuong Vu[1,2], Su-jeong Choi[1], Shuyu Piao[1], Seonhee Kim[1], Minsoo Kim[1,2], Byeong Hwa Jeon[1], Cuk-Seong Kim[1]
[1]Department of Physiology & Medical Science, College of Medicine, Chungnam National University, Daejeon, Korea, [2]Brain Korea 21 FOUR Project for Medical Science, Chungnam National University

S 76 I01-05 Downregulation of CTCF ameliorates tau-induced deficits in *Drosophila melanogaster*
Sung Yeon Park[1,3], Jieun Seo[2], Yang-Sook Chun[1,2,3]*
[1]Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea

S 76 I01-06 Neddylation fine-tunes bone homeostasis by seesawing between the differentiation of osteoblasts and osteoclasts
Jooseung Lee[1], Min Young Lee[1], Jong-Wan Park[1,2,3], Geon Ho Moon[1], Jun Bum Park[1], Hye-Jin Kim[1], Yang-Sook Chun[1,2,3]*
[1]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [2]Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea

Poster Presentation (November 1, Friday)

P01: Basic Neuroscience

S 76 A02-01

Transcriptomic changes by classical fear conditioning in the cerebellum

Jinhee Baek[1,2,3], Jungeun Ji[4,5], Kyoung-Doo Hwang[1,2,3], Junko Kasuya[7,8], Sang Jeong Kim[1,2,3], Ted Abel[7,8,9], Joon-Yong An[4,5,6], Yong-Seok Lee[1,2,3]

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S 76 A02-02

Astrocyte-Driven Modulation of Place Cell Activity in the Hippocampus

Myeongjong Yoo[1,2†], Seung-Woo Jin[3†], Gaeun Park[1,2], Soonho Shin[1,2], Sang-Jeong Kim[1,2], Inah Lee[3], Yong-Seok Lee[1,2]

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S 77 A02-03

Allosteric Shp2 inhibition impairs NMDA receptor-dependent long-term synaptic plasticity

Min-gyun Kim[1,2], Yong-seok Lee[1,2]

Departments of [1]Biomedical Science and [2]Physiology, Seoul National University College of Medicine, Seoul, Korea

S 77 A02-04

Receptive field difference across cell subtypes of S1B L2/3

Yeji Song[1,2], Sang Jeong Kim[1,2,3*]

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Memory Network Medical Research Center, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University College of Medicine, Seoul, Korea

S 77 A02-05

Fear learning induces novel neuronal plasticity and reorganization of population activity in the cerebellum

Min Seok Kim[1,2], Jinhee Baek[1,2], Yong-Seok Lee[1,2,3], Sang Jeong Kim[1,2,3*]

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Memory Network Medical Research Center, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University, Seoul, Korea

S 78 A02-06

Physiological investigation of cerebello-parabrachial-amygdalar circuit for fear learning and memory

Kyoung-Doo Hwang[1,2], Hunter E Halverson[3,4], Jangjin Kim[5], Sang Jeong Kim[1,2], John H Freeman[3,4], Yong-Seok Lee[1,2]

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Science, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Psychological and Brain Sciences, University of Iowa, Iowa City, Iowa, [4]Iowa Neuroscience Institute, University of Iowa, Iowa City, Iowa, [5]Department of Psychology, Kyungpook National University, Daegu, Korea

S 78 A02-07

Critical role of hippocampal-cortical interactions in the representation of social familiarity in mice infralimbic cortex

Gaeun Park[1,2], Min Seok Kim[1,2], Young-Beom Lee[3], Doyun Lee[3], Sang Jeong Kim[1,2,4], Yong-Seok Lee[1,2,4]

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [3]Center for Cognition and Sociality, Institute for Basic Science, Daejeon, Korea, [4]Neuroscience Research Institute, Medical Research Center, Seoul National University, Seoul, Korea

S 78 A02-08

Neuroprotective effect of C1q/TNF-Related Protein9 (CTRP9) after pilocarpine-induced seizures

Hyun Wook Yang[1], Min Kyu Park[1], Hyun Ho Jung[1], Min Woo Lee[2], Jae Woo Shin[3], Dae Soon Son[4], Bo Young Choi[5,6], Hong Ki Song[7,9], Hui Chul Choi[8,9], Sang Won Suh[1,9*]

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S 79 A02-09

Therapeutic Effect of Bee Venom on the Multiple Sclerosis Model in Mice

Jaehong Park[1], Hyunjin Shin[1], Hyeryeong Lee[1], Dong-Wook Kang[1], Miae Lee[1], Sheu-Ran Choi[2], Miok Bae[3], Suk Yun Kang[4], Yeon Hee Ryu[4], Hyun-Woo Kim[1]

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S 79 A02-10

Orexin-A regulates GABA in cultured mice astrocytes

Hyunjin Shin[1], Hyeryeong Lee[1], Jaehong Park[1], Dong-Wook Kang[1], Miae Lee[1], Sheu-Ran Choi[2], Miok Bae[3], Suk Yun Kang[4], Yeon Hee Ryu[4], Hyun-Woo Kim[1]

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S 79 A02-11

Effects of preserving residual ovarian function on the sensory nervous system in a 4-vinylcyclohexene-induced mice model of ovarian failure

Hyeryeong Lee[1], Jaehong Park[1], Hyunjin Shin[1], Dong-Wook Kang[1], Miae Lee[1], Sheu-Ran Choi[2], Miok Bae[3], Suk Yun Kang[4], Yeon Hee Ryu[4], Hyun-Woo Kim[1]

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S 80 A02-12

Indexing changes in soma-glial microcontact associated with pain severity

Chaeeun Kim[1], Hojin Lee[1], Miri Kim[1], Joo Seok Han[2], Juwon Shim[2], Sol-Ji Kim[2], Junwoo Lee[2], Yebeen Kim[1], Minseok Kim[1], Ji Yeon Lim[1], Jungmin Choi[1], Yoon Hee Chung[3], Im Joo Rhyu[1], Sun Wook Hwang[1]

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S 80 A02-13

Targeting the insular cortex for neuropathic pain modulation: Insights into synaptic and neuronal mechanisms

Guanghai Nan[1,2], Nari Kang[1], Un Jeng Kim[1], Myeounghoon Cha[1], Bae Hwan Lee[1,2,3]

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S 80 A02-14

Neurotoxin mediated neuronal dysfunction regulated by lysosomal function

Jinhong Wie*

Department of Physiology, College of Medicine, The Catholic University of Korea, Seoul, Korea

S 81 A02-15

Magnetothermal brain stimulation modulates synaptic plasticity of the primary somatosensory cortex in adult mice

Minhee Jeong[1], Hohyeon Kim[2], Ji-Hyun Jeong[3], Ji-Woong Ahn[3], YoungJi Kwon[1], Soonyong Kwon[1], Seungjun Oh[2], Jungwon Yoon[2], Seungsoo Chung[1]

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P03: Electrophysiology and Ion channel

S 81 B02-01

Convergence of gustatory and visceral input on parabrachial neurons

Young-Kyung Cho[1,2], Ki-Myung Chung[1,2], Kyung-Nyun Kim[1,2]

[1]Department of Physiology & Neuroscience, College of Dentistry, and [2]Research Institute of Oral Science, Gangneung-Wonju National University

S 81 B02-02

The role of presynaptic plasticity at PF-PC synapse on OKR training

Hojeong Lee[1,2], Yong-seok Lee[1,2], Sang Jeong Kim[1,2,3]

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S 82 B02-03

Calcium homeostasis modulator 2 (Calhm2) is the voltage-dependent slowly activating large-pore channel in murine microglia BV2 cells

Si Won Choi[1,2], Kyoung Sun Park[2], Sung Joon Kim[1,2]

[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Wide River Institute of Immunology, Seoul National University College of Medicine, Hongcheon, Korea

S 82 B02-04

Role of the STING-IRF3 pathway in ambient GABA homeostasis and cognitive function

Ramesh Sharma[1,2], Chiranjivi Neupane[1,2], Fei Fei Gao[3], Thuy Linh Pham[2], Yoo Sung Kim[4], Bo-Eun Yoon[4], Eun-Kyeong Jo[5], Kyung-Cheol Sohn[6], Gang Min Hur[6], Guang-Ho Cha[3],Sun Seek Min[7], Cuk-Seong Kim[2], Jin Bong Park[1]*

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S 82 B02-05

STING-IRF3 pathway regulating GABA transporter 1 expression in the spinal cord

Ramesh Sharma[1,2], Thuy Linh Pham[2], Chiranjivi Neupane[1,2], Feifei Gao[3], Guang-Ho Cha[3], Gang Min Hur[4], Hyunjin Kim[5], Min-Ho Nam[5], Sunjung Yang[1], So Yeong Lee[1], Hyun Woo Kim[2], Jin Bong Park[1]*

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S 82 B02-06

Protective effect of tomatidine in isoproterenol-induced cardiac hypertrophy model

Seung Hak Choi[1], Jessa Flores[1], Maria Victoria Faith Valenzuela Garcia[1], Pham Trong Kha[1], Hyoung Kyu Kim[1], Jin Han[1], Jae Ho Kim[2], Jae Boum Youm[1]*

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S 83 B02-07

Inhibition of voltage-dependent K^+ currents by second-generation antipsychotic paliperidone in coronary arterial smooth muscle cells

Junsu Jeong, Won Sun Park

Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 83 B02-08 The second-generation antipsychotic lurasidone inhibits the voltage-dependent K+ channels in coronary arterial smooth muscle cells
Wenwen Zhuang, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 83 B02-09 Unique responses of fixed stoichiometric TRPC1-TRPC5 concatemer to G proteins
Hana Kang[1], Insuk So[1,2*]
[1]Department of Physiology and Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea, [2]Institute of Human-Environment Interface Biology, Seoul National University, Seoul, Korea

S 83 B02-10 Blockade of voltage-gated K^+ channels of rabbit coronary arterial smooth muscle cells by the antipsychotic drug zotepine
Wenwen Zhuang, Minju Park, Junsu Jeong, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 84 B02-11 Inhibition of voltage-dependent K+ channels in rabbit coronary arterial smooth muscle cells by the atypical antipsychotic agent sertindole
Junsu Jeong, Wenwen Zhuang, Minju Park, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 84 B02-12 Second-generation antipsychotic quetiapine blocks voltage-dependent potassium channels in coronary arterial smooth muscle cells
Wenwen Zhuang, Minju Park, Junsu Jeong, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 84 B02-13 Inhibitory mechanisms of aripiprazole on voltage-gated potassium channels in rabbit coronary arterial smooth muscle cells
Junsu Jeong, Wenwen Zhuang, Minju Park, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 85 B02-14 Cryo-EM Structure-Based Investigation of Stoichiometry and Ion Permeability of TRPC1/C4 heteromer
Jinhyeong Kim[1,7], Jongdae Won[2,4,7], Jinsung Kim[1,5,7], Juyeon Ko[1,6], Christine Haewon Park[1,6], Byeongseok Jeong[1], Sang-Eun Lee[1], Hyeongseop Jeong[3], Sun-Hong Kim[2], Hyunwoo Park[2], Insuk So[1*], Hyung Ho Lee[2*]
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P04: Muscle Physiology

S 85 C02-01 DPP-4 inhibitor antidiabetic anagliptin relaxes the rabbit aorta via activation of SERCA pump and Kv channels
Minju Park, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 85 C02-02 The antidiabetic drug teneligliptin induces vasodilation via activation of PKG, Kv channels, and SERCA pumps in aortic smooth muscle
Minju Park, Junsu Jeong, Wenwen Zhuang, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

S 86 C02-03 Vasorelaxant mechanisms of ipragliflozin by activating a Kv channel, the SERCA pump, and the PKA signaling pathway in rabbit femoral artery
Minju Park, Junsu Jeong, Wenwen Zhuang, Won Sun Park
Department of Physiology, Kangwon National University School of Medicine, Chuncheon, Korea

P05: Heart, Respiratory and Circulatrory system

S 86 D02-01 Effects of H2S on Cardiac Mitochondrial Function in STZ-Induced Type 1 Diabetic Rats
Tong Su[1], Li Han Zhu[2], Yin Hua Zhang[1,2*]
[1]Department of cardiovascular, Yanbian University Medical School, [2]Department of Physiology & Biomedical Sciences, Seoul National University College of Medicine

S 86 D02-02 Enhanced Brugada Syndrome Phenotype Driven by Increased Transient Outward K+ Current Due to SCN5A-p.A385T/R504T Mutations
Na Kyeong Park[1], Seong Woo Choi[3#], Sung Joon Kim[1,2#]
[1]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Physiology & Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Physiology, Dongguk University College of Medicine, Gyeongju, Korea

S 86 D02-03 Finasteride prevents neointimal hyperplasia and affects vascular smooth muscle cells proliferation, migration, and apoptosis.
Jeongsook Kim[1], Kyungmi Kim[1], Nishani Jayanika Jayathilake[1], Beno Ramesh Nirujan[1], Kyu Pil Lee[1*]
[1]Department of Physiology, College of Veterinary Medicine, Chungnam National University, Daejeon, Korea

S 87 D02-04 The Role of Sex Hormones in Modulating Cardiac Health Under Normal Physiological Conditions: Insights from the UK Biobank.
Zheng Gong[1], Ling Li[1], Joseph Adu-Amankwaah[2], Lu Fu[2], Hong Sun[2], Yinhua Zhang[1]*
[1]Department of Physiology, College of Medicine, Seoul National University, Seoul, Korea, [2]Department of Physiology, Xuzhou Medical University, Xuzhou, Jiangsu, China

S 87 D02-05 Mutations in KCNE1 promote cardiac alternans in Long QT Syndrome Type 5 rabbits
Tae Yun Kim[1,9,10], Anatoli Y. Kabakov[1], Radmila Terentyeva[2], Dmitry Terentyev[2], Peter Bronk[1], YiChun Lu[1], Cao Thach Tran[1], Allison Navarrete-Welton[1], Katja E. Odening[3], Xuwen Peng[4], István Baczkó[5], András Varró[5,6], Zsuzsanna Bősze[7], Zhilin Qu[8], Gideon Koren[1], Bum-Rak Choi[1]
[1]Cardiovascular Research Center, Cardiovascular Institute, Rhode Island Hospital and Alpert Medical School of Brown University, Providence, RI, USA, [2]Physiology Cell Biol, Dorothy M. Davis Heart and Lung Research Institute, College of Medicine, The Ohio State University, Columbus, OH, USA, [3]Translational Cardiology, Department of Cardiology, Inselspital, Bern University Hospital and Institute of Physiology, University of Bern, Bern, Switzerland, [4]Department of Comparative Medicine, Pennsylvania State University College of Medicine, Hershey, PA, USA, [5]Department of Pharmacology & Pharmacotherapy, University of Szeged, Szeged, Hungary, [6]Department of Pharmacology & Pharmacotherapy, University of Szeged, and HUN-REN Research Group of Cardiovascular Pharmacology, Szeged, Hungary, [7]Precision breeding group, Animal Biotechnology Department, Institute of Genetics and Biotechnology, Hungarian University of Agriculture and Life Sciences, Gödöllő, Hungary, [8]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA, USA, [9]Department of Physiology, Asan Medical Center and University of Ulsan College of Medicine Seoul, Korea, [10]Department of Physics and The Institution of Basic Science, Korea University, Seoul, Korea

S 88 D02-06 Short term effects of furosemide on the target organ damage in Angiotensin II-induced hypertensive rats
Jun Xian Liu, Yin Hua Zhang*
Department of Physiology & Biomedical Sciences, Seoul National University College of Medicine, South Korea

S 88 D02-07 Transcriptional Landscape of hiPSC-derived Cardiomyocytes in Hypertrophic Cardiomyopathy: Insights from Comparative Analysis of GSE89714
Daewoon Yoon[1]*, Moonyoung Lee[2]*, Jungmin Choi[2]**, Jinkyu Park[1]**
[1]Department of Physiology, College of Medicine, Hallym University, Chuncheon, Korea, [2]Department of Biomedical Sciences, College of Medicine, Korea University, Seoul, Korea

S 88 D02-08 CRIF1 Deficiency Improved Homocysteine Production by Disrupting Dihydrofolate Reductase Expression in Vascular Endothelial Cells
Minsoo Kim[1,2], Shuyu piao[1], Seonhee Kim[1], GiangHuong Vu[1,2], Cuk-Seong Kim[1,2]
[1]Department of Medical Science, Chungnam National University, [2]Brain Korea 21 FOUR Project for Medical Science, Chungnam National University

P06: Endocrine and Energy Metabolism

S 89 E02-01 TRPC6 as a Defining Marker of Adipogenic Pericytes Driving Adipose Tissue Function and Systemic Metabolism
Phan Anh Nguyen[1,2,3,4], Kyu-Hee Hwang[1,2,3,4], Duyen Tran Thi Thuy[1,2,3,4], Kyu-Sang Park[1,2,3,4], Seung-Kuy Cha[1,2,3,4]
[1]Department of Physiology, [2]Department of Global Medical Science, [3]Organelle Medicine Research Center, and [4]Institute of Mitochondrial Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

S 89 E02-02 Unraveling the Molecular Pathways of Obesity-Driven Insulin Resistance: The Role of NEDD4-2 in Regulating Calcium Homeostasis
Ok-Hee Kim, Hyung-Oh Gu, Jin-Wook Lee, Hansol Rhu, Hyun Jung Ahn, Byung-Chul Oh
Lee Gil Ya Cancer and Diabetes Institute, Gachon University, College of Medicine, Department of Physiology, Incheon, Korea

S 89 E02-03 Pharmacological Approaches to Insulin Resistance: The Impact of Angiotensin II Receptor Blockers on Intracellular Ca^{2+} Dysregulation
Seung Wan Noh, Bayaraa Amgalan, Yeon Ju Kim, Han-Sol Rhu, Ok-Hee Kim, Byung-Chul Oh
Lee Gil Ya Cancer and Diabetes Institute, Gachon University, College of Medicine, Department of Physiology, Incheon, Korea

S 90 E02-04 Alterations in Adipose Tissue and Adipokines in Heterozygous APE1/Ref-1 Deficient Mice
Hao Jin[2,3]*, Eun-Ok Lee[1,3]*, Sungmin Kim[2,3], Hee Kyoung Joo[1,3], Yu Ran Lee[1,3], Soo Yeon An[2,4], Shuyu Piao[1,3], Kwon Ho Lee[5], Byeong Hwa Jeon[1,2,3]
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P07: Epithelium and Exocrine physiology

S 90 F02-01 Mechanical Stimulation-Induced ATP Release: A Key Mediator of Paracrine Signaling in MCC13 Cells
Mi Seon Seo[1], Ntigura Eustache[1], Kyung Chul Shin[2], Jin Ryeol An[1], Hye Ryeong Lee[1], Solah Park[1], Yeji Lee[1], Sang Woong Park[2], Young Min Bae[1]
[1]Department of Physiology, KU Open Innovation Center, Research Institute of Medical Science, Konkuk University School of Medicine, Chungju, Korea, [2]Neurological Disorders Research Center, Qatar Biomedical Research Institute (QBRI), Hamad Bin Khalifa University (HBKU), Qatar Foundation, Doha, Qatar, [3]Department of Emergency Medical Services, Eulji University, Seongnam, Korea

S 90 F02-02 Genetic suppression of mitochondrial Ca^{2+} uniporter prevents podocyte ferroptosis and glomerulosclerosis
Suyeon Choi[1,2,3], Kyu-Sang Park[1,2,3]
[1]Department of Physiology, [2]Organelle Medicine Research Center, [3]Department of Global Medical Science, Yonsei University Wonju College of Medicine, Wonju, Korea

S 91 F02-03 c-Jun N-terminal kinase as a therapeutic target for glomerulosclerosis in chronic kidney diseases
Suyeon Choi[1,2,3], Soo-Jin Kim[1,2,3], Jung-Mi Hah[4], Kyu-Sang Park[1,2,3]
[1]Department of Physiology, [2]Organelle Medicine Research Center, [3]Department of Global Medical Science, Yonsei University Wonju College of Medicine, Wonju, Korea, [4]College of Pharmacy, Hanyang University, Ansan, Korea

P08: Inflammation and Immune physiology

S 91 G02-01 Oxidative stress and inflammatory responses induced by fine particulate matter in bone marrow-derived macrophages
Septika Prismasari, Hye Young Mun, Jung Yun Kang*
Department of Dental Hygiene, College of Software and Digital Convergence, Yonsei University, Korea

P09: Cellular Physiology and Cancer

S 91 H02-01 The Role of Ei24 in Modulating Calcium Homeostasis Through Interaction with STIM1 and CRAC Channel
Duyen Tran Thi Thuy[1,2,3,4], Phan Anh Nguyen[1,2,3,4], Subo Lee[1,2,3,4], Kyu-Hee Hwang[2,3,4], Ji-Hee Kim[5], Kyu-Sang Park[1,2,3,4], Seung-Kuy Cha[1,2,3,4]
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S 91 H02-02 Combining CYP2J2 inhibition with immune checkpoint blockade for enhanced liver cancer therapy
Yanling Wu, Soo Mi Kim*
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S 92 H02-03 Activation of TMEM16E scramblase induces ligand-independent growth factor receptor signaling and macropinocytosis for membrane restructuring.
Jung-Eun Kim[1], Woori Ko[1], Siwoo Jin[2], Jin-Nyeong Woo[1], Yuna Jung[1], Inah Bae[1], Han-Kyoung Choe[1], Daeha Seo[2], Bertil Hille[3], Byung-Chang Suh[1]*
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S 92 H02-04 Collagen triple helix repeat containing 1 as a key regulator of esophageal cancer progression
Yao Li, Soo Mi Kim*
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S 92 H02-05 Suppression of p21-activated kinase -4 enhances CD274 downregulation in liver cancer
Yuyan Wang, Soo Mi Kim*
Department of Physiology, Institute for Medical Sciences, Jeonbuk National University Medical School, Jeonju, Korea

S 92 H02-06 Senicapoc suppresses TGF-b1-induced metastasis in head and neck squamous cell carcinoma (HNSCC) by blocking KCa3.1 channels
Nhung Thi Hong Van, Joo-Hyun Nam
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S 93 H02-07 The role of recombinant human bmp-2 in colorectal cancer suppression and its safety in surgical applications
Hua Xin Zhao, Soo Mi Kim*
Department of Physiology, Institute for Medical Sciences, Jeonbuk National University Medical School, Jeonju, Korea

S 93 H02-08 Discovery of a novel natural compound, vitekwangin B, with ANO1 protein reduction properties and anticancer potential
Yohan Seo[1], Raju Das[2], Armin Sultana[2], JooHan Woo[2,3,4]
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S 93 H02-09 Potentiating doxorubicin efficacy in colorectal cancer through inhibition of the Akt/GSK3β/mTOR-SREBP1 pathway via HDAC inhibition
Hua Xin Zhao, Soo Mi Kim*
Department of Physiology, Institute for Medical Sciences, Jeonbuk National University Medical School, Jeonju, Korea

S 93 H02-10 Phosphate impacts mitochondrial stress and Ca2+-based filtration in podocytes
Bao T.N. Dang[1,2,3,4], Phan Anh Nguyen[1,2,3,4], Ji-Hee Kim[1,2,3,4], Kyu-Sang Park[1,2,3,4], Seung-Kuy Cha[1,2,3,4]
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S 94 H02-11 Mechanistic elucidation of Genistein targeting lung cancer through network pharmacology and molecular dynamics simulation studies
Raju Das[1], JooHan Woo[1,2,3]
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S 94 H02-12 The Effect of MLN4924 inhibition on IκB-α expression in Renal cell cancer
Yeseon Son[1], Jun Bum Park[2], Yang-Sook Chun[1,2]*
[1]Department of Biomedical Sciences, Ischemic/Hypoxic Disease Institute, [2]Department of Physiology, Seoul National University College of Medicine, Seoul, Korea

S 94 H02-13 Fulvic acid inhibits differentiation of 3T3-L1 adipocytes through activating Ca^{2+} / CaMKII / AMPK pathway
Hyeon Yeong Ju[1],Seung-Eun Song[1], Su-Kyung Shin[2], Ho-Chan Cho[3], Jae-Hoon Bae[1], Seung-Soon Im[1], Dae-Kyu Song[1]*
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S 95 H02-14 Conditioned medium from reprogramed cancer-associated fibroblasts by apoptotic cancer cells inhibits tumor growth in mice via WISP-1 signaling
Kyungwon Yang*, Shinyoung Kim, Jihee Lee Kang
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S 95 H02-15 Interaction between cancer-associated fibroblasts and apoptotic cancer cells suppresses lung cancer cell growth through WISP-1-integrin αvβ3-STAT1 signaling pathway
Kiyoon Kim*, Shinyoung Kim*, Kyungwon Yang, Hee Ja Kim, Da Young Kim, Jihee Lee Kang
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P10: Exercise and Integrative physiology

S 95 I02-01 Regular exercise increases in NAD+ levels in the skeletal muscle and the brain of aging mice
Jimmy Kim[1], Ko Yamanaka[1], Hidefumi Waki[1,2]
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P11: Physiome and Systems Biology

S 95 J02-01 Distributed processing for value-based choice by prelimbic circuits targeting anterior-posterior dorsal striatal subregions in male mice
Kyuhyun Choi[1†], Eugenio Piasini[2,4†], Edgar Díaz-Hernández[1], Luigim Cifuentes-Vargas[1,3], Nathan T. Henderson[1], Elizabeth N. Holly[1], Manivannan Subramaniyan[1], Charles R. Gerfen[5], Marc V. Fuccillo[1*]
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P14: Environmental Physiology and Thermoregulation

S 96 K02-01 Impact of thermotherapy-induced orexin and dopamine changes on metabolic health in postmenopausal obese women
You-jeong Nam[1], Seung-hyun Na[1,2], Sim-sung Kim[1], Jin Kim[2], Young-hyun Jung[2], Jeong-beom Lee[1,2*]
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S 96 L02-01 How do blood pressure medications affect the autonomic nervous system in hypertensive patients? – Using QSART
Sim-sung Kim[1], Kang-soo Cho[1,2], In-ho Lee[3], Sang-hee Hong[4], Jin Kim[2], Young-hyun Jung[2], Jeong-beom Lee[1,2,4*]
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S 97 L02-02 Exploring the efficacy of music therapy in ameliorating depression and sleep disturbances in adolescents with ADHD during the COVID-19 pandemic
Jong-In Park[1], Seunghyun Lee[1], Eon-Ah Choo[1,3], Sim Sung Kim[1,2], You-Jeong Nam[1,2], Mun Jeong Kim[3], Jeong-Beom Lee[1,2,3]
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P15: Others

S 97 M02-01 Metabolite Profiling Using UPLC-QTOF-MS for the Evaluation of Laser Acupuncture in Arthritis
Seung-Ho Seo, Yang Hee You, Chang Su Na
Departments of Korean Medicine, Dongshin University, Naju, Korea

S 97 M02-02 GC-MS-Based Metabolomic Profiling to Assess the Therapeutic Effects of Moxibustion on Obesity
Seung-Ho Seo, Yang Hee You, Chang Su Na
Departments of Korean Medicine, Dongshin University, Naju, Korea

Plenary Lecture

PL-1

Oxygen and acid sensing by arterial chemoreceptors

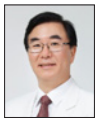
Donghee Kim
Chicago Medical School/RFUMS, USA

Glomus (Type 1) cells in the carotid body serve as peripheral chemoreceptors that sense blood pO_2 and pH (hence pCO_2). These cells convert the chemical stimuli to electrical and Ca^{2+} signals, which regulate the secretion of transmitters that bind receptors expressed at the afferent carotid sinus sensory nerve endings. The carotid sinus and glossopharyngeal nerves carry the impulse to the cardiorespiratory center in the brainstem to regulate ventilation as well as autonomic outflow. Thus, the arterial chemoreceptor reflex ensures that normal blood gas levels are maintained. The cellular mechanism by which changes in pO2 and pH control the secretory activity of glomus cells is complex, involving mitochondria, ion channels and Ca^{2+} signaling. Here we discuss our recent work on these processes that occur within glomus cells. **Ion channels:** Following the early finding that the background K+ channel (TASK: K2P3/9) is sensitive to both hypoxia and acid, Kv and non-selective cation channels were found to participate in the modulation of hypoxia and acid sensing. The role of TASK and other ion channels is discussed. **Ca^{2+} signaling:** Our recent studies have identified spontaneous Ca^{2+} oscillations in glomus cells under basal conditions. Ca^{2+} oscillations required Ca^{2+} influx via L- and T-type Ca^{2+} channels. Oscillations in cell membrane potential (Em) with dependence on Ca^{2+} influx were also identified, suggesting a functional link between cell Em and Ca^{2+} oscillations. We discuss the role of cell Em oscillation as the trigger of Ca^{2+} influx that modulates ER Ca^{2+} release and uptake, which that are associated with Ca^{2+} oscillations. We discuss how hypoxia and acidosis modulate these processes. **Hypoxia-mitochondria-TASK signaling:** Acid inhibits TASK directly by modifying the histidine residues of the protein. In contrast, hypoxia inhibits TASK indirectly via a signal or signals generated from mitochondria. Several molecules (ROS, CO, AMPK, H2S) have been proposed as putative hypoxia signals, but we found no evidence for their role in chemoreception. Using a bioassay, we are testing the possibility that hypoxia decreases [ATP] near the plasma membrane to reduce the activity of TASK that is sensitive to cytosolic [ATP]. We discuss our preliminary findings.

Keywords: Arterial chemoreception, Carotid body, Hypoxia, Acidosis, Ion channels

PL-2

Impairment of homeostasis in neurodegenerative diseases: from bench to clinical trials



Seung Hyun Kim
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Neurodegenerative diseases such as Alzheimer's disease (AD), Amyotrophic Lateral Sclerosis (ALS), Frontotemporal Dementia (FTD), and Parkinson's disease (PD) are influenced by factors like aging, oxidative damage, environmental elements, high-risk genes, and excitotoxicity. Disruptions in ribonucleostasis, proteostasis, immune-inflammatory regulation, and the microbiome also play critical roles in disease pathogenesis and progression. This presentation will discuss serial research topics have conducted over the past 20 years in the field of neurodegenerative diseases including, ALS, AD, and FTD. Key topics will cover the contents from basic research to translational studies and development of therapeutic strategies, focusing on evidence and/or biomarker-based stratified and personalized medicine to restore the function of molecular targets responsible for impaired homeostasis.

Key topics include:

Genetico-Clinical Characteristics of Korean ALS Cohort: Necessity of Stratified and Precision Medicine

Impaired Stress Granule and Phase Transition Dynamics in Protein Misfolding Diseases. Pathogenic mutations of RNA/DNA binding proteins and impairment of phase transition dynamics resulting in Protein misfolding and their potential as therapeutic targets.

Development of Biomarkers for Theragnosis in Neurodegenerative Diseases (AD, ALS, FTD) Discussing our progress in identifying biomarkers to improve diagnostic precision and therapeutic strategies using cell model.

Clinical Application of Cell Therapy for ALS Detailing the translational journey and clinical potential of cell therapy for ALS.

Future Directions for Basic, Translational, and Clinical Research Outlining future research pathways to advance understanding and treatment of neurodegenerative diseases.

This presentation aims to provide a concise overview of our research and its implications for restoring homeostasis in neurodegenerative diseases, emphasizing the translational journey from bench to clinical application

Keywords: Homeostasis, Neurodegnerative diseases, Biomarkers, Therapeutic strategy

Symposia 1. Hypothalamic regulation of body energy homeostasis

S-1-1

Hypothalamic function of IRX3 and IRX5, genetic determinants of human obesity

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Obesity is primarily attributed to excessive food intake. IRX3 and IRX5 have been identified as genetic determinants of obesity, linked to the intronic variants of FTO, which are among the most significant risk factors for human obesity. However, the mechanisms by which these genes influence obesity through changes in food intake remain elusive. My research, utilizing mouse genetics and single-cell genomic analysis techniques, has elucidated the roles of IRX3 and IRX5 as genetic regulators of food intake and hypothalamic neurogenesis: 1) Determines the gene dosage of Irx3 and Irx5 is crucial for the hypothalamic leptin response and the regulation of feeding. 2) Identifies a novel population of radial glia-like neural stem cells in the early postnatal hypothalamus of mice that exhibits predominant expression of Irx3/5. 3) Demonstrates that conditional deletion of both Irx3 and Irx5 in these cells leads to an improved leptin response and enhanced postnatal hypothalamic neurogenesis. Given the association of FTO obesity-risk alleles with increased energy intake in human obesity, my research offers unprecedented mechanistic insights into the genetic control of hypothalamic neurodevelopment in the context of human obesity.

Keywords: Obesity, IRX3/5, Hypothalamus, Feeding control, Neurogenesis

S-1-2

Novel hypothalamic mechanisms for orexin-induced feeding

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Orexin (or hypocretin) is a hypothalamic neuropeptide that regulates wakefullness and appetite. While it was initially suggested that orexin promotes feeding by the hypocretin receptor (Hcrtr) expressed by hypothalamic neurons, the identity of responsible neural circuits still remain to be identified. In particular, Hcrtr2 is highly expressed by the anorexigenic pro-opiomelanocortin (POMC) neurons, but the role of Hcrtr2 expressed by POMC neurons remains unclear. In this study, we investigated the neural mechanisms for orexin-induced hyperphagia. We used multiple approaches including patch-clamp electrophysiology, immunohistochemistry, and *in vivo* feeding studies to gain insight into the neuronal circuits responsible for the orexigenic effects of orexin A. We found that applications of orexin A directly depolarize a distinct subpopulation of POMC neurons. In addition, *in vivo* experiments demonstrated that Hcrtr2 expressed by the POMC neurons is responsible for the orexigenic effects of orexin A. We also identified the neural circuit downstream of POMC neurons and found evidence that opioid receptors are involved in the effects of orexin A. Together, our findings demonstrate that orexin A increases food intake via the activation of a distinct subpopulation of arcuate POMC neurons and the downstream neural circuits.

Keywords: POMC neuron, Beta-endorphin, Opioid receptor, Patch-clamp technique, Heterogeneity

S-1-3

Hypothalamic neural stem cells in aging

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The hypothalamus is the brain region that regulates systemic body metabolism and multiple functions in other brain regions. In adult mice, the hypothalamus harbors neural stem/precursor cell (NSC)-like cells. Along with the dysregulation of body metabolism and physiology that occurs during aging, the NSC population in the hypothalamus declines with age. Here, we introduce a novel protocol that yields scalable and storable hypothalamus-specific NSCs (htNSCs) from hypothalamus-like organoids derived from human pluripotent stem cells (hPSCs). Implanting htNSCs into the medio-basal hypothalami of aged mice conspicuously ameliorated age-related declines in metabolic fitness, physical capacity, and cognitive function and produced corresponding histologic changes in various body tissues. Single transcriptome and immunohistochemical analyses of the grafted hypothalamic tissues showed that the anti-aging effects were attained by correcting glial NF-κB, TNFα, and NLRP3 inflammasome pathways. Collectively, our findings support the potential of anti- or healthy aging therapies that target htNSCs and hypothalamic inflammation.

Keywords: Neural stem cells, Aging, Exosomes, Hypothalamus, Neuro-immunity

Symposia 2. Progress, Challenges and Prospects in Gene Editing

S-2-1

A novel approach using CRISPR-ribonucleoprotein packaged in virus-like particles to generate genetically engineered mouse models

Kyoungmi Kim
Korea University College of Medicine, Republic of Korea

Genetically engineered mouse models (GEMMs) occupy an essential part of research on the causes and treatment of diseases, as well as basic research. Although the production of animal models has been greatly simplified since the development of CRISPR gene editing technology, it is still difficult and limited. Here, we achieved targeted mutagenesis by culturing embryos with virus-like particle (VLP)-based gene editing ribonucleoproteins (RNPs) without any other physical stimulations, presenting it as the CRISPR-VLP-induced targeted mutagenesis (CRISPR-VIM) method. We generated *Plin1*- and *Tyr*-knock-out mice through VLP-based SpCas9 or adenine base editor (ABE)/sgRNA RNPs and identified their phenotype and germline transmission. Additionally, we demonstrated cytosine base editor (CBE)/sgRNA-based C-to-T substitution or SpCas9/sgRNA-based knock-in using VLPs. This method further simplifies and accelerates GEMM generation without specialized techniques or equipment. Consequently, the CRISPR-VIM method can facilitate mouse modeling and be applied in various research fields.

Keywords: CRISPR-ribonucleoproteins (CRISPR-RNPs), Virus-like particles (VLPs), Genetically engineered mouse models (GEMMs), CRISPR-VLP-induced targeted mutagenesis (CRISPR-VIM) method

S-2-2

Mitochondrial genome editing

Hyunji Lee
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Mitochondria is of fundamental importance in programmed cell death, cellular metabolism, and intracellular calcium concentration modulation. Within the mitochondria there is DNA with genetic information important for mitochondrial function called mitochondrial DNA (mtDNA). Inherited mitochondrial disorders via mtDNA mutation cause several diseases in various organs and systems. Nevertheless, mtDNA editing, which plays an essential role in the treatment of mitochondrial disorders, still faces several challenges. Therefore, the development of animal models or treatments for mitochondrial genetic diseases has been quite limited.
Recently, programmable editing tools such as cytosine base editors derived from DddA (DdCBE), transcription activator-like effector (TALE)-linked deaminases (TALED) for mtDNA base editing have emerged with considerable potential for correcting pathogenic mtDNA variants.
I describe recent advances in this field, including structural biology and repair mechanisms, and introduce the advanced strategies required to apply mtDNA base editors to mice and a mitochondrial DNA editing mouse model created using them. These mice are associated with human mitochondrial genetic disorders (Leigh syndrome, MELAS, LHON-MELAS overlap syndrome).
Also, I report that A-to-G-editing TALEDs but not C-to-T-editing DdCBEs induce tens of thousands of transcriptome-wide off-target edits in human cells. To avoid these unwanted RNA edits, I engineered the substrate-binding site in TadA8e, the deoxy-adenine deaminase in TALEDs, and created TALED variants with fine-tuned deaminase activity. The engineered TALED variants not only reduced RNA off-target edits by >99% but also minimized off-target mtDNA mutations and bystander edits at a target site. Unlike wildtype versions, our TALED variants were not cytotoxic and did not cause developmental arrest of mouse embryos.
Ultimately, the potential medical applications and disease modeling of mtDNA editing for the treatment of mitochondrial diseases are discussed.

Keywords: Mitochondrial diseases, MtDNA, Mitochodria, DdCBE, TALED

S-2-3

A functional genomics approach to map extracellular interactions

Hunsang Lee
Korea University

Part 1. Identification of a host receptor for C.sordelli lethal toxin TcsL
Clostridium sordellii lethal toxin (TcsL) is responsible for an almost invariably lethal toxic shock syndrome associated with gynecological *C. sordellii* infections. Here, using CRISPR/Cas9 screening, we identify semaphorins SEMA6A and SEMA6B as TcsL receptors. We show with cryo-EM that TcsL uses the same interface to bind SEMA6A that the highly related *C. difficile* TcdB toxin uses to bind Frizzled receptors. Remarkably, reciprocal mutations in this evolutionarily divergent surface are sufficient to switch receptor specificity between the toxins. We also demonstrate that soluble SEMA6A fragment can protect mice from TcsL-induced edema, validating the physiological role of SEMA6A in toxic shock syndrome and highlighting a potential strategy to block this otherwise untreatable lethal disease.
Part 2. Development of a novel high-throughput receptor-ligand interaction platform.
It is estimated that cells encode for about 3,000 secreted proteins and 2,500 cell surface receptors. Many of secreted proteins act as signaling molecules, such as hormones, growth factors, and other autocrine/paracrine factors. In particular, stem cell secretes many proteins with regeneration capacity. These factors act by triggering a signaling cascade once bound by a cell surface cognate receptor on a target cell. Intuitively, to understand mechanisms underlying these biological processes, secreted proteins need to be paired to their cognate receptors. What is more, it is also a critical step in designing therapeutics, with about 60% of drugs targeting cell surface receptors. However, there are no easily scalable methods for studying receptor/ligand interactions in an unbiased fashion and consequently, a substantial fraction of receptors and ligands remain orphans.
Here, we established a high-throughput receptor-ligand screening platform by combining exotoxin-based fusion protein toxins with genome-scale/cell surfaceome-scale CRISPR-Cas9 screens. The rationale was to generate a recombinant toxin with its native receptor-binding domain replaced with a secreted ligand and utilize it to treat a genome-wide/cell surfaceome-wide pool of knockout cells generated by CRISPR-Cas9. Cells that lack the cognate receptor conferred resistance to the recombinant toxin treatment and identified by next-gen sequencing. Moreover, screens also revealed receptor maturation factors required for their cell surface expression. The developed screening platform is currently being used to systematically decode the extracellular receptor-ligand interaction network.

Keywords: CRISPR screening, Ligand-receptor, Toxins

S-2-4

Controlling and Visualizing Molecualr and Cellular Behavior in Living Cells and Animals

Won Do Heo
KAIST, Republic of Korea

My group has developed various synthetic phase separation tools and optogenetic technologies for visualizing and controlling diverse molecules in live cells and animals. Synthetic phase separation tools were applied to monitor protein-protein interactions. We found synthetic phase separation tools were very powerful and sensitive to discovering many meaningful unknown protein-protein interactions. These provided new insights into understanding cell signalling to induce specific cellular processes. Our optogenetic tools, based on mostly plant light sensing elements, allow finely manipulated molecules and cells in a spatial and temporal resolution. We are applying the new technologies to study the spatiotemporal roles of signalling proteins and second messengers in living cells and the mouse brain. For example, we developed ultra-light-sensitive optogenetic Ca^{2+} modulators named OptoSTIM1 and monSTIM1, encompassing engineered cryptochrome2 for manipulating Ca^{2+} signalling in the brain of awake mice. With an mRNA-modulating optogenetic tool called mRNA-LARIAT, light induces the sequestration of specific exogenous or endogenous mRNAs into large protein clusters, altering mRNA localization and interfering with translation by limiting the ribosome interaction with trapped mRNA. Our ultimate goal is to provide new paradigms for future therapeutics through our optogenetics. I will talk about new approaches in cell biology studies and new strategies for therapeutics for neuronal diseases through remotely and non-invasively delivered light.

Keywords: Optogenetics, MRNA therapy, Bioimaging, Cas13, Calcium

Symposia 3. Innovative new drug development : Basic infrastructural technologies for successful drug development and application of latest technologies in drug screening provided by K-MEDI hub

S-3-1

Small molecules, big discoveries: accelerating drug development with DNA-encoded library screening

Hyewon Seo
K-MEDI Hub, Republic of Korea

DNA-encoded library (DEL) technology has revolutionized drug development due to its broad chemical space coverage, streamlined screening methods, and rapid analysis capabilities. Originating from a seminal work by Brenner and Lerner in the 1990s, which proposed DNA as an encoding tool for chemicals, the real breakthrough came with GSK's groundbreaking report in 2009, demonstrating the practical application of DEL in drug discovery.
Since then, numerous Contract Research Organizations (CROs) have emerged, offering DEL services with diverse business models. These services have undergone significant technical advancements, enhancing the efficiency and effectiveness of DEL screening. In this presentation, we delve into a novel DEL strategy targeting proteins. This includes discussing fragment-based DEL, covalent library approaches, and other focused library concepts aimed at quickly discovering potent hit molecules.
Furthermore, we showcase our recent progress in establishing K-DEL services, marking the introduction of the first public DEL screening service in Korea. Through our endeavors, we aim to bridge the gap between innovative DEL methodologies and practical drug development needs.
In conclusion, DEL technology stands as a cornerstone in modern drug discovery, offering unparalleled opportunities for exploring vast chemical spaces and accelerating hit identification. The evolution of DEL methodologies, coupled with the establishment of accessible screening services like K-DEL, heralds a new era of innovation in drug development. By leveraging these advancements, we pave the way for the discovery of next-generation therapeutics with accelerated development and improved efficiency, ensuring faster access to effective treatment.

Keywords: DNA-encoded library, DEL, Hit identification, Screening methods, K-DEL

S-3-2

Development of human pluripotent stem cell-derived organoids for preclinical studies

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Generally, preclinical models have favored simple, high-throughput in vitro assays and small animal *in vivo* models. Preferring these methods over complex models is due to the need to evaluate millions of potential compounds and the lack of ability to replicate complex human tissue properties *in vitro* at large scale. Consequently, findings from these models have limited applicability to human biology, often leading to expected results that may differ from those observed in human *in vivo* studies. Therefore, there is a need for advances in preclinical models for rapid and accurate drug evaluation. Since the beginning of human pluripotent stem cells (hPSCs)-based studies, there have been many efforts to apply hPSCs for research in a variety of fields, including drug discovery. While hPSC-based differentiated 2D cultures offer simplicity in cultivation and scalability for conducting high-throughput and high-content settings, they lack the diverse cell types and their cell-cell interactions of 3D architecture. To overcome the shortcomings of 2D culture, significant efforts have been made for the development of 3D organoids, which mimic the structure and function of organs. Today, hPSC-derived organoids are a powerful tool for chemical screening and facilitate pre-clinical and clinical discovery due to their capacity to recapitulate a key aspects of human physiology and pathology within a controlled *in vitro* setting. Moreover, organoids can be easily scaled up, rendering them suitable systems for performing high-throughput studies in drug discovery. We have developed robust protocols for differentiating hPSC into three-dimensional organoids such as heart, liver, and blood vessel. These organoids displayed structural and functional resemblance to human tissues. Then, we assessed safety testing using normal heart and liver organoids and efficacy testing models using liver disease models such as non-alcoholic steatohepatitis (NASH). Our organoid-based findings indicated the promise of human heart and liver organoids as a versatile platform for advancing preclinical studies.
In this presentation, I will introduce our comprehensive research findings on the ongoing development of organoid models at K-MEDIhub, as well as show their potential application as non-clinical testing platform.

Keywords: Human pluripotent stem cell, Organoid, Drug discovery, Preclinical studies, NASH

S-3-3

Introduction of research and efficacy evalution technique using in-vivo bioimaging

Hoesu Jung
K-MEDI hub, Republic of Korea

In preclinical studies, bioimaging is a technology that detects and images phenomena at the molecular level occurring in vivo in experimental animals. At the clinical level, imaging diagnosis for a patient's condition is more limited than the techniques used in preclinical studsudies. In particular, it allows the biological information to be observed in real time, non-invasively, and repeatedly. Even without killing the experimental animal, it is possible to cross-check results with in-vivo and ex-vivo experiments.
Optical imaging can be broadly divided into bioluminescent imaging and fluorescent imaging. Bioluminescence imaging uses a luminescent substance called luciferin, which emits light when oxidized by an enzyme called luciferase. Generally, a method is used to inject the luciferase gene into the gene of an experimental material or animal. Fluorescent imaging is the process of detecting and imaging when fluorescent substances within cells, tissues, or living organisms absorb external light and are then excited to emit light of a longer wavelength. In the case of Micro-CT, it is an imaging device that transmits X-rays and uses the differences in absorption to reconstruct structures within the body into a cross- sectional image or a 3-dimensional stereoscopic image. MRI is an imaging device that uses magnets to emits high frequency waves into the body, resonating the hydrogen atomic nuclei in the body parts. It then converts the differences in signals from each tissue into digital information and creates images.
The KMEDIhub Preclinical Center is a core infrastructure facility for the development of new drugs and medical devices, contributing to the medical industry by supporting effectiveness and safety evaluation technology using animal testing in the preclinical trial stage. We provide a variety of research and technical services for the development of medical products by building a variety of imaging equipment, such as high-field MRI for small animals, optical imaging devices, and micro CT.
There are pros and cons to each imaging equipment, so the appropriate imaging equipment and method must be selected according to the experimental design. In tumor experiments, bioluminescence/fluorescence imaging can reveal the distribution of the drug in in-vivo. And images of tumor size reduction can also be obtained. CT images are specialized for viewing bone, muscle, and fat, allowing for the evaluation of bone regeneration or the effectiveness of drugs in animal models with muscle loss. In the case of MRI, we are evaluating the effectiveness of medical material implantation models, changes in lipid metabolites in the liver, volume changes in brain regions related to brain diseases, and evaluating the efficacy of contrast

agents.

Keywords: In-vivo bioimaging, Optical imaging, MRI (magnetic resonance imaging), CT (com puterized tomography)

S-3-4

Development of single-molecule-based, next-generation drug screening technology

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In drug discovery, protein-protein interactions (PPIs) are regarded as important, but undruggable targets. Current biophysical approaches for drug screening against PPIs face inherent limitations. To address this, we have developed a biological nanopore sensor for single-molecule detection of PPIs and its inhibition by small molecule drugs. Using a novel nanopore sensor (YaxAB), we performed drug screening against two anti-tumor therapeutic PPI targets (Bcl-xL-Bak and MDM2-p53 PPIs). The long funnel-shaped structure and nanofluidic charactristics of YaxAB nanopore enable the electro-osmotic trapping of target proteins. Distictive nanopore event distributions observed in the 2D-plot analysis (current blockades vs. noises) revealed the ability of the YaxAB nanopore to discriminate PPI inhibition by small molecule drugs from PPI formation. Additionally, we have developed novel nanopore sensor candidates for the purposes of PPI detection and drug screening. The engineered nanopore sensors exhibited nanofluidic characteristics indicating their potential utility as nanopore sensors for PPI detection. In this study, we suggest that the nanopore candicates can be useful for label-free, ultrasensitive, single-molecule detection of PPIs, opening up a possiblity for low-cost, highly efficient drug discovery against diverse drug targets.

Keywords: Nanopores, Protein-protein interactions, Drug screening, Single-molecule, Label-free

Symposia 4. Channels in Action: Advances in Mechanosensitive Ion Channel Research & Clinical Implications

S-4-1

Structural prediction of tentonin 3, a mechanosensitive channel

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Mechanosensation is essential for the survival of animals. Numerous physiological functions require mechanotransduction process. TTN3 involves in many physiological functions such as proprioception, baroreceptor and beta-cell functions. Tentonin 3 (TTN3/TMEM150c) is activated by mechanical stimuli with slow inactivation kinetics. TTN3 is a pore forming subunit because single channel currents were observed when its protein was incorporated into the lipid bilayer. The unique inactivation kinetics of TTN3 are conserved throughout the vertebrate phyla. Subunit analysis shows that TTN3 is a tetramer. Deep-learning based protein structure programs such as AlphaFold2 predict the molecular structure of TTN3. The predicted structure shows six transmembrane alpha helices. S3~S4 region comprises an ion conduction pathway. Mutations of residues along the putative ion conducting pathway block MA currents. These results combined by mutational study confirm the predicted structure.

Keywords: Tentonin 3, Mechanosensitive channel, TMEM150c, Structure, Mechanotransduction

S-4-2

Tracking back TREK-2 K^+ channels; PIP2, mechanosensitivity and the C-terminal charged residues

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TWIK-related two-pore domain K^+ channels (TREKs) are activated by acidic pH (pHi), membrane stretch, temperature, and arachidonic acid (AA). Phosphatidylinositol 4,5-bisphosphate (PIP2) exerts concentration-dependent biphasic regulations on TREK-2: inhibition by high PIP2, activation by partial decrease of PIP2, and inhibition by further depletion of PIP2. In various types of cells, mechanical stimulation of the plasma membrane activates phospholipase C (PLC) that might regulate ion channels via mechanosensitive degradation of PIP2. We previously found that mouse B cells, especially peritoneal B1 cells, abundantly express TREK-2 that are activated by membrane stretch via PLC activation and PIP2 decrease; the degradation of PIP2 caused by stretch-activated PLC releases TREK-2 from the tonic inhibition by relatively higher intrinsic PIP2. Using the site-directed mutations of the proximal cytoplasmic C-terminal (pCt) of TREK-2, we identified critical charged residues (K330 and RRR335-7) responsible for the biphasic regulation by PIP2. We suggest the triple successive Arg in pCt (R3-pCt) for the stimulatory regulation by the partial decrease of PIP2. The acidic pHi, AA, and high temperature activated the Ala-substituted (R3A-pCt) normally, whereas activation by membrane stretch was significantly attenuated. In hTREK-2, combined neutralization of the inhibitory K330 and R3-pCt (K330A/RRR355-7A) did not recover the suppressed current. In contrast, combined neutralization of pHi-sensing Glu (E332A/R355-7A) induced tonic high current and no further activation by pHi. Interestingly, when the Gly between K330/E332 and R3-pCt was mutated (G334A), hTREK-2 was tonic activated with reversed responses to ATP and acidic pHi. Therefore, we propose that the PIP2-dependent converse regulation of TREKs by Lys and R3-pCt with Gly implies structural flexibility of the pCt in TREK-2.

Keywords: Two-pore K^+ channel, TREK-2, Mechanosensitivity, PIP2, B cell

S-4-3

Signal transduction of Merkel cells in response to mechanical stimuli

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Recent studies indicated that Merkel cells and the mechanosensitive piezo2 ion channel play essential roles in the gentle-touch somatosensation. Merkel cells have been known as neuroendocrine cells with various (neuro) transmitters within their intracellular vesicles. Especially, the synaptic release of some neurotransmitter(s) form Merkel cells to their afferent Aβ endings are recently reported to play an essential role in gentle-touch somatosensation. In spite of these important roles of piezo2 channels and synaptic neurotransmitter(s) between Merkel cells and their afferent Aβ ending, the properties of piezo2 channels such as single channel conductance and mechanical sensitivity and the identity of neurotransmitter(s) between the Merkel cells and their afferent Aβ endings are still unclear.

Here, using patch clamp and fluorescence microscope for calcium measurement that were combined with high speed pressure clamp and nanopositioning mechanical stimuli systems, we describe the biophysical properties of piezo2 in human Merkel cell carcinoma (MCC)-13 cells. We also suggest some candidate (neuro)transmitters released from Merkel cells in response to mechanical stimuli. Piezo2 was a low-threshold, positive pressure-specific, curvature-sensitive, mechanically activated cation channel with a single channel conductance of ~28.6 pS. When a Merkel cell was mechanically stimulated with a step indentation, $[Ca^{2+}]_i$ was increased, which was followed by increases in $[Ca^{2+}]_i$ in the adjacent, surrounding Merkel cells. These paracrine-like action of Merkel cells were prevented by

inhibitors for purinergic receptors. Elisa assay also suggested co-release of norepinephrine and 5-hydroxytryptamine.

Our results are the first to demonstrate single channel recordings of piezo2. We anticipate that our findings will be a starting point for a more sophisticated understanding of roles of piezo2 in gentle-touch sensation. They also suggest co-release of some transmitters including norepinephrine, 5-hydroxytryptamine and ATP from Merkel cells that we stimulated with gentle touch or indentation. Among them, ATP may activate adjacent Merkel cells in a paracrine manner. What function these paracrine regulation of Merkel cells in the structure of Merkel cells-neurite complex plays in a clinical setting needs to be examined in future studies. In addition, whether these paracrine transmitters also take part in the synaptic transmission to drive the afferent Aβ fibers or independent set of transmitter(s) contribute to the paracrine and synaptic transmission independently warrants future study.

Keywords: Merkel cells, Mechanical stimuli, Piezo2, Paracrine, ATP

S-4-4

Mechanosensitive TREK channels: their role in neuroinflammation

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Neuroinflammation is increasingly recognized as a key contributor to neurodegenerative diseases, with mechanical stress from tissue and cellular changes exacerbating disease progression. This study explored the role of TWIK-related two-pore domain K^+ channels (TREKs), mechanosensitive ion channels activated by membrane stretch, in an amyloid-beta (Aβ)-induced neuroinflammation model in mice. Mice were injected with Aβ1-42 into the hippocampus to simulate Alzheimer's disease (AD) symptoms and markers. The results showed significant cognitive impairment, as evidenced by decreased performance in Y-maze and Morris water maze tests, and increased tau protein, BACE1 enzyme expression, and neuroinflammation markers such as Iba-1 and GFAP. Importantly, TREK channels were upregulated following Aβ1-42 injection, with TREK-2 particularly enhanced in hippocampal neurons and responsive to GABAR agonists in GABAergic neurons. TREK knockout mice exhibited reduced AD-like symptoms and pathological markers, indicating a protective effect of TREK channel inhibition on Aβ1-42-induced neurotoxicity. The study highlights TREK channels as promising therapeutic targets to mitigate AD progression, underscoring the need for further research into their mechanistic role in neurodegeneration.

Keywords: Alzheimer's disease, Amyloid-beta, Mechanosensitivity, TWIK-related two-pore domain K^+ channel

Symposia 5. Cutting-edge academic session by the Korean J Physiol Pharmacol

S-5-1

Altered inhibitory circuit of the medial prefrontal cortexin a mouse model of neuropathic pain

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Chronic pain is induced by tissue or nerve damage and is accompanied by pain hypersensitivity (i.e., allodynia and hyperalgesia). Previous studies using in vivo two-photon microscopy have shown functional and structural changes in the cerebral cortex at the cellular and synaptic levels in chronic pain. Alterations in local cortical circuit were revealed during the development of chronic pain, but the underlying mechanisms are not fully understood. We focused on the medial prefrontal cortex (mPFC) which undergoes various plasticity during the development of neuropathic pain. Especially, in the neuropathic pain state, the mPFC activity is decreased and metabotropic glutamate receptor 5 (mGluR5) activity is increased in the mPFC. Here, we investigated whether mGluR5 inactivation restores neuropathic pain in mice and, if so, how this inactivation affects local circuits in the mPFC. First, we confirmed the analgesic effect of mGluR5 inactivation in the mPFC using a pharmacological approach. Then, via electrophysiological recordings, we showed that the spontaneous inhibitory postsynaptic current (sIPSC) frequencies in pyramidal neurons increase during neuropathic pain and that this change is attenuated by applying a mGluR5 antagonist. Furthermore, the application of a mGluR5 agonist increased the sIPSC to layer 5 pyramidal neurons in naïve mice, consistent with the findings in neuropathic pain conditions. To investigate which cell types are responsible for increased inhibition tone, we measured the resting membrane potential of somatostatin (SST) and parvalbumin (PV) interneurons with a mGluR5 agonist. We found that the SST interneurons in the neuropathic pain group were more depolarized than those in the sham group. Optogenetic inactivation of SST interneurons reversed the observed increase in sIPSC of pyramidal neurons of the neuropathic pain model. Conversely, mGluR5 overexpression in SST interneurons in the mPFC of naïve mice caused mechanical allodynia, a representative symptom of neuropathic pain. These results demonstratethat increasedmGluR5 activity in SST interneuronscontributes toneuropathic pain and that cell type-specific modulation can provide new avenues for treating neuropathic pain.

Keywords: Pain, Metabotropic glutamate receptor, Somatostatin, Parvalbumin

S-5-2

Overcoming chemo-resistance of cancer via drug repurposing or natural medicine

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Background: Development of resistance to chemotherapy continues to be a major challenge in cancer treatment, and thus finding mechanisms to overcome chemo-resistance of cancers is responsible for researchers. Benzimidazole anthelmintics have been repurposed and various natural medicines based on ethnopharmacology also suggested to overcome cancers resistant to conventional chemotherapies.
Methods: Previous reports on 5-fluorouracil-resistance acquired SNU-C5 colorectal cancer cells first reviewed based on drug repurposing or natural medicine as a new therapeutic strategy. A brief overview on machine learning in onco-pharmacogenomics will be reviewed.
Results: Natural medicine including yeast extract, aqueous extract of Orostachys japonica, and chitosan oligosaccharide had different anti-cancer effects depend on cancer cells studied. For example, anti-cancer effects were obvious in 5-fluorouracil-resistance acquired SNU-C5 cells with Orostachys japonica, while in wild-type SNU-C5 cells with chitosan oligosaccharide. Repurposed drug, fenbendazole in this session, showed different mechanisms on cancers depending on whether drug resistance is acquired or not. Among various cell death pathways, fenbendazole-induced anti-cancer effects were considered as a ferroptosis-augmented apoptosis in colorectal cancer cells.
Conclusion: Drug repurposing or natural medicine might be a promising field to overcome drug resistance of cancers, at least a potential alternative treatment or an adjuvant, with cost-effective and time-saving strategies.

Keywords: Benzimidazole, Cancer, Drug resistance, Drug repurposing, Natural medicine

S-5-3

The alpha-helical domain of Gα, a new regulator of the heterotrimeric G protein signaling

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Heterotrimeric guanine nucleotide-binding proteins (G proteins) are pivotal mediators in intracellular signaling pathways, comprising three subunits: α, β, and γ. Gα is composed of two distinct domains, a Ras-like domain (RD) and an α-helical domain (AHD), between which the nucleotide-binding pocket is located. Upon interaction with guanine nucleotide exchange factors (GEFs) like G protein-coupled receptors (GPCRs), Gα undergoes conformational changes, leading to GDP release and binding of GTP. GTP binding initiates further structural transitions in Gα, triggering its dissociation from the GEF and Gβγ subunits. These activated Gα and Gβγ induce diverse intracellular signaling cascades. The intrinsic GTPase activity of Gα eventually hydrolyzes GTP to GDP, restoring the G protein to its basal Gαβγ heterotrimeric state. While the RD of Gα is known for its canonical functions, such as GTPase activity and interactions with GTP, Gβγ, GEFs, effector proteins (e.g., adenylyl cyclase), and GTPase-activating proteins, the functions of the AHD, despite its substantial size and sequence variation among Gα subtypes, remain relatively unexplored. Recent studies from my lab have uncovered novel roles for Gα AHD in the context of heterotrimeric G protein signaling. It has been proposed that Gα AHD plays a pivotal role in regulating the GDP/GTP turnover kinetics. Specifically, the conformational dynamics at the N-terminal segment of the αA and αA/αB loop within AHD regulate the GDP/GTP exchange rate, whereas the αA/αB loop in AHD governs the maximum GTP-binding capacity. Additionally, we discovered a novel Gαs AHD-binding protein, MAGE D2. MAGE D2 regulates Gs activation cycle in two ways; it accelerates the GTP-binding induced AHD closing kinetics; and it facilitates GDP release from basal state Gαs. In summary, the recent findings emphasize the significance of Gα AHD as a crucial regulator in G protein signaling.

Keywords: G protein, Alpha-helical domain, Signaling, Protein-protein interaction

S-5-4

Academic writing in the generative AI era

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The advent of large language models (LLMs) and generative AI has revolutionized the landscape of academic writing. This presentation explores the potential applications of LLMs in various stages of the research and writing process, from data collection to manuscript refinement. By leveraging tools such as custom ChatGPT, perplexity, scite.ai, elicit, and consensus, researchers can efficiently gather relevant literature and generate insights. LLMs can also aid in data analysis, figure legend creation, and outlining the structure of scientific articles. The iterative process of using LLMs for writing involves creating an outline, adding details, polishing, and critically evaluating the content. To ensure responsible use, authors should report the use of text generation tools, maintain rigorous note-taking practices to avoid plagiarism, and gradually reduce the reliance on generated content. Privacy and security concerns can be addressed through appropriate data control settings and the use of compliant enterprise solutions. While the effectiveness of LLMs depends on both the user's ability and the model's performance, embracing this technology can significantly enhance the efficiency and quality of academic writing in the generative AI era.

Keywords: Large language models, Generative AI, Academic writing, Research ethics, AI literacy

Symposia 6. Brain and cognitive aging

S-6-1

The role of neurons and glial cells in controlling age-related memory impairment

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Age-related memory impairment (AMI) is a phenomenon that occurs in humans and almost all animals. It is a symptom of a gradual decline in cognitive function compared to younger people as aging progresses. Older adults with AMI show significant impairment in the abilities of learning, memory, attention, thinking, language, and visuospatial organization. Therefore, AMI interferes with healthy aging. The behavioral phenotype of AMI is similar to mild cognitive impairment (MCI), a symptom of neurodegenerative brain disease, and early MCI is difficult to distinguish from AMI. However, while AMI symptoms gradually worsen over time, MCI symptoms worsen rapidly. Approximately 40% of people over 65 years of age suffer from AMI, and approximately 1-2% of these people develop dementia each year. Drosophila, a useful genetic model animal, also exhibits AMI (Yamazaki et al., 2007), and we defined Drosophila AMI as a significant decline in learning ability in middle age. Factors related to AMI include decreased cerebral blood flow and expression of nerve growth factors and polyamines due to aging, as well as decreased chromatin plasticity and increased expression of transposons. Genes associated with AMI in Drosophila are DC0 (PKA) and pyruvate carboxylase. We have conducted screen studies to discover factors regulating aging (lifespan) and AMI. We recently found that a neuropeptide and a mitochondrial metabolic enzyme regulate AMI. The role of neurons and glial cells in which these AMI regulatory factors are expressed will be proposed.

Keywords: Aging, Age-related memory impairment, Drosophila, Learning

S-6-2

Unraveling pathomechanisms underlying ALS: a multiomics-based approach empowered by *Drosophila* genetics

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Amyotrophic lateral sclerosis (ALS) is a late-onset neurodegenerative disease characterized by progressive motor neuron loss. To decipher its pathogenic mechanisms and neuropathic features, researchers have profiled protein, mRNA, and lipid alterations in ALS-affected neurons, with a limited focus on lipids due to technical constraints. Notably, proteomics studies in ALS have primarily aimed to identify direct interacting factors of disease-causing proteins (e.g., TDP-43) or biomarkers in easily accessible samples such as blood or cerebrospinal fluid. Consequently, our current understanding of system-level molecular changes in ALS-afflicted neurons predominantly relies on findings from transcriptomic analyses, thereby limiting our comprehensive grasp of the pathomechanisms underlying ALS. In this presentation, we introduce our ongoing multiomics approach, conducted through collaboration, with a particular emphasis on lipid, protein, and phosphorylated protein profiling, designed to complement prior research. We employ mass spectrometry imaging not only to quantify but also to spatially map lipid molecules within tissues. Importantly, the integration of *Drosophila* genetics into our approach broadens the range of ALS models available, facilitating the connection of multiomics findings with regulatory mechanisms through genetics. We firmly believe that our unique approach illuminates ALS pathophysiology.

Keywords: ALS, Proteomics, Mass spectrometry imaging (MSI)

S-6-3

Protective influence of the APOE Christchurch variant (R136S) against Alzheimer's disease pathology linked to APOE4

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Recently, a study reported resistance to Alzheimer's disease (AD) pathology in an individual homozygous for the APOE Christchurch (Ch) variant (R136S) against the PSEN1 E280A mutation. This raises questions about the protective role of the Ch variant in AD, particularly regarding tau pathology and cognitive impairment, though causal links and mechanisms remain unclear. Moreover, its effectiveness in sporadic AD, especially ApoE4-associated cases, is yet to be explored. To investigate, we employed ApoE3 and ApoE4 isogenic human-induced pluripotent stem cells (hiPSCs), and introduced the Ch variant into ApoE4 hiPSCs using CRISPR/Cas9. Biochemical, transcriptomic, and proteomic analyses of astrocytes differentiated these hiPSCs indicate that the Ch variant is sufficient to mitigate AD phenotypes; such as reduced ApoE levels, impaired Aβ and tau uptake, and cholesterol accumulation. Furthermore, we identify the modification of ApoE and LRP1 interactions as a key mechanisms through which the Ch variant exerts its beneficial effects in AD.

Keywords: Alzheimer's disease, APOE4, HiPSCs, Christchurch variant, LRP1

S-6-4

Increased risk of Alzheimer's disease affected by weight changes but not by body mass index

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Background: Alzheimer's disease (AD) is an intractable and multi-factorial neurodegenerative disorder. Given the globally rapid increase in obesity and its role in AD pathogenesis, understanding the impact of body weight, its changes, and the role of physical activity on AD development can provide important guidance for preventative strategies.
Methods: This population-based retrospective cohort study analyzed data from Korean national health and disability databases, including 3,741,424 individuals aged 30 to 80 years at baseline, who underwent health assessments between 2003 and 2006, followed by biennial check-ups over a decade. Exposures included BMI categories (underweight, normal, overweight, obese) and body weight changes (stable, acute increase, steady increase, weight cycling, acute decrease, steady decrease). Regular physical activity was defined as consistent weekly exercise over ten years. The primary outcome was AD incidence, identified by ICD-10 codes F00 or G30. Hazard ratios (HRs) were calculated using Cox proportional hazard models adjusted for multiple risk factors.
Results: Baseline BMI was not significantly associated with AD incidence after adjusting for confounders, except for underweight (adjusted HR [aHR], 1.10, 95% CI, 1.05-1.15). Weight changes were significantly linked to increased AD risk, particularly weight cycling (aHR, 1.37, 95% CI, 1.35-1.40), acute decrease (aHR, 1.78, 95% CI, 1.55-2.03), and steady decrease (aHR, 1.33, 95% CI, 1.30-1.35). Regular physical activity mitigated these risks, nullifying statistical significance.
Conclusion: Weight changes are significant risk factors for AD, and regular physical activity mitigates these risks. Public health strategies should focus on maintaining stable weight and promoting consistent physical activity.

Keywords: Alzheimer's disease (AD), Body mass index (BMI), Weight changes, Obesity, Regular physical activity

Symposia 7. Neural mechanism underlying learning and memory

S-7-1

Anterior cingulate-amygdala-cerebellum network codes stimulus contingency and task context of trace eyeblink conditioning

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The cerebellum plays a crucial role in learning and other cognitive functions through interactions with forebrain systems. Trace eyeblink conditioning (EBC) is an excellent associative learning paradigm for examining interactions between forebrain systems and the cerebellum. The anterior cingulate cortex (ACC), central amygdala (AM), and cerebellum (CB) are essential for trace EBC, and we previously demonstrated that they all show learning-specific modifications in activity during training. Our previous study recorded neuronal activity in the ACC, AM, and CB simultaneously from multiple tetrodes with paired presentations of the conditional stimulus (CS) and unconditional stimulus (US) during acquisition of trace EBC in rats. We attributed the changes in activity to learning the CS-US contingency but did not report the effects of manipulating the contingency. In the current study, we analyzed data from the same rats during sessions with transitions from CS-US paired trials to CS-alone extinction trials and from CS-alone trials to CS-US trials. All three areas show changes in activity with the changes in contingency, both during the stimuli and during the inter-trial interval. Subsets of ACC, AM, and CB neurons showed higher spike activity during CS-US trials, while others showed higher activity during CS-alone trials both during the trial events and during the inter-trial interval. The findings suggest that the ACC-AM-CB network codes for the stimulus contingency within trials and the task context between trials.

Keywords: Forebrain-cerebellar network, Anterior cingulate cortex, Amygdala, Associative learning, Electrophysiology

S-7-2

Circuit mechanism underlying social memory in mice

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In our laboratory, we are investigating the molecular and cellular mechanisms that underlie learning and memory (L&M) as well as social behaviors in mice. In this presentation, I will introduce the mPFC-to-nucleus accumbens (NAc) pathway, which we have identified as playing a crucial role in social recognition memory in mice. We have observed that in a chronic social isolation model, which selectively affects social recognition without altering sociability, the excitability of NAc-projecting infralimbic (IL) neurons is reduced. Reducing their excitability impairs social recognition in naïve mice, while enhancing it restores social recognition deficits in socially isolated mice. Intriguingly, we found that NAc-projecting IL neurons are activated when a mouse interacts with a familiar conspecific. This suggests that this specific circuit is responsible for social recognition memory in mice. Currently, to investigate the timing and mechanisms underlying this circuit's contribution to social memory, we are performing in vivo calcium imaging in conjunction with chemogenetic and optogenetic circuit modulations.

Keywords: Social behavior, Mouse, Memory, Social isolation

S-7-3

Cellular learning rules for structural knowledge-based decision flexibility

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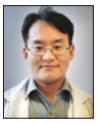
Cognitive flexibility is a fundamental feature of high-level brain function. However, neuronal pathways that control flexibility and the mechanisms by which flexibility is encoded are unknown. Previous studies have reported that neurons in the orbitofrontal cortex (OFC) encode the value of an external environment and lesions in the OFC area in human have led to deficits in choice behavior. Depletion of serotonin in the OFC area caused impaired reversal learning (RL). However, we still do not know how flexibility is represented by individual neurons or synapses. Fundamental questions underlying cognitive flexibility would be to understand a specific brain condition where new information can be updated without losing existing memories. In order to understand these brain mechanisms, we examined neuronal changes within a specific time window of behavior and control the exact timing of serotonin and glutamate release. We specifically targeted the DRN-OFC circuits and controlled their functions in a high spatiotemporal resolution. In brief, we identified the direct long-range projection from the DRN to the OFC anatomically and functionally. Optogenetic stimulation of serotonergic inputs to the OFC facilitated the RL and the inhibition of DRN-OFC circuits slowed down the speed of RL. We also found that the membrane potential of pyramidal neurons was increased by serotonin, resulting in the enhanced spiking probability of the OFC network. Imaging through a miniscope in behaving animals revealed in vivo functions of serotonin in the OFC. Combined two-photon Ca^{2+} imaging and uncaging showed that serotonin boosted Ca^{2+} transients and promoted the synaptic plasticity at dendritic spines. Thus, we revealed that cognitive flexibility may not be encoded as a form of specific cell types or circuit pathways, but rather be represented via state-dependent synaptic plasticity. We believe that these findings are important early steps which will furnish new insights into general cognitive learning.

Keywords: Cognitive flexibility, OFC, Serotonin, Reversal learning, Internal brain state

S-7-4

Role of mesolimbic dopaminergic circuit in social decision-making



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Motivation is essential in an animal's goal-directed behaviors, making animals withstand many hardships. For highly social animals like humans and some rodents, social interaction per se is a powerful driving force to endure effortful conditions. However, the underlying mechanism of motivation for social rewards has not yet been well studied. Effort-based social decision-making (ESDM) task was designed for this study and it was suitable for evaluating the social motivation levels. With this behavior paradigm, we analyzed the effort-based 'HARD' choice behaviors of male mice to meet female. When the interaction time with the female was given as a freely accessible social reward, the male mice chose to meet the female (EFB-). Interestingly, we observed that the male mice chose to meet female even if they had to climb the barrier (EFB+) more frequently than the EFB- group on the last day of the task. To explain these phenomena, we first investigated gene expression levels of dopamine receptor D1 (Drd1a) and D2 (Drd2) in the nucleus accumbens (NAc), the key brain region that mainly receives dopaminergic projections, by quantitative PCR. As a result, Drd1a gene expression, but not Drd2, was significantly higher in the EFB+ group than in other groups. To confirm the role of the D1 receptor in triggering social motivation, we infused D1R antagonist SCH-23390 directly into the NAc and found that 'HARD' choice level was decreased in the EFB+ group. Using in vivo fiber photometry, we measured spontaneous real-time dopamine signal activity in the NAc on the first day and the last day of the task. Consistent with our behavioral results, the doapmine signals during decision-making for 'HARD' choice were reinforced on the last day comapred to the first day. Since the ventral tegmental area (VTA) is the principal region for releasing dopamine, we manipulated the VTA-to-NAc circuit during the decision-making. Optogenetic inhibition reduced the 'HARD' choice level in the EFB+ group. Conversely, activation on the second training day increased the level. Taken together, these data suggest that NAc D1-cells receiving signals from VTA are possibly involved in effort-based decision-making for the social reward.

Keywords: Motivation, Mesolimbic circuit, Dopamine, Effort-based social decision-making

S-7-5

Flexibility and stability: multifaceted role of the posterior parietal cortex in reversal learning

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Reversal learning tasks require animals to cognitively process the reversed rule in association between sensory stimuli and motor actions. The task involves subjects rapidly adapting to changes in stimulus-outcome contingencies. However, the specific brain circuits responsible for reversing the sensorimotor transformation by updating outcome contingencies in association with sensory stimuli remain unclear. Here, we found that the posterior parietal cortex (PPC), which shows distinct projections to the auditory cortex (AC) and the inferior colliculus (IC), plays an important role in auditory reversal learning in mice. By conducting in vivo calcium imaging and analyzing single-neuron encoding by a generalized linear model (GLM), we examined how neurons in each circuit encode task variables, such as auditory stimulus contingency (stimulus-outcome association), reward, licking actions, and stimulus-reward history from the previous trial. Notably, the PPC neurons projecting to the AC (PPCAC) encoded both Go and No-go stimulus-outcome contingencies and updated the stimulus-reward history until the next trial. On the other hand, the PPC neurons projecting to the IC (PPCIC) encoded "Go" stimulus information strongly, which can evoke fast behavioral responses to the reward-associated stimuli. Circuit-specific optogenetic inactivation revealed that the PPCAC was predominantly required for updating behavioral responses after the reversal during the task, while the PPCIC played a key role in transforming auditory information into the reversed motor actions. Taken together, our findings demonstrate distinct roles of cortico-cortical and cortico-collicular top-down projections from the PPC in updating stimulus-reward associations during reversal learning.

Keywords: Posterior parietal cortex, Reversal learning, Reward history, Auditory cortex, Inferior colliculus

Symposia 8. The Present and Future of Digestive Pathophysiology in Korean Medicine

S-8-1

Herbal drug candidate for the antioxidant properties and their metabolism

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The drug interaction between chemical and herbal medicines could confirm the safety of combined prescription of drugs with herbal medicines. System pharmacology could combine the network and molecular tools and reveal the unknown effects of the plant as well as its interaction with

other chemical drugs. This study integrated a systemic assessment and biological validations to verify the therapeutic effects of the herbal preparations on the oxidative damage. Moreover, we confirmed the combined use of synthetic drugs and herbal medicines as assessed by literature, clinical, and non-clinical studies. Our study unveiled the active components in herbs and the molecular mechanisms based on the multiscale interactome. Some traditional herbs inhibited the oxidative damage by acting on the several anti-oxidant signaling pathways. This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (number: HF20C0212).

Keywords: Herbal drug, Antioxidant, System pharmacology, Signaling pathway, DDI

S-8-2

Atractylodes macrocephala Koidz Alleviates Symptoms in Zymosan-Induced Irritable Bowel Syndrome Mouse Model through TRPV1, NaV1.5, and NaV1.7 Channel Modulation

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Irritable bowel syndrome (IBS) is a common disease in the gastrointestinal (GI) tract. Atractylodes macrocephala Koidz (AMK) is known as one of the traditional medicines that shows a good efficacy in the GI tract. We investigated the effect of AMK in a network pharmacology and zymosan-induced IBS animal model. In addition, we performed electrophysiological experiments to confirm the regulatory mechanisms related to IBS. Various characteristics of AMK were investigated using TCMSP data and various analysis systems. AMK restored the macroscopic changes and weight to normal. Colonic mucosa and inflammatory factors were reduced. These effects were similar to those of amitriptyline and sulfasalazine. In addition, transient receptor potential (TRP) V1, voltage-gated Na+ (NaV) 1.5, and NaV1.7 channels were inhibited. These results suggest that AMK may be a promising therapeutic candidate for IBS management through the regulation of ion channels.

Keywords: Zuojin Pill, Inflammatory bowel disease, Dextran Sulfate Sodium, Intestine, Liver

S-8-3

Identifying novel subtypes of functional gastrointestinal disorder by analyzing nonlinear structure in integrative biopsychosocial questionnaire data

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Objective: Due to treatment difficulties in the conventional management of functional gastrointestinal disorders (FGIDs), tailored treatment considering the heterogeneity and biopsychosocial characteristics of FGIDs is needed. Here, we identified biopsychosocial information-based novel subtypes of FGID using integrative questionnaire data.
Materials and Methods: Rome criteria-based Korean Bowel Disease Questionnaire (K-BDQ), traditional Korean medicine diagnosis questionnaire for digestive symptoms (KM), and 36-item Short Form Health Survey (SF-36) data were collected from 198 FGID patients. Multivariate analyses were conducted to assess whether the KM or SF- 36 contain additional information over the Rome criteria and whether this information has statistical relevance with symptom severity. Then, questions related to symptom severity were selected among the three questionnaires by applying a supervised learning model. To identify novel subtypes, nonlinear dimensionality reduction and clustering analyses were conducted on the integrative questionnaire. For optimization of the nonlinear clustering, the trustworthiness, silhouette coefficient, and accordance rate were evaluated. For validation of the clustered result, a machine learning classifier was employed to decode each cluster label.
Results: Comparative analyses among three questionnaires found that SF-36 and KM could supplement the psychosocial aspects lacking in K-BDQ. An integrative questionnaire using clinically relevant information that contributes to the prediction of FGID severity was developed. As a result of nonlinear clustering analysis using the integrative questionnaire data, four subtypes of FGID were identified mild, severe, mind-symptom predominance, and body-symptom predominance subtypes.
Conclusion: This study provides novel subtypes of FGID by analyzing the data-driven, nonlinear structure behind the complexity of FGID patients.

Keywords: Functional gastrointestinal disorders, UMAP, Nonlinear clustering, Subtype identification

S-8-4

Pathophysiology of Stress-Induced Liver Injury and Its Underlying Role

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Besides the brain, the liver is another organ affected by psychological stress. Since ancient times, it has been recognized that liver tissue can be injured under severe psychological stress conditions, a phenomenon often referred to as "anger injuring the liver" (怒傷肝) in many traditional medicine textbooks. Additionally, clinicians sometimes observe elevated serum levels of hepatic enzymes after exposure to severe stress; however, the underlying mechanisms remain unclear.
To enhance our understanding of stress-related liver damage, our team has conducted a series of experiments using multiple animal models. In this presentation, I will present data on how psychological stress induces liver injury and the biological mode of hepatocyte death. Furthermore, I will propose a hypothesis explaining the underlying biological significance beyond.

Keywords: Stress, Liver, Injury, Cortisol, Brain

Symposia 9. Joint Symposium with Korean Society of Pharmacology

S-9-1

Dynamic regulation of mitochondria in cellular senescence

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Mitochondrial homeostasis is critical for various cellular processes and mitochondrial dysfunction is involved in the pathophysiology of cells. Senescent cells exhibit a diverse spectrum of changes in their morphology, proliferative capacity, senescence-associated secretory phenotype (SASP) production, and mitochondrial homeostasis. These cells often manifest with elongated mitochondria, a hallmark of cellular senescence. However, the precise regulatory mechanisms orchestrating this phenomenon remain predominantly unexplored. In this study, we provide compelling evidence for decreases in T-cell-restricted intracellular antigen-1 (TIA-1), a pivotal regulator of mitochondrial dynamics, in models of both replicative senes-

cence and ionizing radiation (IR)-induced senescence. The downregulation of TIA-1 was determined to trigger mitochondrial elongation and enhance the expression of senescence-associated β-galactosidase, a marker of cellular senescence, in human fibroblasts and keratinocytes. Conversely, the overexpression of TIA-1 mitigated IR-induced cellular senescence. Taken together, our findings underscore the significance of TIA-1 in governing mitochondrial dynamics and cellular senescence.

Keywords: Mitochondria, Cellular senescence, Mitochondrial dynamics, Elongation

S-9-2

Finding the equilibrium for the uric acid dynamics

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Most of the natural phenomena follow the law of normal distribution. Continuous variables following normal distribution are composed of heritable and environmental factors. This can be expressed in the form of a polygenic risk score. This rule can be applied to uric acid. Based on the serendipitous finding of hypouricemia during the clinical trials, our group investigated the epidemiologic study to finding the meaning of hypouricemia in the context of public health, we generated polygenic risk score of uric acid in the general population and then found the causative gene through WES for subjects distributed at the extreme ends of the normal distribution. This discovery of GLUT9 became the corner stone of uric acid lowering agent, a treatment for hyperuricemia, the cause of gout.In this lecture, I will also cover clinical pharmacology prospective of uric acid dynamics to find the equilibrium for each individuals.

Keywords: Uric acid, Dynamics, PRS

S-9-3

Senotherapeutic intervention as a treatment of metabolic diseases

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Cellular senescence is a physiological process that occur during embryonic development and wound healing. However, the accumulation of senescent cells by cellular senescence leads to aging and the development of age-related diseases. Cellular senescence is characterized by morphological alterations (flat and larger), functional impairments, a cessation of proliferation, and resistance to apoptosis. Senescent cells produce the senescence-associated secretory phenotype (SASP), which can convert normal cells into senescent cells. Adipose tissue aging is strongly connected to type 2 diabetes because it causes chronic low-level inflammation and fibrosis in adipose tissue, resulting in aging and insulin resistance in the liver and muscles via SASP. Obesity exacerbates this process by hastening adipose tissue aging. Targeting senescent cells through senolytics (eliminate senescent cells) or senomorphics (inhibiting SASP secretion) holds promise for delaying aging and attenuating metabolic diseases, but no clinically approved senotherapeutics are presently available. We discovered a novel senotherapeutic candidate for metabolic disease using clinically applicable 2,150 compounds. Amont these compunds, we selected 15 compounds that increased cell lysis or reduced senescence-associated beta-galactosidase (SA-β-gal) staining using the two-steps screening test in senescent human cells. Among the 15 compounds, we identified homoharringtonine (HHT) that alleviated glucose intolerance and insulin resistance in high-fat diet-induced obese mice. HHT reduced SA-beta gal staining, crown-like structure count, and the SASP expression in the adipose tissue. HHT also reduced adipose tissue aging and improved insulin resistance in naturally aging mice. It also attenuated adipose tissue senescence in human subcutaneous adipose tissue ex vivo. HHT also revealed a delayed aging phenotype in the skeletal muscle, lung and kidney and extended life span in aging mice. Thus, these findings indicate that we have discovered a novel senotherapeutic agent that has a potential to treat type 2 diabetes.

Keywords: Insulin resistance, Homoharringtonine, Senotherapeutics, Aging, Obesity

S-9-4

Therapeutic strategies against age-related fibrotic diseases

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Age-related diseases share common pathophysiologic mechanisms such as oxidative stress, mitochondrial dysfunction, defective autophagy, tissue fibrosis, and cell death. Particularly, in the process of fibrosis, aberrant and persistent TGF-β signaling leads to epithelial-mesenchymal transition (EMT) and fibrotic changes, which could be targets for protecting against degenerative pathologies associated with aging. We have investigated the role of TGF-β-ERK1/2–mTOR–NOX4 signaling and oxidative stress in various tissues including the liver, kidney, and retina, which establish a positive feedback amplification loop, playing a crucial role in EMT and fibrogenesis. Targeting different points of the ERK1/2–mTOR–NOX4 axis with specific inhibitors effectively abrogated the upregulation of fibrogenic markers, oxidative stress, and tissue fibrosis in vivo. Additionally, we newly uncovered that the active form of TGF-β directly binds to integrins, triggering cytosolic Ca^{2+} signaling, leading to the transdifferentiation of hepatic stellate cells and contributing to fibrogenesis. α-Klotho, an anti-aging protein, counters this process by contesting TGF-β1 for integrin binding, preventing the activation of HSCs and liver fibrosis. Mitochondria-derived peptides, including humanin, inhibit TGF-β-mediated oxidative stress and enhance autophagic degradation. All these approaches could provide novel therapeutic strategies to mitigate pathologic EMT and fibrosis related to organism senescence.

Keywords: Liver fibrosis, Glomerulosclerosis, Age-related macular degeneration, Transforming growth factor-β, Oxidative stress

Symposia 10. Exploring Glial Functions in CNS: Understanding Neuron-Glia Interactions

S-10-1

Rejuvenating aged microglia increases amyloid-β clearance

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Age-dependent accumulation of amyloid plaques in patients with sporadic Alzheimer's disease (AD) is associated with reduced amyloid clearance. Older microglia have a reduced ability to phagocytose amyloid, so phagocytosis of amyloid plaques by microglia could be regulated to prevent amyloid accumulation. Furthermore, considering the aging-related disruption of cell cycle machinery in old microglia, we hypothesize that regulating their cell cycle could rejuvenate them and enhance their ability to promote more efficient amyloid clearance. First, we used gene ontology analysis of microglia from young and old mice to identify differential expression of cyclin-dependent kinase inhibitor 2A (p16ink4a), a cell cycle factor related to aging. We found that p16ink4a expression was increased in microglia near amyloid plaques in brain tissue from patients with AD and 5XFAD mice, a model of AD. In BV2 microglia, small interfering RNA (siRNA)-mediated p16ink4a downregulation transformed microglia with enhanced amyloid phagocytic

capacity through regulated the cell cycle and increased cell proliferation. To regulate microglial phagocytosis by gene transduction, we used poly (D,L-lactic-co-glycolic acid) (PLGA) nanoparticles, which predominantly target microglia, to deliver the siRNA and to control microglial reactivity. Nanoparticle-based delivery of p16ink4a siRNA reduced amyloid plaque formation and the number of aged microglia surrounding the plaque and reversed learning deterioration and spatial memory deficits. We propose that downregulation of p16ink4a in microglia is a promising strategy for the treatment of Alzheimer's disease.

Keywords: Alzheimer's disease,Cell cycle, Microglia senescence, Phagocytosis, P16ink4a

S-10-2

Conductivity and nano-topography of nanotube platforms modulate astrocyte functions

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Multi-walled carbon nanotubes (CNT) have been applied to the nervous system to modulate neuronal growth and electrical properties. However, their application was invasive, and effects on the function of astrocytes have not been studied. Therefore, we developed non-invasive CNT platforms for cells with different nanotopography and conductivity. Using CNT platforms, we investigated whether the CNT platform could affect the function and characteristics of cerebellar and hippocampal astrocytes. Astrocytes on CNT showed improved cell adhesion with upregulated integrin and intracellular Ca^{2+}. Interestingly, cerebellar astrocytes showed improved gliotransmission by increasing intracellular Ca^{2+} via TRPV1. We observed enhanced glutamate uptake via increased glutamate transporters in hippocampal astrocytes on CNT platforms. Also, we acquired increased passive conductance from astrocyte whole-cell patch clamp recording through upregulated two-pore potassium channel expression. Our findings suggest that the characteristics and functions of astrocytes vary across brain regions and are differently regulated when applied with nanomaterials. Therefore, our CNT platform-modulated astrocyte functions may lead to a new direction for neuromechanobiology and neuron glia interaction.

Keywords: Astrocyte, CarbonNanoTube (CNT), Glia, Nanobiotechnology, NeuroMechanobiology

S-10-3

The role of Tweety-homolog (TTYH) family in astrocyte volume regulation

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Brain volume regulation is a vital homeostatic process that maintains ionic and osmotic balance, which is critical for the proper functioning and health of the nervous system. Astrocytes play a central role in this regulation, utilizing a variety of ion channels, transporters, abundant water channels, and specialized membrane structures known as caveolae to manage cell volume. Despite their crucial role in regulating brain volume, much is still unknown about the molecular mechanisms of how astrocyte sense and regulate the volume changes. In this study, we reveal that Tweety-homologs (TTYH1, TTYH2, TTYH3) is pore-forming subunits of stretch-activated anion channels in astrocytes. Using a combination of electrophysiology and FRET-based biosensor imaging, we demonstrated that under whole-cell patch configurations, Cl- current activated by positive-pressure through patch-pipette are temporally synchronized with membrane stretch. Simultaneous gene-silencing of Ttyh1/2/3 results in the abolition of both cell swelling and Cl- conductance, underscoring their essential role in astrocyte volume regulation. Additionally, we unveil the physical interaction between TTYH 1/2/3 and caveolin-1, critical for maintaining the structural integrity of caveolae as observed by transmission electron microscopy. Cryo-electron microscopy further reveals the formation of both tetrameric and dimeric complexes of TTYH family at the cell membrane. Each TTYH subunit comprises 5 transmembrane domains, and we have demonstrated that a conserved positively charged residue at 213 in the transmembrane domain within these subunits of TTYH1 plays an essential role in Cl- conductance. Our findings are reinforced by single channel conductance recording in hTTYH1-reconstituted lipoprotein, confirming the TTYH family as bona fide anion channels. Our results provide unprecedented insights into the molecular mechanisms underlying astrocyte volume regulation.

Keywords: Astrocyte, Volume regulation, Tweety-homolog family, Cl- channel, Membrane stretch

S-10-4

Tracking oligodendroglial development through advanced imaging techniques

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Understanding the intricate processes of oligodendroglial development and maturation in the context of brain development and leukodystrophy is crucial for advancing neuroscience research and therapeutic interventions. In this study, we explored the dynamics of oligodendroglial development in mouse and human brain, as well as in human cerebral organoids, using non-invasive methodologies including 3D magnetic resonance fingerprinting (MRF) and volumetric confocal imaging techniques. When we quantified myelin water fraction (MWF) during normal brain development of C57BL/6 mice, we found that the increase in MWF values correlated well with the histologic myelin immunoreactivity in the cortex and the corpus callosum according to developmental stages. Moreover, MWF values and proteolipid immunoreactivity were significantly decreased in megalencephalic leukoencephalopathy with subcortical cyst 1 (MLC1) knockout mice. We also tracked myelin maturation in a total of 81 children of varying ages using 3D MRF-derived MWF, underscoring the potential of 3D MRF-derived MWF as a rapid and non-invasive quantitative indicator of brain myelin content. We then visualized the development of oligodendrocytes in live human cerebral organoids by utilizing a high-speed scanning confocal microscope, coupled with advanced computational image processing. This approach enabled us to monitor the intricate dynamics of neuron and oligodendrocyte development within cerebral organoids across an approximately two-month trajectory. Taken together, these technological advances can mark a significant advancement in the field of neuroscience, providing powerful tools for deciphering oligodendroglial development.

Keywords: Brain development, Oligodendrocyte, MR fingerprinting, Myelin water fraction, Advanced confocal imaging technique

Symposia 11. Tissue-Specific Immunity: Exploring the Physiological Landscapes Across Different Organs

S-11-1

Human MAIT cells undergo clonal selection and expansion during thymic maturation and aging

You Jeong Lee

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Unlike conventional T cells that recognize agonistic self-peptide for thymic selection, mucosal-associated invariant T (MAIT) cells depend on gut-derived bacterial metabolites. They harbor canonical TCRs but a highly diverse CDR repertoire, but it is not well understood how this diversity is shaped in the thymus. To address this issue, we analyzed clonal selection and differentiation of human MAIT cells during their thymic maturation and compared it with other types of innate T cells— iNKT and γδ T cells. Our analysis reveals that MAIT and iNKT cells embark on a common developmental pathway, unlike the transcriptionally unique γδ T cells. Significantly, only the CD8+ MAIT cells, but not iNKT and γδ T cells, progress to stage 3, accompanying clonal expansion concomitant with aging. While iNKT cells employ a strict combination of canonical sets of TCRs from the immature stage, MAIT cells demonstrate a reduction in TCR Vβ and Jα diversity upon thymic maturation, suggesting they are clonally selected. Furthermore, we discovered that about 10% of thymic MAIT cells had dual TCRs—one polyclonal and the other MR1-specific—implying they might recognize broad antigens in the periphery. Collectively, these results show that a clonal selection by extrathymic antigens and occasional dual TCRs shape a highly diverse TCR repertoire of human MAIT cells.

Keywords: MAIT, INKT, Γδ T cells, Thymus, Repertoire

S-11-2

Inflammatory Niche in Lung tissue regeneration and pathogenesis

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Tissue regeneration is a multi-step process mediated by diverse cellular hierarchies and states that are also implicated in tissue dysfunction and pathogenesis. Alveolar type 2 (AT2) cells function as stem cells by self-renewing and differentiating into alveolar type 1 (AT1) cells that are essential for gas-exchange in the lung. However, how AT2 cells are activated from the quiescence and which trajectory they follow to differentiate into AT1 cells remain unknown. Here, we leveraged single-cell RNA sequencing in combination with in vivo lineage tracing and organoid models to finely map the trajectories of alveolar lineage cells during injury repair and lung regeneration. We identified how injury remodels immune system and inflammatory niches driven my macrophage dynamics orchestrate tissue regeneration during injury repair in the lungs. We also identified a distinct AT2-lineage population, Damage-Associated Transient Progenitors (DATPs), that arises during alveolar regeneration. Further, we found that chronic inflammation prevents AT1 differentiation, leading to aberrant accumulation of DATPs and impaired alveolar regeneration in chronic human lung diseases. Overall, my study reveals how inflammation coordinates the lung tissue regeneration by directly reprogramming stem cell activity or regulating neighboring niches to modulate the plasticity of lung stem cells.

Keywords: Lung fibrosis, Alveolar stem cells, Regeneration, Organoid co-culture, Cell state transition

S-11-3

Portal immune system: key guardians against gut-derived toxins

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Liver fibrosis is characterized by the extensive deposition of extracellular matrix such as fibril collagen, causing dysfunction and failure of the liver. Gut-derived bacterial endotoxin induces inflammation-mediated progression of liver fibrosis by flowing in hepatic portal venous system. Our body establish innate immune systems to protect against endotoxin-induced damages, but gut-derived endotoxin can overcome our defense systems. HDL synthesis also occurs in the liver and small intestine; but, distinct functions for intestinal HDL are unrevealed. Here, we discovered that HDL in the portal vein was mainly composed of small-sized HDL3 and showed strong effects on neutralization of LPS endotoxin in hepatic portal venous system. In a mouse model of liver diseases which induces dramatic liver inflammation and fibrosis via TLR4, loss of intestine-derived HDL worsened liver injury, whereas liver pathology was improved by therapeutic challenge of low-dose oral LXR agonist that elevated and depended upon intestinal HDL production. Additionally, we found novel innate immunity system in portal vein to effectively remove bacteria translocation. Hepatic portal venous immune systems show distinct immune cell population, and are developed to strongly remove foreign components. Thus, we found that protection of the liver from injury in response to gut-derived signals like LPS is a major function of intestinally synthesized HDL and portal innate immunity.

Keywords: Liver, HDL, Immunity, Portal venous system

Symposia 12. Novel therapeutic strategies for cardiovascular diseases – stem cell, miRNA, mitochondria and beyond

S-12-1

Heart regeneration - making breakthroughs & renewed optimism

Hun-Jun Park

The Catholic University of Korea, Republic of Korea

Ischemic heart disease remains the primary cause of morbidity and mortality worldwide. Despite significant advancements in pharmacological and revascularization techniques in the late 20th century, heart failure (HF) prevalence after myocardial infarction (MI) has gradually increased over the last two decades. After ischemic injury, pathological remodeling results in cardiomyocytes (CMs) loss and fibrosis, which leads to impaired heart function. Unfortunately, there are no clinical therapies to regenerate CMs to date, and the adult heart's limited turnover rate of CMs hinders its ability to self-regenerate. Over the past few decades, there have been some breakthroughs and renewed optimism about cardiac regeneration. Spheroids are 3D structures that can be generated from stem cells or tissue-derived cells in vitro, and they can recapitulate some of the structural and functional characteristics of the corresponding organs. In the context of cardiac regeneration, spheroids have been proposed as a potential approach for generating functional heart tissue for transplantation. Cardiac spheroids can be generated by differentiating human pluripotent stem cells (hPSCs) into various cardiac cell types including CMs, endothelial cells (ECs) and cardiac fibroblasts (CFs), and assembling them into 3D structures that resemble the architecture of the heart. Increasing interest has been directed towards non-CM cell types in driving myocardial renewal. We will discuss the therapeutic potential of 3D cardiac spheroids derived from hPSCs for cardiac regeneration and the limitations to establish their safety and efficacy in preclinical and clinical settings including optimization, maturation, and integration with the host tissue.

Keywords: Ischemic heart disease, Microenvironment, Cardiomyocytes, Cardiac spheroids, Cardiac regeneration

S-12-2

Estrogen through GPER mitigates stress-induced cardiac inflammation and metabolic disorders

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Background: Cardiac dysfunction, a significant contributor to various forms of excessive stress-related cardiac diseases. Sex disparities in mortality regarding stress-induced cardiac dysfunction remains elusive, but clinically males exhibit higher mortality rates, potentially linked to hormonal differences. Nucleotide bound oligomeric domain like receptor protein 3 (NLRP3) inflammasomes and Peroxisome Proliferator-Activated Receptor Delta (PPARδ) are key players in cardiac inflammation and metabolism and their activation has been demonstrated to favor stress induced cardiac dysfunction outcomes. While estradiol (E2) is abundant and beneficial in females, its impact on inflammatory and dysmetabolism in the heart with regards to sex during stress remains unknown. This study is to investigate sex-specific differences and the impact of E2 /GPER-1 and β2-adrenoceptor (β2AR) signaling on the inflammation and metabolism in the heart of female mice during stress; To evaluate the therapeutic potential of GPER-1 activation for males under stress conditions.
Method: Female and male C57BL/6J mice were employed, along with β2AR-/-, GPER-1-/- and NLRP3-/- mice. Various treatments, including ovariectomy, E2 supplementation, PPARδ and GPER-1 agonist administration, were utilized to investigate sex-specific responses and mechanisms during isoprenaline induced stress of LPS induced sepsis. Echocardiography was employed to assess cardiac function, while western blot analysis was utilized for protein detection. Periodic Acid-Schiff (PAS) and oil red staining were used to visualize glycogen and lipids, respectively. Statistical analyses were conducted using GraphPad Prism 8.0.2 software, employing one-way or two-way ANOVA were used. Significance was defined as p-values less than 0.05.
Results and Conclusions: (1) Estrogen reduces the activation of NLRP3 inflammasomes in the myocardium during stress and improves lipid accumulation. β2AR mediates the effect of estrogen. (2) Under stress conditions, the activation of NLRP3 inflammasomes occurs prior to lipid accumulation. It is an important cause of stress-induced myocardial lipid accumulation. (3) Estrogen through the activation of GPER exhibited significant cardioprotective effects in female mice challenged with LPS. (4) Activating GPER specifically in males alleviated the adverse cardiac outcomes observed during LPS challenge. The cardioprotective effect of activating GPER may be related to reduction of NLRP3.

Keywords: Estrogen, Inflammation, Metabolism, Cardiac function, Sex-specific differences

S-12-3

Mitochondrial transplantation for ischemic related cardiovascular diseases

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Recently, mitochondria transplantation (MT) is emerged as a novel therapeutic strategy targeting ischemic cardiovascular diseases, but the roles of MT in the donor hearts for transplantation remain unidentified. Here, we tested the efficacy of human platelet-derived mitochondria (pl-MT) and mesenchymal stem cell-derived mitochondria (MSC-MT) on mitochondrial and cardiac function of the donor hearts for heart transplantation. Incubation of donor rat hearts with pl-MT ex vivo for 9 hrs or with MSC-MT incubation of mice hearts for 9 hrs resulted in the internalization of MT in cardiomyocytes and the enhancement of cardiac mitochondrial activity and ATP production. Contractility and conduction velocity of the hearts were improved with MT. We will discuss detailed mechanisms of mitochondrial changes following MT in both young and aged mice hearts. Our study provides the proof of principle for exogenous mitochondria transplantation as an enhancer of the donor heart

Keywords: Mitochondria transplantation, Heart transplantation, Donor heart

Symposia 13. Young Faculty Presentation Part 1. Neuroscience

S-13-1

AI in neurobiology: from neuron classification to reinforcement learning models

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This presentation explores two areas of research at the intersection of machine learning (ML) and neuroscience. The first focuses on research that utilizes ML techniques for the classification of neurons. In this part, we describe how we can use electrophysiological data as the main input for different ML algorithms and evaluate their effectiveness in predicting molecular biological markers of neurons. In the second section, we shift our attention from the realm of reinforcement learning (RL) to an exploration of successor representation (SR) algorithms. An intriguing correlation between neuroplasticity in hippocampal microcircuits and the temporal difference learning algorithm in RL lies at the center of this discussion. We will also examine the SR algorithm under different conditions, including different synaptic weight initializations and robustness in the face of noisy input. This talk aims to shed light on the synergistic potential of ML and neuroscience in unraveling the complexity of brain function.

Keywords: Machine learning, Successor presentation, Reinforcement learning, Robustness, Temporal difference learning

S-13-2

Identifying a biomarker for cognitive performance

Alan Jung Park
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Deciphering the function of the brain is fundamental to understand our cognition. Our behavior is an outcome of complex interactions that occur in milliseconds across brain networks. Hence, conventional cell biology-based approaches cannot uncover the enigma of the brain. With recent technological advances, the field of cognitive neuroscience moves toward interdisciplinary research combining biology, engineering, and computer science. In this talk, I will introduce an interdisciplinary research to unravel brain circuit mechanisms underlying cognitive behavior and discuss ongoing research to identify biomarkers that predicts individual's cognitive performance.

Keywords: Biomarker, Schizophrenia, Theta wave, Brain circuit, Cognition

S-13-3

Functional significance of *NRGN*, a schizophrenia risk gene, in regulating synaptic plasticity and calcium channel activity

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Schizophrenia is one of the leading causes of disability worldwide, and its highly heritable nature implies genetic underpinnings. Genome-wide association studies identified NRGN as a risk gene associated with schizophrenia in multiple populations, and individuals carrying the NRGN risk variant exhibit decreased hippocampal activation during contextual learning. Neurogranin, encoded by the schizophrenia risk gene NRGN, is a neuron-specific, calmodulin-binding protein abundant in the postsynaptic compartments. The expression of neurogranin is reduced in the postmortem brains of patients with schizophrenia, implicating the hypofunction of neurogranin in schizophrenia. Interestingly, the expression levels of neurogranin are rapidly increased in response to elevated neuronal activity in the hippocampus, and the activity-dependent translation of neurogranin is required for contextual memory formation. However, the overall impact of neurogranin levels on the induction of synaptic plasticity remain elusive. Through an integrative approach using whole-cell patch clamp and quantitative phosphoproteomic analysis, we found that neurogranin bidirectionally modulate long-term potentiation (LTP) in the hippocampus by shifting the phosphorylation pattern of postsynaptic density proteins, including glutamate receptors and selective ion channels. In particular, synaptic PP2B activity was required for mediating the deficit in LTP caused by reduced neurogranin levels, thus revealing a novel mechanistic link of a schizophrenia risk gene to cognitive deficits. Lastly, currently ongoing studies highlighting the significance of neurogranin levels in controlling the activity of L-type calcium channels will be discussed.

Keywords: Neurogranin, Schizophrenia, Spike-timing-dependent plasticity, Phosphoproteome, L-type calcium channel

S-13-4

Pathologic α-Synuclein-NOD2 interaction and RIPK2 activation drives microglia-induced neuroinflammation in Parkinson's disease

Bo Am Seo
Yonsei University Wonju College of Medicine, Republic of Korea

Pathological aggregation of α-Synuclein (α-Syn) and neuroinflammation are closely linked to Parkinson's disease (PD). However,the specific regulators of the neuroinflammation caused by pathological α-syn remain obscure. In this study, we show that NOD2/RIPK2 signalingis a crucial regulator of neuroinflammation in PD. Pathological α-syn binds to NOD2, causing self-oligomerization and complex formation with RIPK2, leading to RIPK2 ubiquitination and activation of MAPK and NF-kB. Notably, this NOD2/RIPK2 signaling is particularly active in microglia of human PD brains andthe α-Syn preformed fibril (α-Syn PFF) mouse model. Depleting NOD2 or RIPK2 reduces neuroinflammation and protects against dopamine neuron degeneration in a pathologic α-Synmouse modelby blocking the formation of neurotoxic reactive astrocytes caused by microglia activation. The discovery of NOD2/RIPK2 signaling as a key regulator of neuroinflammation in PDprovides a new understanding of α-Syn-driven neuroinflammation and neurodegeneration in PD and a potential new therapeutic strategy.

Keywords: Parkinson's disease, Microglia, Neurotoxic reactive astrocyte, Neuroinflammation, NOD2/RIPK2

Symposia 14. Young Faculty Presentation Part 2. Cancer and Metabolism

S-14-1

Unveiling the role of SON-mediated RNA splicing in genetic diseases and tumorigenesis

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Dysregulation of RNA splicing has emerged as a promising target for the treatment of genetic disease and cancer. However, the functional importance of RNA splicing and splicing factors in genetic diseases and various cancers has not been properly identified. Zhu-Tokita-Takenouchi-Kim (ZTTK) syndrome, an intellectual disability syndrome first described in 2016, is caused by heterozygous loss-of-function variants in SON, a DNA/RNA binding protein. Our investigation revealed haploinsufficiency in SON affecting multiple genes, including those involved in the development and metabolism of various organs. Given the diverse functions of SON, it is reasonable to expect that pathogenic variants in this gene can manifest a wide spectrum of clinical symptoms. Since SON is aberrantly overexpressed in cancers, particularly glioblastoma multiform (GBM), we explored its role in this highly aggressive brain tumor. Our findings indicate that SON regulates oncogenic RNA splicing through two distinct regulatory mechanisms. Firstly, SON directly binds to and removes the intron of PTBP1, known as an oncogene, thereby increasing its expression and enhancing PTBP1-mediated oncogenic RNA splicing. Secondly, SON interreacts with various hnRNPs to form a novel RNA splicing complex that antagonizes RBFOX2 splicing complex, resulting in oncogenic exon exclusion. Knockdown of SON inhibits proliferation and clonogenicity in vitro and tumor formation in vivo orthotopic xenografts models. These findings underscore the importance of SON-mediated RNA splicing in normal development and tumorigenesis and suggest its potential significance in other cancers. Therefore, SON and its associated complexes represent promising therapeutic targets for treatment of cancer and genetic diseases.

Keywords: SON, RNA splicing, ZTTK syndrome, Glioblastoma, PTBP1

S-14-2

Tumor-targeted therapy using engineered mesenchymal stem cells remodels tumor microenvironment

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Tumor cells interact with surrounding immune cells and stromal cells to generate the tumor microenvironment (TME) favorable to cancer growth. As cancer progresses, the TME becomes immune suppressive, resulting in a significant reduction in the number and functionality of tumor infiltrating lymphocytes (TILs). To address this, immunotherapies such as immune checkpoint blockade (ICB) and cytokine therapy have been explored. However, the therapeutic effect is limited in advanced solid tumor and severe adverse toxicity is often observed at therapeutic doses. Mesenchymal stem cells (MSCs), known for their capacity of tumor tropism, are encouraging vehicles to deliver therapeutics into the TME. In this study, we reported that newly designed MSCs become a potent cellular therapy for the targeted adjustable delivery of cytokines and immune-activating molecules into the TME. Tumor-targeted production of therapeutics remodels the TME to reinvigorate CD8 TILs and increase immune responses against tumor. Furthermore, engineered MSC therapy mediated TME remodeling overcomes the resistance in advanced solid tumor to ICB and adoptive T cell transfer (ACT). Overall, this next generation of MSC opens new avenues to improve the TME and rejuvenate CD8 TILs and thus potentiate ICB and ACT.

Keywords: Tumor microenvironment, Mesenchymal stem cell, Cytokine, Immune checkpoint blockade, T cell

S-14-3

In vivo mapping of subcellular proteomes in mice

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To facilitate the understanding of metabolic changes associated with disease, we have developed new in vivo tools that enable tissue-specific profiling of subcellular proteomes. First, we describe a method to profile in vivo mitochondrial proteomes utilizing transgenic mice expressing MTS-APEX2 (MAX-Tg), a peroxidase-based proximity labeling enzyme containing a mitochondrial matrix targeting sequence. Upon label activating conditions, MTS-APEX2 successfully biotinylate proteins in muscle tissues. Mass analysis of biotinylated proteomes confirmed specific and efficient labeling of the mitochondrial proteome and revealed tissue-specific patterns of the matrix proteome. Of these, we newly identified that RTN4IP1 is localized to the mitochondrial matrix and regulate CoQ biosynthesis. Second, we also generated iSLET (in situ Secretory protein Labeling via ER-anchored TurboID) mice which labels secretory pathway proteins, via proximity labeling activity by ER lumen targeted TurboID, an engineered biotin ligase. We expressed iSLET in the mouse liver and demonstrate efficient labeling of the liver secreted proteome which could be tracked and identified within circulating blood plasma. We expect MAX-Tg and iSLET mice will facilitate our understanding of mitochondrial function and interorgan communication.

Keywords: TurboID, Mitochondria, Secretory protein, Coenzyme Q, Insulin resistance

S-14-4

Exercise-induced-lactate promotes fatty acid oxidation by the TCA cycle and mitochondrial respiration in muscles of obese mice

Jin-Ho Koh
Yonsei University Wonju College of Medicine, Republic of Korea

Lower oxidative capacity in skeletal muscles (SKMs) is a prevailing cause of metabolic diseases. Exercise not only enhances the fatty acid oxidation (FAO) capacity of SKMs but also increases lactate levels. Given that lactate may contribute to tricarboxylic acid cycle (TCA) flux and impact monocarboxylate transporter 1 in the SKMs, we hypothesize that lactate can influence glucose and fatty acid (FA) metabolism. To test this hypothesis, we investigated the mechanism underlying lactate-driven FAO regulation in the SKM of mice with diet-induced obesity (DIO). Lactate was administered to DIO mice immediately after exercise for over 3 weeks. We found that increased lactate levels enhanced energy expenditure mediated by fat metabolism during exercise recovery and decreased triglyceride levels in DIO mice SKMs. To determine the lactate-specific effects without exercise, we administered lactate to mice on a high-fat diet (HFD) for 8 wk. Similar to our exercise conditions, lactate increased FAO, TCA cycle activity, and mitochondrial respiration in the SKMs of HFD-fed mice. In addition, under sufficient FA conditions, lactate increased uncoupling protein-3 abundance via the NADH-NAD þ shuttle. Conversely, ATP synthase abundance decreased in the SKMs of HFD mice. Taken together, our results suggest that lactate amplifies the adaptive increase in FAO capacity mediated by the TCA cycle and mitochondrial respiration in SKMs under sufficient FA abundance.

Symposia 15. Young Faculty Presentation Part 3. Infection and Immunology

S-15-1

Sesamin enhances apoptosis of activated T cells by physically interacting with MCL-1 and shows therapeutic effect on allergic dermatitis

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Sesamin is a lignan compound in plants that has various pharmacological effects, including reducing diabetes-associated injuries, cholesterol metabolism, and antitumor effect with anti-proliferative and pro-apoptotic properties. Nevertheless it has been investigated T cell-mediated disorders usually occur when the apoptosis pathway of activated effector T cells is not controlled well, however, it is still unknown whether sesamin attenuates T cell-mediated diseases with promotion of apoptosis on activated T cells. Quantitative PCR and flow cytometry results demonstrated sesamin suppresses IL-2 production and CD69 expression from activated T cells. In silico analysis showed Myeloid cell leukemia 1 (MCL-1) is predicted as target molecule of sesamin and pulldown assay validated it physically interacts with MCL-1 in T cells. Results from Western blot and immunoprecipitation assay confirmed sesamin regulates T cell activation by modulating MCL-1 activity and such inhibition blocks heterodimer interaction between MCL-1 and Bak in activated T cells. We found sesamin selectively induces cell death pathway only in activated T cells. To confirm our hypothesis, atopic dermatitis (AD) animal model as T cell-mediated disease induced by dinitrochlorobenzene (DNCB)/house dust mite extract was used. Oral administration of sesamin improves AD by attenuating pathological manifestations, expression of atopic genes and systemic immune response. Western blot analysis also confirmed such improvements are significantly co-related with promotion of cell death and modulation of MCL-1 activity by oral administration of sesamin. Therefore, these results suggest sesamin has a therapeutic potential for T-cell mediated disease through physical interaction with MCL-1 which promotes apoptosis of activated T cells exclusively.

Keywords: Sesamin, Atopic dermatitis, T cell activation, MCL-1, Proliferation

S-15-2

Tofacitinib Uptake by patient-derived intestinal organoids predicts individual clinical responsiveness

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Despite increasing therapeutic options in the treatment of ulcerative colitis (UC), achieving disease remission remains a major clinical challenge. Nonresponse to therapy is common and clinicians have little guidance in selecting the optimal therapy for an individual patient. This study examined whether patient-derived materials could predict individual clinical responsiveness to the Janus kinase (JAK) inhibitor, tofacitinib, prior to treatment initiation. For this, in 48 patients with UC initiating tofacitinib, we longitudinally collected clinical covariates, stool, and colonic biopsies to analyze the microbiota, transcriptome, and exome variations associated with clinical responsiveness at week 24. We established patient-derived organoids (n = 23) to determine how their viability upon stimulation with proinflammatory cytokines in the presence of tofacitinib related to drug responsiveness in patients. We performed additional biochemical analyses of organoids and primarytissues to identify the mechanism underlying differential tofacitinib sensitivity. The compositionof the gut microbiota, rectal transcriptome, inflammatory biomarkers, and exome variations were indistinguishable

among UC patients prior to tofacitinib treatment. However, a subset of patient-derived organoids displayed reduced sensitivity to tofacitinib as determined by the ability of the drug to inhibit STAT1 phosphorylation and loss of viability upon cytokine stimulation. Remarkably, sensitivity of organoids to tofacitinib predicted individual clinical patient responsiveness. Reduced responsiveness to tofacitinib was associated with decreased levels of the cationic transporter MATE1, which mediates tofacitinib uptake. Therefore, Patient-derived intestinal organoids predict and identify mechanisms of individual tofacitinib responsiveness in UC. Specifically, MATE1 expression predicted clinical response to tofacitinib.

Keywords: Ulcerative colitis, Tofacitinib, JAK-STAT inhibitor, Human intestinal organoids, MATE1

S-15-3

Principles and applications of atomic force microscopy in studying virus entry mechanism

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Viruses are intracellular pathogens that depend on host organisms for all stages of their replication cycle. During millions of years of evolution and adaptation to their hosts, viruses acquired the relevant molecular factors to exploit and control cellular functions. Receptor-mediated virus entry into a host cell is a complex multistep process where the virus must overcome various obstacles to access host machinery for replication. Elucidating the complex interplay of viruses and their receptors is important to gain a full understanding of the entry process. Virus infection is a multistep process in which the dynamics of each step are crucial, and therefore conducting experiments using living cells maintained under physiological conditions is essential. Moreover, the molecular and mechanistic basis of virus binding to the cell surface and entering the host cell is still not fully deciphered. Using confocal-combined atomic force microscopy, I study virus infection mechanism from virus binding to cell surface receptors to the endocytosis of virus. The studies are to establish a full picture of the initial attachment and entry steps. The investigation covers the dynamics, kinetics, and thermodynamics of the virion interaction during the cell surface binding step, as well as during endocytosis.

Keywords: AFM, Virus, Binding, Entry, Infection

S-15-4

In vivo imaging of invasive aspergillosis with 18F-fluorodeoxysorbitol positron emission tomography in small animals

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Invasive aspergillosis is a critical complication in immunocompromised patients with hematologic malignancies or with viral pneumonia caused by influenza virus or SARS-CoV-2. Although early and accurate diagnosis of invasive aspergillosis can maximize clinical outcomes, current diagnostic methods are time-consuming and poorly sensitive. Here, we assess the ability of 2-deoxy-2-^{18}F-fluorosorbitol (^{18}F-FDS) positron emission tomography (PET) to specifically and noninvasively detect *Aspergillus* infections. We show that ^{18}F-FDS PET can be used to visualize *Aspergillus fumigatus* infection of the lungs, brain, and muscles in mouse models. In particular, ^{18}F-FDS can distinguish pulmonary aspergillosis from *Staphylococcus aureus* infection, both of which induce pulmonary infiltrates in immunocompromised patients. Thus, our results indicate that the combination of ^{18}F-FDS PET and appropriate clinical information may be useful in the differential diagnosis and localization of invasive aspergillosis.

Keywords: 2-Deoxy-2-^{18}F-fluorosorbitol (^{18}F-FDS), Invasive aspergillosis, *Aspergillus fumigatus*, Positron emission tomography, Molecular imaging

Symposia 16. Inflammation and aging

S-16-1

Role of interaction between cancer-associated fibroblasts and apoptotic cancer cells in lung cancer suppression

Jihee Lee
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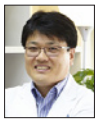
The interplay between apoptotic cancer cells and the tumor microenvironment (TME) influences cancer growth, progression and metastasis. We demonstrate that treatment with conditioned medium (CM) from lung cancer-associated fibroblasts (CAFs) exposed to apoptotic cancer cells suppresses proliferation and promotes apoptosis in lung cancer cells via WSP-1-integrin αvβ3-STAT1 signaling pathway. *In vivo* administration of CM from CAFs exposed to apoptotic 344SQ cells (ApoSQ-CAF CM) potently suppressed tumor growth, reduced tumor-supportive tumor-associated macrophages (M2 TAMs) and the phenotype transition of M2 into M1-like TAMs within the TME, whereas WISP-1-immunodepleted ApoSQ-CAF CM reversed these effects. Furthermore, WISP-1 signaled through integrin α5β3-STAT1 to inhibit survival and promote apoptosis in M2 macrophages and induce the phenotype change of M2 into M1-like macrophages in a paracrine manner. Thus, these data suggest that CM from apoptotic cancer cell-exposed CAFs may be an effective therapeutic strategy by targeting both tumor cells and M2 TAMs.

Keywords: Cancer-associated fibroblasts, Apoptotic cancer cells, Tumor-associated macrophages, Tumor growth, Efferocytosis

S-16-2

Novel target for antiaging intervention in the elderly:from the aspect of mid old cells



Tae Jun Park
Ajou University School of Medicine, Republic of Korea

The biological process of aging is thought to result in part from accumulation of senescent cells in organs. However, the present study identified that the numbers of full-senescent cells were not increased in normal elderly tissue. Instead, fibroblasts and smooth muscle cells that were neither proliferative nor fully senescent were prevalent in tissues of the elderly, which we termed "mid-old" cells. Upregulation of pro-inflammatory genes (*IL1β*, *SAA1*) and downregulation of anti-inflammatory genes (*SLIT2*, *CXCL12*) were detected in mid-old cells. In the stroma, SAA1 promotes development of the inflammatory microenvironment via upregulation of MMP9, which decreases the stability of epithelial cells present on the basement membrane, decreasing epithelial cell function. Strikingly, the microenvironmental change and the functional decline of mid-old cells could be rejuvenated by a young cell-originated protein, SLIT2. We provided the functional reverse of mid-old cells rather than elimination of senescent cells as a new concept about rejuvenation.

Keywords: Aging, Rejuvenation, Mid-old cell, SLIT2, SAA1

S-16-3

Supramolecular Senolytics via Intracellular Oligomerization of Peptides

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Senescence is an important factor in many common diseases globally, especially in several age-related diseases. Senolytics, a type of drug that can eliminate senescent cells, is promising in regard to developing new treatments for senescence-related diseases. However, there are limitations in the current usage of these drugs in terms of low specificity and the induction of severe side effects. In the current study, we developed supramolecular senolytics to address these concerns. We utilized intracellular oligomerization systems, which selectively occurs in senescent cells because of elevated ROS levels, to generate self-assembling senolytics. The underlying mechanisms of this method were further investigated using mouse models to assess the impacts of mitochondrial ablation in retinal tissues as a treatment method for age-related macular degeneration. The results of this study are very promising and indicate that specific targeted mitochondrial ablation using self-assembling senolytics could be a potentially novel treatment strategy for age-related macular degeneration, as well as other senescence-related diseases.

Keywords: Senolytic, Anti-aging, Supramolecular chemistry, Peptide-self-assembly, Mitochondria

S-16-4

Senescent microglia: a universal target in brain aging and neurodegenerative diseases

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Brain aging is a recognized risk factor for neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease). However, the complex relationship between brain aging and the development of these conditions is not yet fully understood. Cellular senescence is believed to contribute to cellular dysfunction and chronic inflammation, known as inflammaging. According to the threshold theory of senescent cell accumulation, susceptibility to neurodegenerative diseases is linked to the rates of senescent cell formation and their clearance within the brain. Microglia play a key role in removing senescent cells, and the buildup of senescent microglia may accelerate brain aging, exacerbating inflammaging and increasing the risk of neurodegenerative diseases. In this symposium, I suggest that microglia senescence, which is particularly sensitive to aging, might be a central factor in the progression of neurodegenerative diseases. Targeting senescent microglia presents a promising approach for alleviating these conditions.

Keywords: Brain aging, Senescent microglia, Neurodegenrative diseases, Dna damage, Rejuvenation

Symposia 17. Exploring novel pain circuits from the periphery to the brain

S-17-1

Translational neurophotonics for visualizing and manipulating the nervous system

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Neurophotonics, a field at the intersection of neuroscience and photonics, offers state-of-the-art tools for visualizing and modulating the nervous system. These tools are essential in tackling complex neurologic diseases, including neuropathic pain. The use of in vivo imaging techniques in animal disease models has shed light on neural functionalities, fostering the development of therapies that bridge the gap between bench-side research and bedside application.

Our research centers on the advancement of laser speckle imaging (LSI) for the precise measurement of cerebral blood flow, a potential biomarker for the characterization of vascular diseases. Utilizing a focal photothrombosis, we developed an innovative optical speckle image velocimetry (OSIV) method for the quantitative imaging of blood flow. These imaging modalities reveal cerebral dynamics in real-time, offering critical insights into the pathological processes that affect the nervous system.

Moreover, the investigation employs a cross-disciplinary strategies to confront the complexities of intractable pain—a significant contemporary healthcare challenge. Our methods include developing neuropathic pain animal models and applying photobiomodulation to mitigate chronic pain. Additionally, we harness neuromodulation technologies and employ artificial intelligence for quantitative pain assessment.

More broadly, our work exemplifies the translational capacity by revealing the mechanisms underlying brain diseases and forging new paths for intervention. We engage with preclinical animal models to address conditions such as ischemic stroke and chronic pain, meeting clinical demands. By harnessing sophisticated optical technologies, we aim to enhance our comprehension of neural disorders and formulate effective, non-invasive prevention and treatment strategies. This research is anticipated to refine therapeutic approaches and facilitate their smooth transition into clinical practice, thereby setting the stage for future neurophysiological advancements.

Keywords: Neurophotonics, In vivo imaging, Neuropathic pain, Laser speckle imaging, Photobiomodulation

S-17-2

Neuroimmunity in Pain: Role of Natural Killer Cells

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Recently, role of neuroimmune interaction has been the subject of significant interest in pain research. We have demonstrated the resolution of persistent painful peripheral neuropathy through the clearance of partially damaged sensory nerves by innate immune natural killer (NK) cells (Davies et al., 2019, 2020). Based on this work, I will present sciatic partial crush injury (PCI) model as a new preclinical model which is suitable to study both peripheral nerve regeneration and pain in the spinal system (Kim et al., 2021, 2023a), and also discuss potential therapeutic targets for NK cells which might be utilized for the treatment of chronic neuropathic pain (Kim et al., 2023b). Further translational and clinical research, along with mechanistic studies in preclinical models, are required to address whether NK cell immunotherapy is a promising alternative to opioid drugs for the effective management of chronic neuropathic pain.

Keywords: Neuropathic pain, Natural killer cell, Peripheral neuropathy,

Crush injury, Immunotherapy

S-17-3

Nocifensive behavior-associated activation of cerebellar Bergmann glia modulate chronic neuropathic pain

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The cerebellum is activated during physiological and pathological states of pain in human brain imaging studies. However, the neural circuits and molecular mechanisms underlying the processing of pain information in the cerebellum remain unknown. Using two-photon microscopy and optogenetics in mice, we found that the locus coeruleus (LC) terminals in the cerebellar cortex release noradrenaline (NA) in response to cutaneous noxious electrical stimuli. Most Bergmann glia (BG) accumulated this LC-NA noxious information by increasing intracellular calcium in an integrative manner. This global calcium activation of BG, referred to as "flare," was also elicited in response to an intraplantar capsaicin injection. Miniature microscopy from awake mice revealed temporal association between pain-evoked calcium activation of BG and a nocifensive licking behaviour. Chemogenetic inactivation of LC terminals or BG in the cerebellar cortex suppressed BG flares and reduced licking. BG-specific knockdown of α1 adrenergic receptors also suppressed capsaicin-induced BG flares and licking. Additionally, these BG manipulations displayed analgesic effects on chronic neuropathic pain caused by nerve injury. Finally, chemogenetic activation of BG or an intraplantar capsaicin injection reduced Purkinje cell firings, which may disinhibit the output activity of the deep cerebellar nuclei. These results suggest that BG in the cerebellar cortex play an essential role in computing noxious information ascending from the LC and modulating pain-related behaviours by controlling the activity of the cerebellar neural circuits.

Keywords: Cerebellum, Pain, Glia, Noradrenaline, Locus coeruleus

S-17-4

Metabotropic glutamate receptors in the brain show characteristic patterns in neuropathic pain state

Geehoon Chung
Neurogrin, Republic of Korea

Patients with neuropathic pain often suffer from persistent and severe pain even after the initial nerve injury has subsided. This can be attributed to maladaptive changes in the nervous system. This presentation focuses on changes in brain regions, with a particular focus on the metabotropic glutamate receptor 5 (mGluR5). It explores the brain mechanisms underlying (1) impairment of pain modulation by the periaqueductal gray (PAG) and rostral ventromedial medulla (RVM), (2) comorbid expression of pain and negative moods by the medial prefrontal cortex (mPFC), and (3) prolonged tactile hypersensitivity by the primary somatosensory cortex dysgranular zone (S1DZ). The talk also discusses how data from animal experiments can be utilized to address issues related to the development of diagnostic and therapeutic tools.

Keywords: Neuropathic pain, Metabotropic glutamate receptor, Brain imaging, PET, Pattern analysis

Symposia 18. Revealing underlying mechanism of metabophyiology through Multi-omics analysis

S-18-1

The role of NAD+ recycling at the nexus of glucose and lipid metabolism

Wondong Kim
Hanyang University, Republic of Korea

In glycolysis, glucose metabolism is coupled to the reduction of cytosolic nicotinamide adenine dinucleotide (NAD+) to NADH. Under aerobic conditions, the transfer of electrons into mitochondria and ultimately to the mitochondrial electron transport chain (ETC) can regenerate NAD+, whereas the cytosolic reduction of pyruvate to lactate can regenerate NAD+ when mitochondrial respiration is impaired. In addition to modulating membrane fluidity, HUFAs can be released from membrane lipids and then converted to eicosanoids and other bioactive molecules that play diverse roles in health and disease. As such, the significance of D5D and D6D activity has largely been viewed in terms of the biologic actions of their enzymatic end products. Dietary intake and transcriptional control of FADS1 and FADS2 expression are established determinants of cellular HUFA content. We show that changes in cytosolic NAD+ and NADH redox states also influence delta-5 and -6 desaturases (D5D and D6D) activity, establishing a bidirectional link between glycolysis and polyunsaturated fatty acid desaturation. These findings alter the existing paradigm of NAD+ regeneration in glycolysis and highlight a key biologic role for D5D and D6D action independent of their end products. Consistent with this, a type 2 diabetes risk haplotype in SLC16A11 that reduces pyruvate transport (thus limiting lactate production) increases D5D and D6D activity in vitro and in humans, demonstrating a chronic effect of desaturase mediated NAD+ recycling. Using aptamer-based proteomics and LC-MS-based metabolomics, we established a role for kidney-derived glycerol-3-phosphate (G-3-P) in mineral metabolism and outline potential targets to modulate FGF23 production during kidney injury in humans and mice. G-3-P is a downstream product of glycolysis, a ubiquitous metabolic process, and G-3-P production is coupled through cytosolic NAD+ recycling. These findings place NAD+ recycling at the nexus of glucose and lipid metabolism and provide a mechanism for metabolic reprogramming in human metabolic disease.

Acknowledgement: This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (2022R1C1C101178913 and RS-2023-00217123).

Keywords: Glucose metabolism, NAD+ recycling, Fatty acid desaturation, Glycerol-3-phosphate, Chronic kidney disease

S-18-2

Fibrotic tumor microenvironment promotes metastatic tumor growth in fatty liver

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Liver metastasis extremely worsens the prognosis for patients with colorectal cancer (CRC). Our previous study demonstrated that fatty liver promotes metastatic tumor microenvironment (TME) via extracellular vesicles and yes-associated protein (YAP). The underlying mechanism of CRC liver metastasis enhanced by fatty liver is not fully understood. Here, we demonstrate fatty liver modulates fibrotic TME to enhance metastatic cancer activity through hyaluronan (HA) synthase 2 (HAS2), regulated by cancer YAP. HFD-induced fatty liver increases the myofibroblastic cancer-associated fibroblast (CAF) infiltration and the production of extracellular matrix (ECM) collagen and HA. First, we investigated the role of HAS2 in liver metastasis enhanced by fatty liver by using hepatic stellate cell (HSC)-specific *Has2*-deleted (*Has2*$^{\Delta HSC}$) mice. *Has2*$^{\Delta HSC}$ mice had reduced metastatic tumor growth,

CAF activity, ECM production, and M2 macrophage infiltration, enhanced by fatty liver. In addition to the known function of cancer YAP-mediated M2 macrophage infiltration, our study revealed cancer YAP also regulates CAF activity and HAS2 expression via CTGF. Our single cell analyses further revealed the link of CAF-derived HAS2 with M2 macrophages and CRC cells through CD44; these cells further associate with exhausted CD8 T cells via PD-L1/PD-1 interaction. Lastly, we verified that 4-methylumbelliferone and 4-methylumbelliferyl glucuronide, both HA synthesis inhibitors, reduced metastatic activities of CRC, CAF, YAP, and M2 macrophages, enhanced by fatty liver. In conclusion, we determined fatty liver promotes fibrotic TME for enhancing liver metastasis; fibrotic TME regulated by CAF, YAP, and HAS2 enhances metastatic potential of CRC in the liver.

Keywords: Colorectal cancer, Cancer-associated fibroblast, Connective tissue growth factor, Extracellular matrix, YAP

S-18-3

Nearby nutrients dictate metabolism and maintain open chromatin landscape to support cancer growth

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POSTECH, Republic of Korea

There is current dire need to develop effective therapies for pancreatic ductal adenocarcinoma (PDA), a highly lethal malignancy on the rise with extremely poor prognosis. Although targeting tumor metabolism has been the focus of intense investigation for over a decade now, tumor metabolic plasticity and a high risk of toxicity have challenged this anti-cancer strategy. Here we show using genetic and pharmacological approaches in human and murine *in vitro* and *in vivo* models, that PDA has a distinct dependence on *de novo* ornithine synthesis (DNS) from glutamine via ornithine aminotransferase (OAT), which supports polyamine synthesis and is required for tumor growth. This directional OAT activity is normally largely restricted to infancy and contrasts with the reliance of most adult normal tissues and other cancer types on arginine-derived ornithine for polyamine synthesis. We find that this dependence associates with arginine depletion in PDA tumor microenvironment, and is driven by mutant KRAS, which induces the expression of OAT and polyamine synthesis enzymes, leading to alterations in the transcriptome and open chromatin landscape in PDA tumor cells. The distinct dependence of PDA but not normal tissue on OAT-mediated DNS provides an attractive therapeutic window for treating pancreatic cancer patients with minimal toxicity.

Keywords: Cancer metabolism, Tumor microenvironments, Metabolomics, Glutamine, Polyamine

S-18-4

Host and microbial compensation in a model of leucine breakdown deficienty

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Dankook University, Republic of Korea

In humans, defects in leucine catabolism cause a variety of inborn errors in metabolism. Here, we use Caenorhabditis elegans to investigate the impact of mutations in mccc-1, an enzyme that functions in leucine breakdown. Through untargeted metabolomic and transcriptomic analyses we find extensive metabolic rewiring that helps to detoxify leucine breakdown intermediates via conversion into previously undescribed metabolites and to synthesize mevalonate, an essential metabolite. We also find that the leucine breakdown product 3,3-hydroxymethylbutyrate (HMB), commonly used as a human muscle-building supplement, is toxic to C. elegans and that bacteria modulate this toxicity. Unbiased genetic screens revealed interactions between the host and microbe, where components of bacterial pyrimidine biosynthesis mitigate HMB toxicity. Finally, upregulated ketone body metabolism genes in mccc-1 mutants provide an alternative route for biosynthesis of the mevalonate precursor 3-hydroxy-3-methylglutaryl-CoA. Our work demonstrates that a complex host-bacteria interplay rewires metabolism to allow host survival when leucine catabolism is perturbed.

Keywords: Leucine, HMB, Metabolism, Inborn errors of metabolism

Young Investigator Oral Presentation

Y-01

Nuclear aggregation of profilin-1 impairs the phagocytic function of DNA damage-induced senescent microglia

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The accumulation of DNA damage is a defining characteristic of cellular senescence. Furthermore, senescent microglia play a pivotal role in the pathogenesis of neurodegenerative diseases associated with brain aging. Nevertheless, the mechanisms regulating DNA damage repair in microglia remain poorly characterized. This study demonstrates that profilin-1 (PFN1), an actin-binding protein, translocates from the cytoplasm to the nucleus in response to DNA double-strand breaks induced by doxorubicin. This nuclear relocation of PFN1 is accompanied by an increase in nuclear F-actin formation following DNA damage. It is noteworthy that double-strand break repair in microglia is rapidly mediated through the non-homologous end joining (NHEJ) pathway. Our findings indicate that the impairment of PFN1 function, whether through the knockdown PFN1 or inhibition of its nuclear transport, results in the disruption of DNA repair efficiency in microglia. In DNA damage-induced senescent microglia, the increased nuclear localization of PFN1 was associated with a reduction in phagocytic function, linked to the formation of nuclear F-actin. However, the actin-depolymerizing agent cytochalasin D did not induce the relocation of PFN1 back to the cytoplasm, and PFN1 remained aggregated at DNA damage foci. Our findings suggest that while nuclear PFN1 plays a role in repairing DNA double-strand breaks, its failure to return to the cytoplasm in senescent microglia leads to impaired phagocytic function due to nuclear aggregation.

Acknowledgement: This work was supported by a grant (2023R1A2C1006622 to MSK) and the K-Brain Project (RS-2023-00265515 to MSK) of the National Research Foundation (NRF) funded by the Ministry of Science and ICT (MSIT), Republic of Korea. We would like to thank the CheongNyeong Research Foundation (CNRF) for providing a scholarship to Rim C.

Keywords: Senescent microglia, Profilin-1, DNA damage repair, Phagocytosis, Neurodegenerative diseases

Y-02

POMC neuron-specific mitochondrial methionyl-tRNA formyltransferase deficiency improves energy metabolism through enhanced sympathetic activity

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Mitochondrial methionyl-tRNA formyltransferase (MTFMT) is essential for the efficient translation of mtDNA-encoded proteins and may also influence stress response, inflammation, and proteostasis. All these processes are key regulators of pro-opiomelanocortin (POMC) neurons, which play a central role in maintaining global energy homeostasis. To explore MTFMT's role in POMC neurons, we generated tissue-specific knock-out (POMCMtfKO) mice using the Cre-loxP system. Male POMCMtfKO mice exhibited a significant reduction in body weight compared to their wild-type littermates, as a consequence of decreased food intake combined with increased energy expenditure. These mice showed increased glucose metabolism with improved glucose tolerance and insulin sensitivity, raised serum glucagon/insulin ratio, elevated hepatic glucose production, and depleted glycogen stores in the liver and skeletal muscle. Additionally, POMCMtfKO mice had decreased adiposity, browning of inguinal white adipose tissue, and increased thermogenesis, corresponding with elevated tyrosine hydroxylase staining. All these changes could be mediated by an increase in sympathetic tone, as confirmed by elevated resting serum norepinephrine levels. However, the metabolic changes observed were not as strong under high-fat diet conditions and absent during caloric restriction. These findings suggest that MTFMT knockout induces chronic, low-level stress, which activates POMC neurons and enhances metabolism by modulating the autonomic nervous system.

Keywords: Pro-opiomelanocortin (POMC) neurons, Mitochondrial methionyl-tRNA formyltransferase (MTFMT), Energy homeostasis, Sympathetic nervous system

Y-03

Astrocytic FoxO1 in the hypothalamus regulates metabolic homeostasis

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*These author contributed equally to this work.

Astrocytes play important role in the regulation of brain energy metabolism. Forkhead box transcription factor O1 (FoxO1) is a master regulator of cellular metabolism and hypothalamic FoxO1 controls food intake and energy balance. However, role of astrocytic FoxO1 in the regulation of brain energy metabolism and systemic homeostasis is unknown. Here, we report that FoxO1 is critical to maintain the glycolytic nature of astrocytes by regulating the pyruvate dehydrogenase kinase/pyruvate dehydrogenase (PDK/PDH) axis. FoxO1 inhibition shifts the cellular glucose metabolism of astrocytes towards oxidative metabolism, increasing cellular production and release of astrocytic ATP into extracellular environment. Accordingly, astrocytic FoxO1 ablation induces an overactivation of hypothalamic neuronal circuits leading to overfeeding and impaired glucose regulatory mechanism in response to metabolic changes under fasting-refeeding condition and predisposes mice to glucose dyshomeostasis and diet-induced obesity. Targeted deletion of hypothalamic astrocyte FoxO1 replicates such metabolic alterations, suggesting that astrocytic FoxO1 in the hypothalamus plays a key role in the control of brain energy metabolism and whole-body glucose homeostasis.

Keywords: Astrocyte, FoxO1, Energy metabolism, Glucose homeostasis, Hypothalamus

Y-04

Neurophysiological mechanisms of synaptic and cognitive dysfunction in phenylketonuria

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Phenylketonuria (PKU), one of the inborn errors of metabolism (IEMs) characterized by elevated blood phenylalanine (Phe) levels, is a common cause of intellectual disability. However, the mechanisms by which elevated Phe levels impair cognitive function remain unclear. In this study, we demonstrate that submillimolar Phe disrupts synaptic plasticity through the hy-

peractivation of GluN2B-containing NMDA receptors (NMDARs). L-Phe exhibited dose-dependent, bidirectional effects on NMDA-induced currents but did not affect synaptic NMDAR activity in hippocampal CA1 neurons. The hyperactivation of extrasynaptic GluN2B by L-Phe led to an activity-dependent downregulation of AMPA receptors (AMPARs) during burst or sustained synaptic activity. L-Phe administration reduced neural activity and learning performance, effects that were mitigated by pretreatment with GluN2B inhibitors. Furthermore, pharmacological and virus-mediated suppression of GluN2B reversed impaired learning in PKU model (Pah^{Enu2}) mice. Collectively, these findings suggest that pathological Phe concentrations in cerebrospinal fluid perturb extrasynaptic NMDAR function and synaptic plasticity in individuals with PKU and that GluN2B inhibition may represent a potential therapeutic strategy to improve cognitive function in PKU patients.

Keywords: Phenylketonuria, PKU, Cognitive impairment, GluN2B, Extrasynaptic NMDAR, Synaptic plasticity, LTP, AMPAR downregulation

Y-05

Distinct modulation of calcium-activated chloride channel TMEM16A by a novel drug-binding site

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TMEM16A is a calcium-activated chloride channel with significant role in epithelial fluid secretion, sensory transduction, and smooth muscle contraction. Several TMEM16A inhibitors have been identified; however, their binding sites and inhibitory mechanisms remain unclear. Using magnolol and honokiol, the two regioisomeric inhibitors, as chemical probes, we have identified a novel drug-binding site distinct from the pore region, in TMEM16A, which is described here. With electrophysiology, unbiased molecular docking and clustering, molecular dynamics simulations, and experimental validation with mutant cycle analysis, we show that magnolol and honokiol utilize different drug-binding sites, pore and non-pore pockets. The pore blocker utilizes amino acids crucial for chloride passage, whereas the non-pore blocker allosterically modulates the pore residues to hinder ion permeation. Among 17 inhibitors tested, 11 were pore blockers and six were non-pore blockers, indicating the importance of this newly identified non-pore pocket. Our study provides insights into drug-binding mechanism in TMEM16A together with a rationale for future drug development.

Keywords: TMEM16A, Anoctamin 1, Drug binding site, MD simulation, Autodock

Y-06

Roles of CALHM channels: Exploring ATP release hemichannel vs. Electrical gap junction, or both?

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The Calcium homeostasis modulator (CALHM) is a recently discovered voltage-dependent, nonselective ion channel that has garnered significant attention due to its implications in neuronal activity and taste perception. Over the past few years, our research has focused on investigating the electrophysiological characteristics of the CALHM ion channel, which encompass temperature sensitivity, pH dependency, and structural stability. Notably, CALHM exhibits a uniquely slow voltage-dependent activation that is influenced by factors such as temperature, pH, and $[Ca^{2+}]_e$. It is worth emphasizing that the conditions required for CALHM activation are exceptionally stringent in comparison to conventional ion channels. Under typical physiological conditions of temperature and pH, only strong depolarization exceeding 30 mV can elicit a discernible current through CALHM. These unique electrophysiological characteristics present formidable challenges when endeavoring to uncover the physiological functions of CALHM ion channels.

In this study, we have explored the intriguing hypothesis that the CALHM ion channel may function as a gap junction, supported by several compelling reasons: 1) CALHM shares a higher structural similarity with large-pore channels, including proteins known to participate in gap junction formation. 2) Cryo-EM investigations have revealed a head-to-head structural arrangement of CALHM2 and CALHM4, suggesting the potential for gap junction formation. 3) Hemichannel currents within the CALHM family are activated under rigorous conditions, and even CALHM2 fails to exhibit any current in transient-expression systems.

In the present research, we conducted measurements of gap-junction currents using the dual whole-cell patch clamp technique to validate the potential for CALHM to form gap junctions. Remarkably, we observed trans-junctional currents in HeLa cells expressing CALHM2, characterized by a symmetrical bell-shaped voltage-dependency, a typical hallmark of gap junction. These findings suggest that CALHM channels may indeed serve as critical components of gap junctions, potentially harboring physiological functions not as hemichannels but within the context of gap junctions.

Keywords: CALHM, Gap junction, Ion channel, Trans-junctional current

Y-07

Inhibition of Lactate Dehydrogenase A stimulates lipid catabolism and thermogenesis via AMPK and NADH in mouse brown adipose tissue

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Lactate dehydrogenase (LDH) isoforms A and B are key regulators of glycolysis, catalyzing the reversible conversion of pyruvate to lactate. Recent studies have shown that lactate upregulates mitochondrial function and thermogenesis in brown adipose tissue (BAT). However, the regulatory roles of LDH in adipose tissue metabolism have not been thoroughly investigated. In this study, we demonstrated that LDH-A is predominantly expressed in mouse BAT. Genetic suppression of LDH-A impaired glycolysis and upregulated mitochondrial proteins, including uncoupling protein 1 (UCP1) and electron transport chain (ETC) proteins, in differentiated brown adipocytes. LDH-A knockdown decreased cellular ATP levels, stimulating AMP-activated kinase (AMPK) signaling, which led to increased expression of peroxisome proliferator-activated receptor gamma coactivator 1α (PGC1α) and attenuated lipogenesis through acetyl-CoA carboxylase inactivation. These metabolic alterations in LDH-A suppression were blocked by compound C, an inhibitor of AMPK. Similarly, sodium oxamate, a competitive inhibitor of LDH-A, inhibited glycolysis, depleted ATP content, and activated AMPK in brown adipocytes. Oxamate also upregulated mitochondrial proteins, including UCP1, augmented fatty acid oxidation, and enhanced proton leak due to uncoupling of respiratory chain via UCP1. Exogenous lactate, similar to LDH-A inhibition, raised NADH/NAD^+ ratio and upregulated UCP1. Supplementation of pyruvate blunted the changes in NADH/NAD^+ and UCP1 by oxamate as well as lactate. Intraperitoneal injection of oxamate into normal chow and high-fat diet mice showed body weight reduction with improved insulin sensitivity and glucose tolerance. Oxamate *in vivo* activated AMPK, increased NADH/NAD^+, and upregulated UCP1 and ETC proteins, with β-oxidation, lipolytic, and thermogenic genes in BAT. Furthermore, oxamate application decreased lipid droplet size and number in the liver and adipose tissues and markedly induced browning of inguinal white adipose tissue, resulting in accelerated heat generation under cold stress (4 ℃). Taken together, our findings suggest that LDH could be a promising thera-

peutic target for obesity and chronic metabolic diseases through improving thermogenesis and lipid catabolism.

Y-08

Cancer cells induce lipolysis by secreting cytokine CCL to obtain free fatty acids from fat tissue for cancer proliferation and migration

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In our previous research, we demonstrated that free fatty acids (FFAs) derived from human adipocyte derived stem cells (hADSCs) increase metastasis of cancer cells by upregulating Hypoxia-inducible factor-1α (HIF-1α). For further study, we cocultured cancer cells with hADSCs to find out the trigger inducing lipolysis of hADSCs. Herein, we could mimic tumor micro-environment by using a PDMS 3D organoid co-culture system which is appropriate for observating cross-talk of two different cells (cancer cells and hADSCs).
In this present study, we revealed that cancer cells cocultured with hADSCs secrete a specific C-C motif cytokine (CCL), leading to lipolysis of hADSCs, so that cancer cells are able to use more FFAs to enhance their proliferation and metastasis. At the beginning, it was confirmed that HIF-1α increase in cancer cells when they are stimulated by FFAs from hADSCs. Also, the increased HIF-1α upregulates CCL by functioning as a transcriptional factor and increasing mRNA level of CCL. With cytokine array, we also found increased protein level of CCL in the conditioned media obtained from where cancer cells and hADSCs are cocultured, comparing where cancer cells are cultured only.
Interestingly, the CCL secreted from cancer cells again stimulates hADSCs. As a result, Peroxisome proliferator-activated receptor (PPAR) which is a transcriptional factor regulating lipolysis related genes is upregulated in hADSCs, inducing lipolysis. It was validated that the protein stability of PPAR increase by diminished binding with E3 ubiquitin ligase, HUWE1, when CCL is treated to hADSCs. Furthermore, with lipid staining, it was identified that the amount of lipid droplets of hADSCs is reduced by CCL treatment. Besides, when neutralizing antibody of CCL or PPAR inhibitor are treated to block CCL or PPAR function, the decreased lipid droplets are recovered. Also, the mRNA level of lipolysis related genes which are down-stream of PPAR, increases by CCL treatment, but it is recovered by the neutralizing antibody of CCL or PPAR inhibitor, verifying that CCL which is secreted from cancer cells, induces lipolysis of hADSCs.
In result, the more FFAs are derived from hADSCs, the more migration and proliferation are induced, making a vicious cycle between cancer cells and hADSCs. This was confirmed in vivo as well, showing that high fat dieted mice have more aggressive tumor than normal fat dieted mice. Additionally, in high fat dieted group, the volume of inguinal subcutaneous white adipose tissue which is adjacent to tumor shrank when it is compared with the other fat tissue which is not close with tumor. This result indicates that when there is stimulation of increased FFAs to tumor, the tumor can induce lipolysis from fat tissue for its growth.
In conclusion, it is shown that cancer cells can upregulate lipolysis of fat tissue via the chemokine, CCL to derive more FFAs from fat tissue and to consume the FFAs for its proliferation and migration. Therefore, this finding can support poor prognosis of cancer patients who have obesity.

Keywords: Cancer proliferation and migration, Obesity, Cytokine, Lipolysis, Cell to cell cross-talk

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Y-09

Gaussian filter-based image denoising detects hidden sweat glands and enhances accuracy of active sweat gland density (ASGD) measurements

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The quantitative sudomotor axon reflex test (QSART, Iontophoresis of 10 % ACh with 2mA*5min) is widely used in perspiration studies. However, it faces challenges such as suboptimal image quality and misidentification of hidden sweat glands as background noise. This study applied Gaussian filtering to reveal hidden active sweat gland density (ASGD) and enhance image clarity. 29 participants (18 males and 11 females) of ASGD data were collected from eight body regions – chest, abdomen, upper back, lower back, upper arm, forearm, thigh, and calf – on both left and right sides of the body. Improvement in image visibility was assessed after applying Gaussian filtering to collected images. Additionally, image reliability was analyzed by evaluating difference in ASGD between left and right sides of the body with the Wilcoxon signed-rank test and intraclass correlation coefficient (ICC). Results demonstrated that Gaussian filtering markedly increased ASGD detection across all eight body regions. Furthermore, both symmetry and reliability of sweat gland images showed improvements post-filtering. This research demonstrates that applying Gaussian filtering can effectively expose previously obscured sweat glands and significantly enhance the clarity and precision of ASGD detection. Moreover, our findings identify the 0.5 × 0.5 cm^2 unit as an optimal measurement scale for ASGD research, better than the 0.25 × 0.25 cm^2 unit. The introduction of this advanced measurement module with its superior accuracy has the potential to advance active sweat gland research with QSART. This module can be applied in various scientific fields.
Keywords: Active sweat gland density, QSART, Image enhancement, Gaussian filter

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Y-10

Compartment-specific protein expression and function of neuronal mitochondria

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Neurons have a distinct morphology characterized by axons and dendrites, enabling them to transmit signals to and from other neurons. Mitochondria, essential for cellular energy production and signaling, also exhibit compartment-specific shapes and physiological roles. Despite these observations, the functional distinctions between axonal and dendritic mitochondria remain underexplored. In this study, we are investigating the unique functional characteristics of axonal and dendritic mitochondria and their potential underlying mechanisms using three different approaches. First, we employed a mitochondria-targeting genetically encoded Ca^{2+} indicator (mito-jGCaMP8m) to measure mitochondrial Ca^{2+} signals in dendrites and axons following electrical stimulation. In addition, to earn more consistent data, spontaneous activities were blocked, but not evoked potentials. Second, we compared protein expression levels between axonal and whole-cell, including somatodendritic compartments by plating neurons on a porous membrane, then harvested the upper and lower membrane parts as whole-cell and axonal fractions, respectively. Lastly, we are currently exploring the functional importance of distinct mitochondrial Ca^{2+} regulation in a compartment-dependent way using live imaging and electrophysiological methods. We found that axonal mitochondria exhibit faster Ca^{2+} release rates and demonstrate ER-independent Ca^{2+} uptake. In contrast, dendritic mitochondria show slower Ca^{2+} release rates and predominantly depend on the endoplasmic reticulum (ER) for Ca^{2+} uptake. Furthermore, we identified several candidate genes potentially responsible for these functional differences. Collectively, our data would suggest fundamental cellular mechanisms to understand the distinct physiological roles of axonal and dendritic mitochondria.

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Keywords: Mitochondria, Axon, Dendrite, Calcium imaging, Mitochondrial calcium uniporter (MCU) complex

Y-11

Non-invasive neuromodulation of cerebrospinal fluid flow

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Cerebrospinal fluid (CSF) flow is essential for maintaining brain homeostasis, and its dysfunction is strongly linked to neurodegenerative diseases. As a highly active organ, the brain continuously generates metabolic waste, necessitating the efficient removal of by-products. Impaired CSF circulation is believed to be a key factor in the development of various neurological disorders, and restoring this circulation is considered a promising therapeutic strategy.
To modulate CSF flow using non-invasive methods, we employed two neuromodulatory techniques: transcutaneous auricular vagus nerve stimulation (taVNS) and transcranial focused ultrasound (FUS) stimulation. To provide direct, real-time evidence of CSF flow enhancement with the neuromodulation techniques, we utilized multi-level of in vivo imaging techniques, including two-photon microscopy and wide-field optical imaging to visualize CSF tracer dynamics.
Our results demonstrated that taVNS improved cognitive function impaired by surgically induced transient global cerebral ischemia, while also increasing CSF influx and flow velocity. This enhancement in CSF dynamics may facilitate brain clearance, contributing to a more favorable prognosis following ischemic events. On the other hand, FUS, applied at the skull base to enable cortical in vivo imaging, enhanced CSF flow and improved efflux dynamics, as confirmed by in vivo two photon and wide-field CSF tracer imaging, without causing any tissue injury or blood brain barrier damage.
These findings indicate that non-invasive neuromodulation techniques show promise as therapeutic approaches for enhancing CSF flow and could be translated into clinical treatments for neurodegenerative diseases.

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Keywords: Cerebrospinal fluid, Neuromodulation, Vagus nerve stimulation, Focused ultrasound stimulation

Y-12

Comparison of modulation efficiency with electrical stimulation between normal and degenerated primate retina

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With electrical stimulation, retinal prostheses bypass dysfunctional photoreceptors and activate the surviving bipolar or retinal ganglion cells (RGCs). Therefore, the effective modulation of RGCs is crucial for developing retinal prostheses. Substantial research has been performed on the ability of an electrical stimulus to generate a reliable RGC response. However, different experimental conditions show varying levels of how well the electrical stimulation evokes RGC spikes. Therefore, in this study, we attempted to extract an indicator to understand how the electrical stimulation effectively evokes RGC spikes. Six cynomolgus monkeys were used: three as controls and three as an N-methyl-N-nitrosourea (MNU)-induced retinal degeneration model. The retinal recordings were performed using 8 × 8 multi-electrode arrays (MEAs). Electrical stimulation consisted of symmetrical biphasic pulses of varying amplitudes and durations. The number of stimulation conditions that resulted in significantly higher post-stimulation firing rates than pre-stimulus firing rates was defined as the modulation efficiency ratio (MER). The MER was significantly lower in degenerated retinas than in normal retinas. We investigated the relationship between the variables and the MER in normal and degenerated primate RGCs. External variables, such as duration and inter-electrode distance, and internal variables, such as average firing rates and statistics (mean, standard deviation, and coefficient of variation [CV]) of inter-spike intervals (ISIs) of spontaneous spikes, were used. External variables had similar effects on MER in normal and degenerated RGCs. In contrast, internal variables affected MER differently in normal and degenerated RGCs. While in normal RGCs, they were not related to MER, in degenerated RGCs, the mean ISIs were positively correlated with MER, and the CV of ISIs was negatively correlated with MER. The most critical variable affecting MER was the mean ISI. A shorter ISI indicates hyperactive firing in the degenerated retina, which prevents electrical stimulation from evoking more RGCs. We believe this hyperactivity in degenerated retinas results in a lower MER than that in the normal retina. Our findings can be used to optimize the selection of stimulation channels for in vitro MEA experiments and practical calibration methods to achieve higher efficiency when testing retinal prostheses.

Keywords: Retinal prosthesis, Retinal ganglion cell, Electrical stimulation, Spontaneous firing, Inter-spike interval, Modulation efficiency

Y-13

Role of the STING-IRF3 pathway in ambient GABA homeostasis and cognitive function

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Targeting altered expression and/or activity of GABA transporters (GATs) provide therapeutic benefit for age-related impairments, including cognitive dysfunction. However, the mechanisms underlying the transcriptional regulation of GATs are unknown. In the present study, we demonstrated that the stimulator of interferon genes (STING) upregulates GAT1 and GAT3 expression in the brain which resulted in cognitive dysfunction. Genetic and pharmacological intervention of STING suppressed the expression of both GAT1 and GAT3, increased the ambient GABA concentration, and therefore, enhanced tonic GABAA inhibition of principal hippocampal neurons, resulting in spatial learning and working memory deficits in mice in a type I interferon (IFN I)-independent manner. Stimulation of the STING-GAT pathway efficiently restored cognitive dysfunction in STING-deficient mice models. Our study uncovered for the first time that the STING signaling pathway regulates GATs expression in a cell autonomous manner and therefore could be a novel target for GABAergic cognitive deficits.

Keywords: GATs, Memory, STING-IRF3 pathway, Tonic GAGAA current

Y-14

GLP-1 and its Derived Peptides Mediate Pain Relief Through Direct TRPV1 Inhibition Without Affecting Thermoregulation

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Hormonal regulation during food ingestion and its association with pain prompted the investigation of the impact of glucagon-like peptide-1 (GLP-1) on transient receptor potential vanilloid 1 (TRPV1). Both endogenous and synthetic GLP-1, as well as a GLP-1R antagonist, exendin 9–39, reduced heat sensitivity in naïve mice. GLP-1-derived peptides (liraglutide, exendin-4, and exendin 9–39) effectively inhibited capsaicin (CAP)-induced currents and calcium responses in cultured sensory neurons and TRPV1-expressing cell lines. Notably, exendin 9–39 alleviated CAP-induced acute pain, as well as chronic pain induced by complete Freund's adjuvant (CFA) and spared nerve injury (SNI), in mice without causing hyperthermia associated with other TRPV1 inhibitors. Electrophysiological analyses revealed that exendin 9–39 binds to the extracellular side of TRPV1, functioning as a noncompetitive inhibitor of CAP. Exendin 9–39 did not affect proton-induced TRPV1 activation, suggesting its selective antagonism. Among the exendin 9–39 fragments, exendin 20–29 specifically binds to TRPV1, alleviating pain in both acute and chronic pain models without interfering with GLP-1R function. Our study revealed a novel role for GLP-1 and its derivatives in pain relief, suggesting exendin 20–29 as a promising therapeutic candidate.

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Keywords: Transient receptor potential vanilloid 1, Glucagon-like peptide-1, Exendin 9–39, GLP-1-derived peptides, Sensory neurons, Pain relief

Y-15

Impaired mitophagy flux and mitochondrial dysfunction in pulmonary arterial hypertensive smooth muscle and their recovery by KV7.4 activator URO-K10

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Pulmonary arterial hypertension (PAH) induces various changes in signaling and metabolic pathways in pulmonary artery smooth muscle cells (PASMC), leading to ionic remodeling such as downregulation of K+ channels. However, we reported that KV7 channel activity is maintained or even upregulated in PAH PASMCs. In this context, targeting KV7 channels with agonists presents a promising therapeutic approach for the treatment of PAH. In the monocrotalin-induced PAH rats (MCT-PAH), Kv7.4 activator URO-K10 was applied using osmotic mini-pump (MCT-PAH/UK10). Both body weight increase and survival rate were improved in MCT-PAH/UK10. Also, RV hypertrophy and pulmonary arterial thickening were attenuated. Electron microscopy revealed increased mitochondrial fission and mitophagy in PAH-MCT, which were prevented in MCT-PAH/UK10. Consistent with these findings, immunoblot studies revealed upregulation of DRP1, TOMM20, and LAMP2, with their levels were normalized in MCT-PAH/UK10. Oxidative phosphorylation analysis revealed decreased levels of maximal respiration, spare respiratory capacity, and OCR/ECAR in PASMCs primarily cultured from PAH-MCT rats, which were restored in MCT-PAH/UK10. Both mitochondrial membrane potential (Ψm) and mitochondrial ROS were increased in PAH-MCT, and reversed in MCT-PAH/UK10. Immunoblot studies showed an increased LC3-II/LC3-I ratio, p62, and PINK1/PARKIN signaling, indicating increased autophagosome formation but incomplete mitochondrial degradation, which was resolved through URO-K10 treatment. Taken together, these findings suggest that URO-K10 not only improves pulmonary vascular function but also restores mitochondrial homeostasis, offering a novel therapeutic strategy for the treatment of pulmonary arterial hypertension.

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Keywords: Pulmonary arterial hypertension, Mitochondria dysfunction, MitoKv7.4, Mitophagy

Y-16

Effects of caffeine ingestion and thermotherapy on blood orexin circulation in humans

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Caffeine and orexin can affect awakening, neuroendocrine, and sympathetic nerve function. Our previous study has reported that caffeine intake can

increase human body temperature. However, little is known about the combined effects of thermotherapy and caffeine intake on human serum orexin concentrations. Forty-two healthy male subjects with age of 26.72±5.05 years, height of 174.10±7.09 cm, and body weight of 74.68±8.91 kg participated in this study. They were randomly assigned to a control (CON) group (n=21) and a caffeine (CAFF) group (n=21). After thermotherapy (half-body immersion in a hot water bath at 42±0.5 ℃), circulating orexin level increased more ($p<0.05$) in the CAFF group than in the CON group. Positive relationships between mean body temperature and orexin were observed before and after heat stimulation ($p<0.001$). Caffeine intake boosted the upregulation of serum orexin concentrations in subjects undergoing thermotherapy.

Keywords: Caffeine, Orexin, Thermotherapy, Neuroendocrine, Sympathetic nervous system

Y-17

Anti-inflammatory effects of fermented and aged mountain-cultivated ginseng sprouts via suppression of MAPK-NF-κB pathway in lipopolysaccharide-stimulated RAW264.7 macrophages

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Fermented and aged mountain-cultivated ginseng sprouts (FAMCGS) exhibit superior antioxidant and anti-inflammatory properties compared to mountain-cultivated ginseng sprouts (MCGS). However, the mechanisms behind these properties of FAMCGSE remain unclear. This study explores the anti-inflammatory effects of FAMCGS extract (FAMCGSE) on LPS-stimulated RAW 264.7 macrophages and the underlying mechanisms. MTT assay confirmed that FAMCGSE (0 to 0.1%) maintained cell viability without inducing morphological changes. Pretreatment with FAMCGSE significantly mitigated LPS-induced morphological alterations dose-dependently. RT-PCR and Western blot analyses showed that FAMCGSE significantly reduced the mRNA and protein levels of proinflammatory mediators such as TNF-α, IL-1β, IL-6, iNOS, and COX-2. Additionally, FAMCGSE decreased the production of TNF-α, IL-1β, IL-6, nitric oxide, and PGE2 in LPS-activated RAW264.7 cells. Mechanistically, FAMCGSE inhibited the phosphorylation of mitogen-activated protein kinases (MAPKs; ERK, p38, and JNK) and prevented the LPS-induced nuclear translocation of NF-κB, with effects comparable to compound K (CK) or dexamethasone. Notably, FAMCGSE was particularly effective in inhibiting ERK and JNK activation, with less impact on p38, suggesting a specific inhibitory action on certain MAPK pathways. These findings highlight FAMCGSE's potential as an inhibitor of MAPK and NF-κB pathways, indicating that FAMCGSE, including its main component CK, may be a promising therapeutic agent for inflammation-related conditions.

Keywords: Fermented and aged mountain-cultivated ginseng sprout, Inflammation, Macrophage, MAPK, NF-κB

Y-18

Effects of thermotherapy on irisin and lipid metabolism in middle aged obese woman

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Many women gain weight as they transition and approach menopause. Weight gain during menopause is predominantly due to a reduction in physical activity. For obese menopausal women, appropriate therapy about controlling weight and increasing lipid metabolism is required to prevent metabolic syndrome. Although exercise is a notable treatment for this effect, it may be difficult for obese women to perform exercise after menopause due to environmental or physical constraints. We would like to suggest thermotherapy as an alternative. The main aim of this study was to analyze how thermotherapy (half bath in hot water, 42±0.5℃, 3-4 times/week, 30 min/time, 15 times for 4 weeks) affects the adiponectin, free fatty acid and irisin expression in menopausal overweight-obese women. We observed that thermotherapy significantly increased adiponectin, free fatty acid and irisin levels. We also found that the increased lipid metabolism with thermotherapy was associated with adiponectin. Also, the role of other hormones on lifestyle and eating behavior in menopausal overweight-obese women can be further explored to identify obesity and lifestyle-related diseases.

Keywords: Thermotherapy, Irisin, Adiponectin, Lipid metabolism

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주요 Reference

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- Biochemical and Biophysical Research Communications, (2022), 606, 94-99
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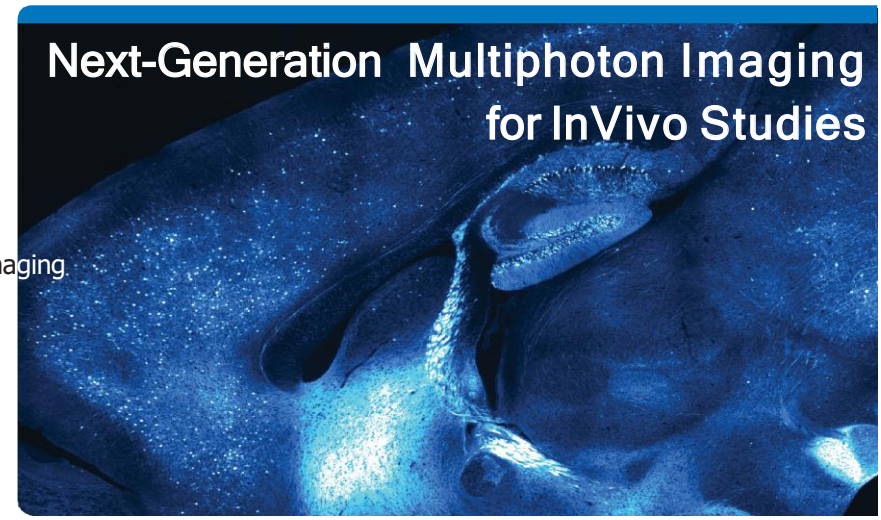

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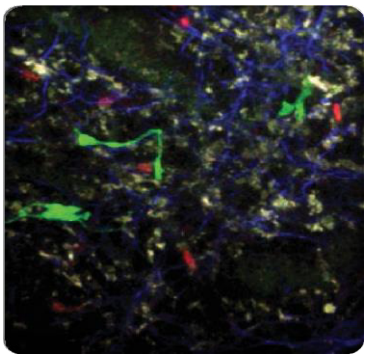

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