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The Korean Journal of
Physiology &
Pharmacology

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

Abstract Book

초록집 다운로드

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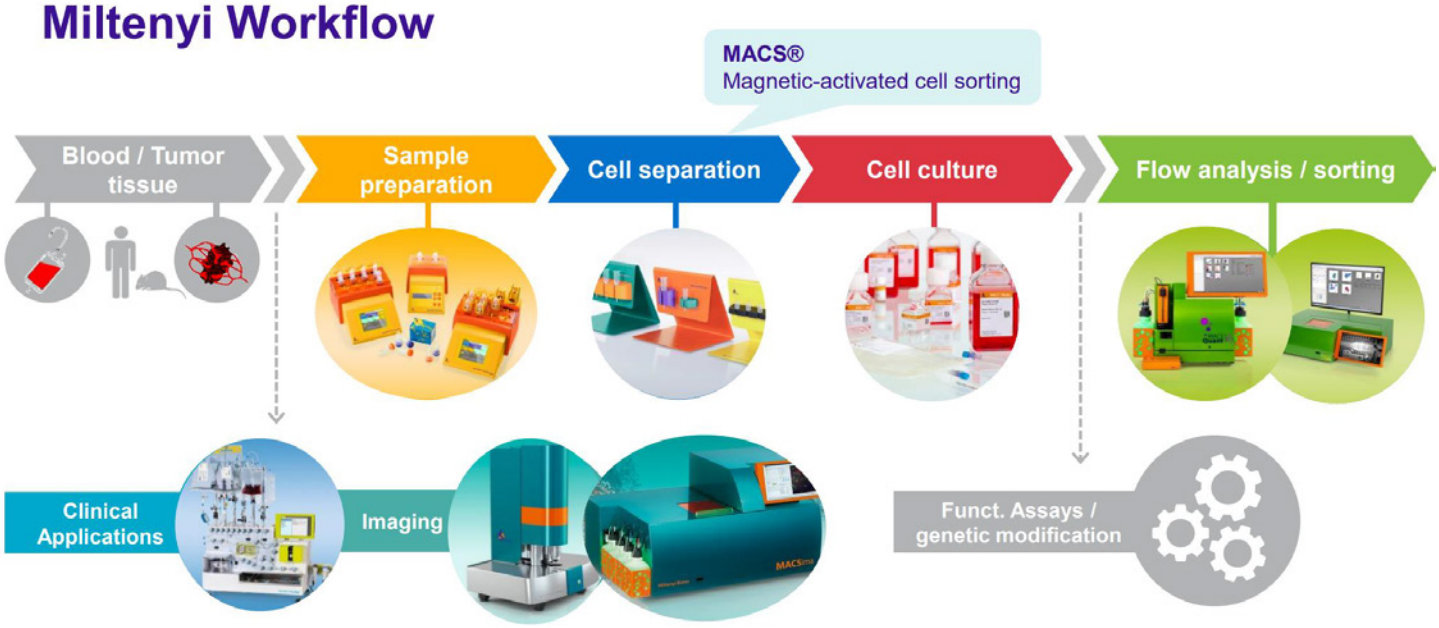
Miltenyi Biotec

Miltenyi Workflow



DoGenBio

EZ-Cytox

MTT 보다 간편하고 빠르게! MTS, XTT 보다 정확하게
Cell viability, proliferation, cytotoxicity를 측정하는 kit

Oxidative Stress Assay Kit

01 EZ-Superoxide Dismutase (SOD) Assay Kit
02 EZ-Glutathione (GSH/GSSG, Total) Assay Kit
03 EZ-Catalase Assay Kit
04 EZ-Hydrogen Peroxide/Peroxidase Assay Kit
05 EZ-Lipid Peroxidation (TBARS) Assay Kit
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
09 EZ-Total Cholesterol Assay Kit
10 EZ-Triglyceride Quantification 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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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
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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

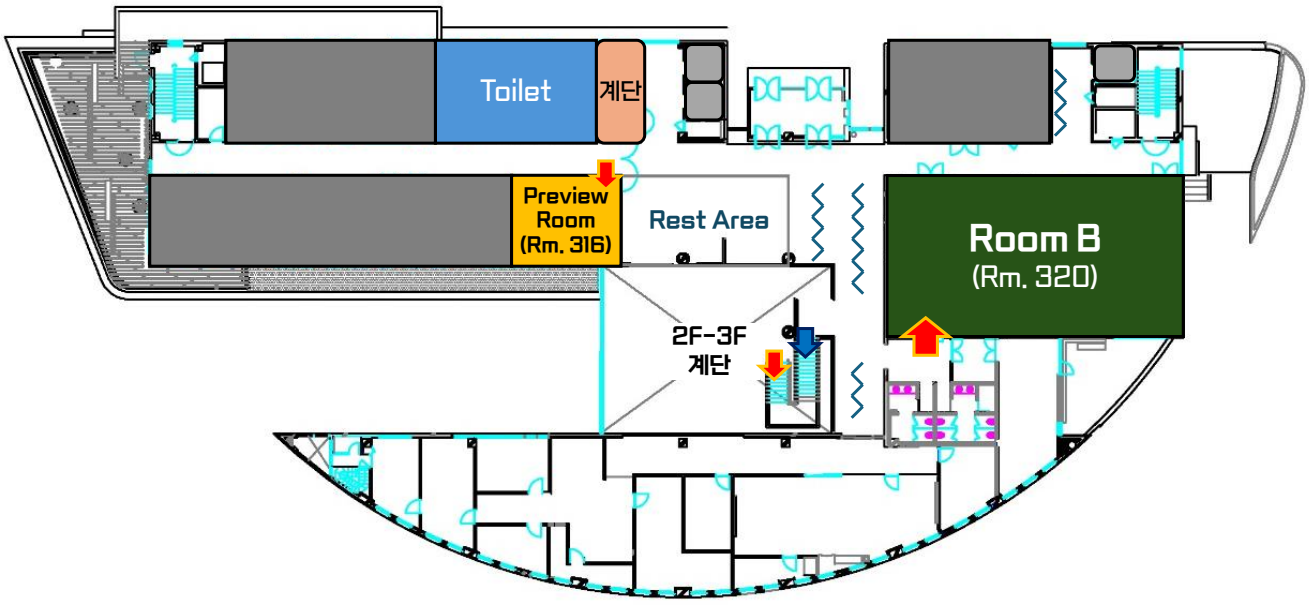
4F	Room C (Rm. 418)	Poster Exhibition (Corridor)		
3F	Room B (Rm. 320)	Poster Exhibition (Lobby)	Preview Room & VIP Room (Rm. 316)	
2F	Registration	Room A (유광사 홀)	Sponsorship Booths	주 출입구(외부 현관)

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
2
9
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.

DanBi Ahn[1,2], Eun Ah Jo[2], Hee Young Kim[2]

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S 55 A01-08

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

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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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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

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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]

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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*]
[1]Department of Physiology, Inflammation-Cancer Microenvironment Research Center, Ewha Womans University College of Medicine, Seoul, Korea,
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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*]
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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]
[1]Department of Physiology, Dongguk University Wise College of Medicine, Gyeongju, Korea, [2]Channelopathy Research Center (CRC), Dongguk University College of Medicine, Goyang, Korea, [3]Medical Cannabis Research Center, College of Medicine, Dongguk University Wise, Goyang, Korea

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]*
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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
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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

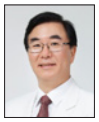
Donghee Kim
Chicago Medical School/RFUMS, USA

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
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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

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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
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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

Bae Jun Oh
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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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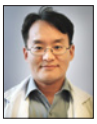
Cognitive flexibility is a fundamental feature of high-level brain function. However, neuronal pathways that control flexibility and the mechanisms by which flexibility is encoded are unknown. Previous studies have reported that neurons in the orbitofrontal cortex (OFC) encode the value of an external 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

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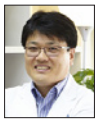
The interplay between apoptotic cancer cells and the tumor microenvironment (TME) influences cancer growth, progression and metastasis. We demonstrate that treatment with conditioned medium (CM) from lung cancer-associated fibroblasts (CAFs) exposed to apoptotic cancer cells suppresses proliferation 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
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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
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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

Min-Sik Lee
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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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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A01-01

Calcium dynamics of cerebellar Purkinje neurons encode social interaction state

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The ability to perceive internal mental states and predict the consequences of future actions is critical for survival and maximizing social rewards. Social prediction, defined as the ability to predict internal mental states based on emotionally charged stimuli, is essential for planning action sequences and estimating behavioral outcomes. Recent studies have shown that the cerebellum functions as a prediction module during social interaction, and cerebellar prediction is crucial for estimating mental states, including intentions, emotions, and desires. Climbing fibers provide an instructive signal and encode prediction errors during learning. However, the role of climbing fibers projecting to Purkinje neurons during social interaction remains largely unknown.

Here, we show that climbing fiber-induced dendritic calcium activity in Purkinje neurons encodes social interaction states. To observe climbing fiber-triggered calcium dynamics in Purkinje neuron dendrites during social interaction, we performed two-photon calcium imaging of individual dendrites using a miniature two-photon microscope in freely behaving mice. We present evidence for a social state encoder in a subset of Purkinje neurons and use kernel density estimation of calcium dynamics from neuronal ensembles in the cerebellum to demonstrate social-selective calcium dynamics.

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Keywords: Cerebellum, Social, Prediction, Decoder

A01-02

Genome-wide sequencing of isolated glial cells suggests age-related changes in oxidative phosphorylation in *Drosophila melanogaster*

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Learning and memory abilities decline with aging, and this phenomenon is known as age-related memory impairment (AMI). Fruit flies also exhibit AMI, and we recently discovered and reported that in long-lived wild-type fruit flies (w^{1118}), AMI manifests as a significant decline in learning ability in middle age. While neurons have long been considered to play a central role in AMI, recent studies have highlighted the emerging role of glial cells, which support neurons by assisting with immune function, signaling, and energy metabolism. In our study, we aimed to investigate age-related changes in gene expression within neurons or glial cells to identify new factors and mechanisms within glial cells that regulate AMI. We genetically labeled the nuclear membranes with a green fluorescent protein and dissociated brain cells from young (10 days after eclosion, dae) and middle-aged (30 dae) flies. Using fluorescent-activated cell sorting (FACS), neurons or glial cells were collected and followed by next-generation sequencing (NGS). Analysis of the NGS data revealed that aging in neurons was associated with increased inflammatory signaling through the Toll and Imd pathways. On the other hand, G-protein coupled receptor (GPCR) signaling pathways in glial cells were more activated. GPCRs influence neural plasticity and regulate immune cell activity, mediating inflammatory responses. Interestingly, when we selected and analyzed genes with age-specific changes in expression within glial cells, we found that four genes, which function as proton transmembrane transporters in mitochondria, were upregulated. These genes were found to play a role in regulating oxidative phosphorylation. These findings suggest a new possibility that the energy metabolism of glial cells may influence neuronal activity and contribute to the regulation of AMI.

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Keywords: Aging, Neuron, Glia, Mitochondria, GPCR, Neuroinflammation

A01-03

Bergmann glia inhibit Purkinje cell activity through interneuron

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Bergmann glia (BG), a type of radial glial cell in the cerebellar cortex, serve multiple roles. They have been found to influence Purkinje cells by modulating synaptic inputs, controlling excitability via extracellular potassium levels, and directly impacting Purkinje cells through neurotransmitter release. In this study, we utilized GFAP-promoter-driven AAV virus to genetically express hM3Dq in BG. Our results indicate that the interaction between BG and Purkinje cells is mediated by NMDA and GABAA receptors. Additionally, calcium imaging revealed that BG activation triggers MLI activation. In summary, we propose that glutamate released by BG prompts GABA release from MLI, leading to the inhibition of Purkinje cell activity. These findings offer insights into the cellular mechanisms through which BG modulate neuronal function in the cerebellum.

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Keywords: Purkinje cell, Bergmann glia, Interneuron, Cerebellum

A01-04

Chemogenetic modulation of the prelimbic cortex to the nucleus accumbens core circuit reduces cocaine-induced increase of risk choice behavior

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Decision-making is critically impaired in individuals with abnormal psychiatric conditions like gambling disorder and substance abuse. These impairments are associated with deficits in top-down executive control governed by the medial prefrontal cortex (mPFC) and its fronto-striatal connections to the nucleus accumbens (NAc), particularly involving the prelimbic (PrL) region of the mPFC and the NAc core. This study employed Designer Receptors Exclusively Activated by Designer Drugs (DREADDs), a chemogenetic technique, to examine whether modulating the activity of the PrL to NAc core neural circuits affects risk-taking behaviors. Rats were trained on a rat gambling task (rGT) until their choices among four options, each with varying probabilities of rewards and punishments, showed stable preferences. Subsequently, based on their preferences, the rats were categorized into two groups—risk-averse and risk-seeking—and exposed to two different experimental conditions. One group of rats underwent a cocaine sensitization regime to observe changes in decision-making following cocaine

administration and neuronal modulation with Gi and Gq DREADDs. The other group experienced neuronal modulation without cocaine exposure. The results indicated that cocaine typically led risk-averse rats to make riskier choices. Interestingly, this effect was significantly reduced by activating the Gi DREADD in the PrL-NAc core circuit, an outcome not mirrored by activating the Gq protein. Moreover, there were no notable changes in decision-making when neuronal activity was modulated without cocaine. These results indicate that the PrL-NAc core circuit is one of the major target area exacerbated by chronic cocaine leading to risky decision-making and further suggest that this effect can be controlled by neuronal activity modulation to this circuit.

Keywords: Rat gambling task, Sensitization, Prelimbic cortex, Nucleus accumbens, DREADD

A01-05

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

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Noonan syndrome (NS) is the most common developmental disorder among Rasopathies and exhibits a high prevalence of autism spectrum disorder (ASD). However, the neural mechanisms underlying ASD-like behavioral phenotypes in NS are not well understood. Ptpn11D61G/+ mice, which display NS-like symptoms such as short stature, heart deficits, and learning and memory impairments, have been used as a mouse model of NS. In this study, we report that *Ptpn11*$^{D61G/+}$ mice show male-specific abnormal auditory sensory processing, which are one of the key features of ASD. Only male *Ptpn11*$^{D61G/+}$ mice, not female mutant mice, exhibited lowered sensitivity in auditory brainstem responses, they showed increased startle responses to acoustic stimuli, reduced habituation of startle response, and impaired sensorimotor gating in the pre-pulse inhibition (PPI) of startle response. As a potential mechanism underlying sex-specific impairment of auditory processing in *Ptpn11*$^{D61G/+}$ mice, we found profound phospho-proteomic changes associated with synaptic organization and function in medial prefrontal cortex (mPFC) of male *Ptpn11*$^{D61G/+}$ mice. Specifically, phosphorylation of αCaMKII at Thr286 is significantly decreased in male *Ptpn11*$^{D61G/+}$ mice compared to wild-type littermates but not in female mutants. Our results suggest a significant association of αCaMKII hypoactivity with sensory processing impairments in male *Ptpn11*$^{D61G/+}$ mice. Our study provides new insights into the neural mechanisms underlying ASD-like behaviors in *Ptpn11*$^{D61G/+}$ mice. Furthermore, these findings have implications for understanding the sex-specific phenotypes in ASD.

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Keywords: Autism Spectrum Disorder, RASopathy, Sensory processing, Prepulse inhibition

A01-06

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

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Understanding the neurobiological alterations associated with neuropathic pain is crucial for developing treatments, but the underlying mechanisms remain incompletely 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 pyramidal neuron activity decreases, while metabotropic glutamate receptor 5 (mGluR5) activity increases 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) frequency in pyramidal neurons increased during the neuropathic pain state and that this change was attenuated by applying a mGluR5 antagonist. Also, 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. Additionally, SST interneurons in the neuropathic pain group were more depolarized compared to those in the sham group through mGlur5 activation. Optogenetic inactivation of SST interneurons reversed the increase in sIPSC frequency of pyramidal neurons in the neuropathic pain group. Conversely, overexpression of mGluR5 in SST interneurons in the mPFC of naïve mice resulted in mechanical allodynia, a representative symptom of neuropathic pain. These findings demonstrate that increased mGluR5 activity in SST interneurons contributes to neuropathic pain and that cell type-specific modulation can provide new avenues for treating neuropathic pain.

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Keywords: Neuropathic pain, MPFC, Interneuron, Electrophysiology

A01-07

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

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Acute or chronic exposure to cocaine causes addictive behaviors by reducing GABAergic input to dopaminergic neurons in the Ventral Tegmental Area (VTA) and increasing dopamine release in Nucleus Accumbens (NAc). A circuit comprising of lateral hypothalamus (LH) and lateral habenula (LHb) mediates aversion behaviors by acting on mesolimbic dopaminergic system. Therefore, we investigated whether an LH-LHb circuit modulates cocaine-induced locomotor activity and which neuropeptides mediates the LH-LHb modulation of cocaine behaviors. Optogenetic activation of LH-LHb strongly inhibited cocaine-enhanced locomotor activity, which

was prevented by local injection of either glutamate or orexin receptor antagonist into LHb. in vivo extracellular recordings proved that optogenetic activation of LH-LHb increased single-unit discharges from LHb neurons and the evoked activities were prevented by local injection of either glutamate or orexin receptor antagonist into LHb. Our findings revealed that the reduction of cocaine-induced locomotion by LH-LHb stimulation was mediated by glutamate and orexin in LH.

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Keywords: Hypothalamus-habenula circuit, Acute cocaine behavior

A01-08

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

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Social recognition is an essential function required to recognize specific individuals and retain information about them to exhibit normal social behavior. A previous study showed that female and male mice exhibit different responses to stressful circumstances, such as chronic social stress, including both behavioral and neurophysiological changes. Despite these clear sex-specific differences in social stress responses-such as distinct behavioral and neurophysiological alterations-the effects of social isolation followed by regrouping on these components remain poorly understood. In this study, we demonstrated that inactivating the social recognition-specific mPFC subpopulation in females caused social recognition deficits similar to those in males, as shown by the three-chamber test and chemogenetic inactivation, highlighting its crucial role for both female and male mice. Additionally, we revealed that single housing (SH) followed by regrouping exhibited comparable excitability with group housing mice in these neurons of female mice, while male mice did not, with whole-cell patch clamp recordings. Furthermore, we observed that female SH mice initially displayed social recognition deficits in the three-chamber test following single housing; however, they were able to recover their social recognition abilities after regrouping, in contrast to male mice which did not show such recovery. These findings suggest that while both male and female mice rely on the same mPFC subpopulation for social recognition, females exhibit greater neuronal resilience following social isolation and are more capable of recovering social recognition abilities after regrouping, in contrast to males who show persistent deficits.

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Keywords: Resocialization, Social isolation, Social recognition, Infralimbic cortex, Nucleus accumbens

A01-09

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

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Excitotoxicity in neurodegenerative diseases is closely linked to the overproduction of reactive oxygen species (ROS) and dysregulated calcium (Ca^{2+}) homeostasis. Excessive Ca^{2+} influx overwhelms the cell's buffering capacity, leading to mitochondrial dysfunction and the activation of pro-apoptotic pathways. While targeting Ca^{2+} regulation remains a promising therapeutic approach, the development of effective and safe treatments for neurodegenerative diseases like Alzheimer's and Parkinson's has been challenging. For instance, Isradipine, a voltage-gated calcium channel blocker, failed to show efficacy in Phase 3 clinical trials for Parkinson's disease despite early promise. Given these limitations, we aimed to regulate calcium sources at a higher level than traditional voltage-gated calcium channels, with the goal of delaying or potentially preventing neurodegenerative disease progression. Here, we investigated the TRPC channels as a potential protein target to delay the progression of neurodegenerative symptoms. Utilizing live cell imaging, we were observed intracellular ROS, calcium levels, and mitochondrial dysfunction over a period of 12 hours or more in SH-SY5Y cells. Upon treatment with primary ROS generators such as tBHP and 6-OHDA, a peak in ROS production was observed, followed by a marked decline in mitochondrial membrane potential and a concomitant rise in intracellular Ca^{2+} levels, ultimately leading to cell death. In contrast, treatment with secondary ROS inducers like Rotenone and PMA, which induce ROS production via mitochondrial pathways, did not result in alterations in Ca^{2+} levels, yet cell death was still observed. Surprisingly, this cell death signaling was delayed by treatment with Pico145, a TRPC4/C5 blocker, or Isradipine. Furthermore, the combination treatment with Pico145 and Isradipine resulted in a marked suppression of cell death.

In conclusion, our results highlight the different mechanisms through which primary and secondary ROS generators contribute to neurodegenerative cell death, with calcium dysregulation being a critical factor. The delay in cell death following Pico145 and Isradipine treatment, as well as the pronounced suppression observed with their combined administration, underscores the therapeutic potential of concurrently targeting TRPC and voltage-gated calcium channels. This synergistic intervention presents a compelling strategy for attenuating neuronal degeneration and holds promise for the development of novel therapies for neurodegenerative diseases.

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Keywords: Excitotoxicity, TRPC channel, Calcium dysregulation, Reactive oxygen species, Neurodegenerative disease

A01-10

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

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The Kv2.1 voltage-activated potassium (Kv) channel is a significant delayed-rectifier potassium channel in the mammalian central nervous system, where its activation and inactivation mechanisms are essential for modulating intrinsic neuronal excitability. Phosphatidylinositol 4,5-bisphosphate (PIP2) is a membrane phospholipid that modulates the activity of several ion channels, forming nanoscopic PIP2-cation clusters that affect numerous physiological processes. Similarly, Kv2.1 channels are prominently clustered in the somata and dendrites of principal pyramidal neurons, where they modulate neuronal excitability. Here, we assessed the impact of PIP2-mediated Kv2.1 clustering using cellular physiological and pharmacological methods. Our findings indicate that de-clustering of Kv2.1 via the non-clustering Kv2.1-S586A mutant, results in the loss of its co-localization with PIP2. This suggests that the clustering of Kv2.1 channel affects interaction with PIP2, while de-clustering diminishes interaction with PIP2, while de-clustering diminishes interaction with PIP2. Additionally, we depleted PIP2 by activating the muscarinic pathway activation treated with oxotrem-

orine methiodide (Oxo-M). Our findings suggest that PIP2 plays a significant role in the regulation of Kv2.1 clustering.

Keywords: Kv2.1, PI(4,5)P2, Clusters

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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Kv2.1 is a voltage-gated potassium channel that serves a critical structural function in the soma and proximal dendrites of mammalian neurons. Kv2.1 channels form dense clusters on the cell surface, incorporating non-conductive channels, suggesting that functions extend beyond mere membrane potential regulation. Astrocytes are the predominant cells in the mammalian brain and are essential for sustaining the health and functionality of the central nervous system (CNS). They possess the ability to respond to synaptic inputs and modulate neuronal activity by elevating intracellular calcium concentrations. The interaction between neurons and astrocytes together with the processes governing these interactions is inadequately comprehended. This work examined the regulation mechanisms of kv2.1 in the interaction between neurons and astrocytes through neurophysiological approaches. Our data indicate that clustered Kv2.1 channels control direct interaction between neurons and astrocytes. We determined that the clustering of Kv2.1 was crucial for this interaction, in contrast to de-clustering Kv2.1 channels. This interaction significantly affects the functional properties of astrocytes. Consequently, comprehending the mechanism by which Kv2.1 channel clusters regulate interactions between neurons and astrocytes is crucial for developing novel therapeutic strategies for neurodegenerative diseases.

Keywords: Kv2.1, Clusters, Neuron-astrocyte interaction

A01-12

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

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The majority of patients with neuropathic pain, whether peripheral or central, exhibit hypersensitivity to various stimuli, including innocuous cold and mechanical sensations. While the role of peripheral nociceptors in cold hyperalgesia is relatively well understood, the underlying mechanisms of cold hyperalgesia in patients with central pain syndrome remain largely unexplored. The parabrachial nucleus (LPBN) is crucial for both autonomic and behavioral thermoregulatory responses, and the lateral hypothalamus (LH) is known to regulate thermoregulatory behavior. Therefore, we investigated the role of the LPBN-LH pathway in the development of cold hyperalgesia in mice. Optogenetic stimulation of LPBN-LH projections for 10 minutes using a blue laser induced cold hyperalgesia within 10 minutes, lasting for at least 2 months. This effect was reversible through optogenetic inhibition of the LPBN-LH pathway. Our fiber photometry studies indicated that LPBN-projecting neurons in the LH were activated by cold stimuli. These findings suggest that the LPBN-LH pathway serves as a central neurocircuitry involved in the generation of cold hyperalgesia.

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Keywords: Lateral parabrachial nucleus, Lateral hypothalamus, Cold hyperalgesia

A01-13

Physiological profiling of cannabidiol reveals profound inhibition of sensory neurons

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Cannabidiol (CBD), the main nonpsychoactive cannabinoid of cannabis, holds promise for nonaddictive treatment of pain. Although preclinical studies have been encouraging, well-controlled human trials have been largely unsuccessful. To investigate this dichotomy and better understand the actions of CBD, we used high-content calcium imaging with automated liquid handling and observed broad inhibition of neuronal activation by a host of ionotropic and metabotropic receptors, including transient receptor potential (Trp) and purinergic receptors, as well as mediators of intracellular calcium cycling. To assess the effect of CBD on overall nociceptor electrical activity, we combined the light-activated ion channel channelrhodposin in TRPV1-positive nociceptors and a red-shifted calcium indicator and found that 1 μM CBD profoundly increased the optical threshold for calcium flux activation. Experiments using traditional whole-cell patch-clamp showed increase of nociceptor activation threshold at submicromolar concentrations, but with unusually slow kinetics, as well as block of voltage-activated currents. To address a more integrated capacity of CBD to influence nociceptor sensitization, a process implicated in multiple pain states, we found that submicromolar concentrations of CBD inhibited sensitization by the chemotherapeutic drug vincristine. Taken together, these results demonstrate that CBD can reduce neuronal activity evoked by a strikingly wide range of stimuli implicated in pain signaling. The extensive effects underscore the need for further studies at substantially lower drug concentrations, which are more likely to reflect physiologically relevant mechanisms. The slow kinetics and block raise biophysical questions regarding the lipophilic properties of CBD and its action on channels and receptors within membranes.

Keywords: Cannabidiol, Chronic Pain, DRG, Calcium Signaling, Patch-clamp

A01-14

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

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Traumatic brain injury (TBI) is a severe neurological condition resulting from external physical impacts that cause significant brain damage. The pathological process of TBI involves increased neuronal cell death, primarily driven by cerebrovascular damage, inflammatory responses, and oxidative stress. A critical mechanism contributing to this damage is the activation of phosphodiesterase 5 (PDE5), an enzyme that reduces levels of cyclic guanosine monophosphate (cGMP). This reduction in cGMP leads to vasoconstriction and diminished cerebral blood flow, further exacerbating neuronal injury by downregulating neuroprotective signaling pathways. Nitric oxide (NO) and zinc are key factors in the pathophysiology of TBI-induced neuronal death. NO, a gaseous neurotransmitter, plays a crucial role in regulating cerebral blood flow, neuronal communication, memory formation, and intracellular signaling. Zinc, an essential trace element, is involved in neurotransmission, synaptic plasticity, and cellular signaling. Under pathological

conditions such as TBI, the roles of NO and zinc can shift from protective to harmful. For instance, the reduction in cerebral blood flow following TBI disrupts the delivery of NO to neurons, impairing nitrogen homeostasis. This disruption triggers excessive PDE5 activity, leading to further reductions in cGMP and subsequent neuronal damage. Additionally, the decreased cGMP levels impair the transcription of neuroprotective factors such as nuclear factor erythroid 2-related factor 2 (NRF2) and haem oxygenase-1 (HO-1). This impairment leads to glutathione depletion and the accumulation of free zinc within neurons, resulting in oxidative stress and further neuronal death. In this study, we investigated the neuroprotective potential of AR1001, a PDE5 inhibitor, administered subcutaneously at a dose of 2 mg/kg following TBI. Our hypothesis was that AR1001 would mitigate neuronal damage by enhancing cGMP levels, thereby improving NO-mediated vasodilation and reducing zinc-induced oxidative stress. To test this hypothesis, we conducted histological and biochemical analyses using Fluoro-Jade B (FJB) staining to detect neuronal degeneration, N-(6-methoxy-8-quinolyl)-para-toluenesulfonamide (TSQ) staining to assess zinc accumulation, and nNOS immunohistochemical staining to evaluate NO production

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Keywords: AR1001, Phosphodiesterase 5 (PDE5), Nitric oxide (NO), Zinc, Nuclear factor erythroid 2-related factor 2 (NRF2)

A01-15

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

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Background: Traumatic brain injury (TBI) is a major health concern, often resulting in significant brain damage and functional impairments. A key contributing factor to TBI-induced neuronal injury is the overactivation of AMPA glutamate receptors, leading to an increased influx of calcium and zinc ions. This study investigates the neuroprotective potential of L-theanine, known for its antioxidant potential and ability to enhance glutathione synthesis, against hippocampal damage in a TBI rat model.
Methods: Rats subjected to TBIs were treated with two dosages of L-theanine (100 and 200 mg/kg) and an AMPA receptor inhibitor, NBQX (30 mg/kg). The neuronal damage assessment, conducted 24 hours post-injury, involved a histological analysis, focusing on the factors of neuronal death, oxidative damage, and glial cell activation. The statistical analysis included the performance of an ANOVA followed by a Bonferroni post hoc test, with the data presented as mean ± SEM values and the significance determined at $p < 0.05$.
Results: Treatment with L-theanine was observed to significantly mitigate the zinc accumulation, neuronal death, and cognitive impairments associated with TBI. These benefits are likely attributed to the inhibition of AMPA receptor activity and reduction in neuroinflammation, possibly enhanced as a result of increased glutathione production.
Conclusion: This study suggests that L-theanine can perform a neuroprotective role in TBI, modulating AMPA receptor activation and diminishing neuroinflammation. Its antioxidant and anti-inflammatory properties further enhance the material's potential use as a therapeutic agent for reducing hippocampal damage caused as a result of a TBI.

Acknowledgement: The research was supported by the Hallym University Research Fund, Republic of Korea (MHC-202402-003) awarded to Sang Won Suh.

Keywords: Traumatic brain injury(TBI), L-theanine, AMPA receptors, Neuroinflammation, Glutathione

A01-16

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

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An ideal therapeutic approach would be to selectively target only the pathological subclusters within cells composing injured tissue, ensuring both efficacy and safety. These subclusters are defined by specific gene expression profiles, but the current technology for accurately deriving such profiling remains incomplete. In this study, we aimed to address this issue with a focus on the brain. Specifically, we sought to identify genes exclusively expressed within particular brain cell subclusters using single-cell RNA sequencing data from the mouse nervous system (SRP135960). These genes could serve as "single targets," while multiple genes co-expressed within the same subcluster could be classified as "multi-targets." Next, we focused on developing a targeting algorithm designed to regulate specific phenotypes or pathological conditions related to brain function. Concentrating on subclusters within the dorsal root ganglia (DRG), we identified uniquely expressed genes in the context of neuropathic pain (GSE154659) by analyzing gene expression profiles. We then utilized databases containing information on subcellular localization, gene families, and druggability to compile a list of target candidates with higher clinical relevance. This information facilitates a precise histological understanding of the pathologic components in the DRG, enabling the attenuation of pain-specific phenotypes without affecting normal somatosensory functions. Moreover, this methodology, validated in the DRG, could be extended to address other neurological diseases and is expected to be further improved by deep learning models in terms of prediction accuracy.

Keywords: Brain subclusters, Single target gene, Multiple target genes, Algorithm, DRG, Pain

B01-01

Altered Glutamatergic Signaling and Neuroinflammation in an ADHD Model

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Attention-Deficit/Hyperactivity Disorder (ADHD) frequently coexists with epilepsy, suggesting potential shared mechanisms between neurodevelopmental deficits and increased seizure susceptibility. G protein-coupled receptor kinase-interacting protein 1 (GIT1) has been implicated in synaptic development, and its deficiency has been linked to both ADHD-like behaviors and altered seizure dynamics. This study aimed to explore the effects of GIT1 deficiency on seizure susceptibility, synaptic development, and neuroinflammatory responses. In a pilocarpine-induced status epilepticus (SE) model, Git1+/- mice exhibited a delayed onset of seizures and prolonged latency to SE compared to Git1+/+ controls. At the cellular level, Git1+/- mice displayed reduced PSD95-labeled synaptic puncta and impaired neurite outgrowth during early developmental stages (3–5 days in vitro). These delays in synaptic maturation were associated with diminished glutamatergic signaling, which likely contributed to the prolonged seizure latency ob-

served in the Git1+/- mice. Moreover, Git1+/- mice showed elevated levels of neuroinflammatory markers, such as glial fibrillary acidic protein (GFAP) and pro-inflammatory cytokines (IL-1β, TNF-α), indicating an increased neuroinflammatory response. This heightened inflammation may exacerbate excitotoxic damage following SE, suggesting that while GIT1 deficiency delays seizure onset, it also increases the risk of long-term neuronal damage due to inflammation. In summary, Git1 deficiency impairs synaptic development and reduces glutamatergic signaling, leading to a delay in seizure susceptibility. However, the accompanying rise in neuroinflammation heightens the risk of excitotoxic injury following prolonged seizures. These findings provide insight into how neurodevelopmental deficitis and inflammatory processes may link ADHD-related symptoms with altered seizure dynamics.
(This work was supported by the National Research Foundation of Korea (NRF) funded by the Korean government (MSIT) (NRF-2019M3C7A1031455 and NRF-2022R1F1A1075083).)

Keywords: ADHD, Status epilepticus, Glutamate, Neuroinflammation

B01-02

Obesity augments seizure severity and neuroinflammatory responses in status epilepticus

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Obesity, marked by a body mass index (BMI) of 30 or higher, is a growing global health challenge linked to a variety of complications, including an elevated risk for neurodegenerative diseases. Status epilepticus (SE), a life-threatening condition characterized by prolonged seizures, affects millions globally and is closely associated with neuroinflammation and neuronal damage. Although obesity is acknowledged as a comorbidity in epilepsy, its precise influence on SE remains inadequately understood.
In this study, we explore the effects of obesity on SE by employing leptin-deficient ob/ob mice, a widely used model of temporal lobe epilepsy. Pilocarpine was administered intraperitoneally to both normal C57BL/6J (+/+) and obese leptin-deficient ob/ob (C57BL/6J -/-) mice. Our results demonstrated a significantly earlier onset of seizures and a more rapid progression to SE in the ob/ob mice. Fluoro Jade B staining highlighted increased neuronal degeneration in the hippocampal CA1 and hilus regions of the ob/ob mice. Additionally, immunofluorescence staining and Western blot analysis revealed heightened glial cell activation, as evidenced by an upregulation in GFAP expression. Neuroinflammatory markers, including IL-1β, TNF-α, LCN2, and p-STAT3, were also significantly elevated in the ob/ob mice, further indicating an intensified neuroinflammatory response. Moreover, necroptosis, a regulated cell death pathway involving p-MLKL, was markedly increased in the obese mice. These findings suggest that obesity enhances susceptibility to SE and amplifies neuroinflammatory and neurodegenerative processes, potentially worsening the overall neurological outcome. This work advances our understanding of how obesity influences SE pathology and provides insight into potential therapeutic targets for managing SE in obese individuals.
(This work was supported by the National Research Foundation of Korea (NRF) funded by the Korean government (MSIT) (NRF-2021R1F1A1063448).

Keywords: Obesity, Status epilepticus, Hippocampal cell death, Inflammation, Necroptosis

B01-03

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

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Diabetic peripheral neuropathy (DPN), a common complication of diabetes, affects nearly half of diabetic patients, leading to sensory impairments and chronic pain. Current treatments for DPN are limited, emphasizing the need for novel therapeutic approaches. This study investigates the efficacy of photobiomodulation(PBM) known as near-infrared low-level laser therapy (LLLT) as a potential non-invasive treatment for DPN. Our study demonstrated that near-infrared PBM produced significant therapeutic effects in both in vitro and in vivo models of DPN. In glucose-induced toxicity models using PC12 cells, PBM significantly improved cell viability and neurite outgrowth, as assessed by the MTT assay and neurite outgrowth assay, respectively. Immunocytochemistry revealed a reduction in IL-1β expression, highlighting the anti-inflammatory effects of PBM at the cellular level. In the streptozotocin-induced rat model of DPN, PBM significantly reduced pain sensitivity, as shown by the Von Frey test, indicating its potential for alleviating neuropathic pain. Immunohistochemical analysis of the L5 dorsal horn of the spinal cord showed reduced levels of Glial Fibrillary Acidic Protein and Connexin 43, markers associated with neuroinflammation and glial activation, suggesting that PBM not only reduces pain but also addresses the underlying neuroinflammatory processes. Collectively, these findings suggest that PBM may offer a novel, non-invasive therapeutic approach for mitigating pain, inflammation, and nerve damage in diabetic peripheral neuropathy, providing a promising direction for future treatments.

Keywords: Diabetic peripheral neuropathy, Near-infrared low-level laser therapy, Photobiomodulation, Neuroinflammation

B01-04

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

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The comorbidity is a frequent challenge in neurodegenerative diseases, where patients often experience a combination of motor and psychiatric symptoms. In Parkinson's disease (PD), this is particularly challenging, as motor symptoms are treated with dopaminergic therapies while other non-motor complications necessitate additional pharmacological interventions. The concurrent use of multiple drugs in PD increases the risk of pharmacokinetic and pharmacodynamic interactions, which can lead to exacerbation of motor symptoms or diminished effectiveness of the primary treatment. Meanwhile, depression frequently accompanies PD, and selective serotonin reuptake inhibitors (SSRIs) are often prescribed to manage these depressive symptoms. Here, we investigate the potential for SSRIs to worsen motor symptoms in PD patients and propose that this effect may be linked to neurodegeneration caused by calcium toxicity, triggered by the hyperactivation of canonical transient receptor potential (TRPC) type 5 channel. This hyperactivation likely disrupts the basal ganglia circuitry, leading to neuronal death and a subsequent decline in motor control.
To explore the role of TRPC5 in PD pathology, we first assessed TRPC5 expression in basal ganglia neurons, finding high expression levels in both dopaminergic and GABAergic neurons. Behavioral tests using a rotenone-in-

duced PD model revealed that TRPC5 knockout mice showed significantly reduced Parkinsonian motor deficits compared to wild-type controls. Moreover, when SSRIs were administered to these PD model mice, motor function significantly worsened in the group treated with both rotenone and SSRIs, compared to those treated with rotenone alone. This deterioration was accompanied by a marked loss of dopaminergic and GABAergic neurons. In contrast, TRPC5 knockout mice were far less susceptible to the toxic effects of fluoxetine, showing no significant motor dysfunction or neuronal loss. To further clarify the impact of SSRIs on TRPC5, we measured whole-cell currents in TRPC5-overexpressing cells and found that fluoxetine significantly enhanced TRPC5 activity. This effect was synergistically amplified in TRPC5 expression, leading to a substantial increase in intracellular calcium levels. Our findings suggest that TRPC5 hyperactivation significantly contributes to the worsening of motor symptoms and neuronal loss in PD when SSRIs, such as fluoxetine, are administered. These results underscore the importance of cautious SSRI prescription in PD patients and indicate that targeting TRPC5 may provide a potential therapeutic strategy to mitigate these adverse effects.

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Keywords: Parkinson's disease, Calcium toxicity, TRPC5, SSRI antidepressants, Motor dysfunction

B01-05

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

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Dopamine receptors (D1, D2, D3, D4, and D5) are involved in many neurological processes, including cognition, memory, learning, and motor control, as well as neuroendocrine signaling. Of these, D1 and D2 play a major role and are respectively responsible for dopamine reception and inhibition. DRD2 plays a major role in the neural circuitry that mediates behavioral control, an ability that is essential for adaptive responding and is impaired in a variety of common neurological disorders. To determine which of the dopamine receptors are present in the brain regions that coincide with the survival of dopaminergic neurons and alpha-synuclein expression, we identified various types of dopamine receptors in the human brain atlas database. Remarkably, only DRD2 is highly expressed in healthy adult substantia nigra brain region as homodimer form and inversely correlates with the expression of α-Synuclein. Moreover, when alpha-synuclein is abnormally expressed in dopaminergic neurons, DRD2 loses its function and activates caspase-3, which is associated with cell death. We confirmed this scientific phenomenon by treating dopaminergic neurons with alpha-synuclein PFFs. Furthermore, we applied protein structure analysis modeling software to obtain evidence that the DRD2, alpha-synuclein, and caspase-3 molecules are very tightly linked. Thus, our founding suggests that DRD2 plays a critical role in dopamine neurotransmitter influx in dopaminergic neurons, and that it is deeply involved in the activation of alpha-synuclein molecules and caspase-3.

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Keywords: Dopamine receptors, DRD2, Alpha-synuclein, Caspase-3, Parkinson's disease

B01-06

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

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Chronic neuropathic pain from nervous system injury is hard to manage. Transcutaneous auricular vagus nerve stimulation treats cognitive disorders and neuropathic pain with few side effects, but its mechanisms are still unknown. In this study, the role of taVNS in neuropathic pain induced by partial sciatic nerve ligation (PSL) and its underlie mechanism will be examined. Electrical stimulation to the auricular branch of the cymba concha was administered under anesthesia for 20 minutes daily for consecutive 3 days. Development of chronic pain after the surgery was evaluated through von Frey test and two-photon microscopy. Application of taVNS was revealed to significantly reduce the chronic pain in 3 days. Histological examination showed changes c-Fos expression after taVNS in serotonergic pathway, involving the central amygdala and nucleus of the dorsal raphe. The pain-relief effects of taVNS were prevented by systemic serotonin depletion using PCPA, suggesting critical role of serotonin in taVNS-mediated analgesic effect on chronic pain.

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Keywords: Chronic neuropathic pain, Transcutaneous auricular vagus nerve stimulation, Pain relief, Serotonin

C01-01

Rectification profile alterations in TREK channel mutants

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Dysfunction of TREK/TRAAK channels, members of the two-pore domain K+ (K2P) channel family, is linked to the the pathophysiology of pain and mood disorders. Understanding their gating mechanisms and activity properties is essential for developing more effective and selective modulators. A previous study identified gain-of-function mutants in TREK-1 and TRAAK, where the TM2.6 glycine residue was mutated to aspartate (TREK-1 G171D, TRAAK G133D), resulting in slight inward rectification. This study extends the analysis to the single-channel properties of a similar TREK-2 TM2.6 mutant (G196D), comparing it to TREK-1 G171D and TRAAK G133D. Additionally, species-specific differences in TREK-1 rectification patterns were examined. The TM2.6 GxxxD mutants of TREK/TRAAK channels exhibited significantly increased channel activity compared to their respective wild-type channels ($p < 0.05$). TREK-1 G171D formed two distinct channel phenotypes: TREK-1L, which maintained conductance at positive membrane potentials similar to the wild-type, and TREK-1S, which showed substantially lower conductance. TREK-2 G196D demonstrated more pronounced inward rectification than its wild-type counterpart. The TRAAK G133D mutant exhibited significantly altered single-channel properties, including enhanced inward rectification, increased channel activity, and extended mean open time. Species differences were also observed: TREK-1 displayed outward rectification in both mouse and human, but not in rat. Furthermore, TWIK was found to reduce the outward rectification pattern of TREK-1. These findings indicate that the TM2.6 GxxxD mutations in TREK/TRAAK channels lead to enhanced inward rectification and increased channel activity, with species-specific variations in rectification patterns, offering valuable insights for the development of targeted modulators for TREK/TRAAK-related pathophysiology.

Keywords: Two-pore domain K^+ channel, TREK-1, TREK-2, TRAAK, Rectification

C01-02

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

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Diabetic retinopathy (DR) is the leading cause of vision loss among working-age adults worldwide, primarily resulting from chronic hyperglycemia that induces microvascular damage in the retina. Our previous study demonstrated a significant reduction in the expression levels of TWIK-related K+ (TREK) channels in the dorsal root ganglion (DRG) and trigeminal ganglion (TG) from a painful diabetic peripheral neuropathy (pDPN) model. This model was produced by a high-fat diet (HFD, 60 kcal%) combined with a single dose of streptozotocin (60 mg/kg) for 40 weeks. TREK channels, which are mechanosensitive, contribute to setting the resting membrane potential and regulating electrical activity in both excitable and non-excitable cells. However, their expression changes in the retina in the pDPN model remain largely unexplored. This study aimed to investigate the alterations of TREK channels in the retina of the pDPN model. In the pDPN model, H&E staining revealed a reduction in total retinal thickness and a loss of retinal ganglion cells (RGCs) compared to the normal diet (NFD) and HFD groups. Additionally, a high number of TUNEL-positive cells and elevated levels of reactive oxygen species were observed in the retina of the pDPN model. Both TREK-1 and TREK-2 channels were expressed in the mouse retina, primarily localized in horizontal cells and RGCs. Furthermore, platelet-derived growth factor receptor alpha (PDGFRα)-positive cells, which express TREK channels, were distributed in the outer plexiform layer. In the pDPN model, TREK channel expression was significantly reduced compared to the NFD and HFD groups. Knockdown of TREK channels in retinal and endothelial cells resulted in decreased cell viability and proliferation. These findings suggest that reduced TREK channel activity aggravates the pathological changes in the retina of the pDPN model, potentially accelerating the progression of retinal damage in diabetic peripheral neuropathy.

Keywords: Diabetic peripheral neuropathy, Retinopathy, TREK channels

C01-03

Interventricular Differences in Inotropic Responses Induced by Isoproterenol in Rat Cardiomyocyte

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Sympathetic stimulation of cardiac β-adrenergic receptor (β-AR) induces positive inotropy, which is mediated by augmented L-type calcium current ($I_{Ca,L}$) and SR Ca^{2+} uptake etc. Despite the increasing recognition of right ventricular (RV) dysfunction in cardiovascular diseases such as pulmonary hypertension, the physiological mechanisms underlying RV function remain less understood compared to the left ventricle (LV). The purpose of this study was to compare the response in contractility of the RV and LV myocytes to β-AR stimulation. The cardiomyocytes sarcomere length shortening (DSL) with 2 Hz stimulation was evaluated using IonOptix system. In response to cumulative increase of Isoproterenol (ISO) level, the RV myocytes showed more sensitive DSL increase with increased relaxation speed. ELISA study showed higher increase of cAMP by 100 nM ISO in RV than LV myocytes. In whole-cell patch clamp recordings, the relative increase of action potential duration by 100 nM ISO and $I_{Ca,L}$ were more prominent in RV than LV myocytes. Our present study demonstrates the more prominent β-AR inotropic response in the RV myocytes including higher level of the initial step of signaling cascade. Further investigations such as myofilament Ca^{2+}-sensitivity regulation are requested to understand the biventricular differences in β-AR effects and their changes in RV dysfunction.

Keywords: Cardiomyocyte, Excitation-contraction coupling, B-adrenergic receptor, Action potential, Sarcomere length

C01-04

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

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The substantia gelatinosa (SG) of the trigeminal subnucleus caudalis (Vc) serves as the initial relay point for orofacial nociceptive inputs through thin myelinated Aδ and unmyelinated C primary afferent fibers. Citronellol is a monoterpenoid alcohol present in the essential oil of many medicinal plants, such as *Cymbopogon citratus*. Although many studies have reported that citronellol has analgesic effects, the mechanism by which citronellol acts on the SG neurons in the Vc has not yet been fully elucidated. To investigate this, the whole-cell patch-clamp technique was used to explore the antinociceptive mechanism underlying citronellol's effects on the SG neurons in the Vc of mice.

Under high-chloride pipette solution, citronellol consistently generated inward currents that persisted even in the presence of tetrodotoxin (a voltage-gated Na^+ channel blocker), 6-cyano-7-nitroquinoxaline-2,3-dione (a non-NMDA glutamate receptor antagonist), and DL-2-amino-5-phosphonopentanoic acid (a NMDA glutamate receptor antagonist). However, the citronellol-induced inward currents were partially inhibited by picrotoxin, a $GABA_A$ receptor antagonist, or strychnine, a glycine receptor antagonist, and were almost fully blocked when both were applied together. Additionally, citronellol enhanced both GABA-induced and glycine-induced responses. Taken together, these results suggest that citronellol exerts inhibitory effects via GABA or glycine receptors on SG neurons in the Vc and may have potential as a therapeutic agent for orofacial pain.

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Keywords: GABA receptor, Glycine receptor, Monoterpenoid, Patch-clamp, Orofacial pain

C01-05

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

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Beta-ionone is a monocyclic monoterpenoid compound derived from fruits and vegetables. Within the biomedical domain, many studies demonstrated the diverse pharmacological activities of beta-ionone, including anti-inflammatory, anti-proliferative, anti-metastatic effects, and apoptosis induction. In contrast, the nociceptive effect of beta-ionone was not deeply

studied. Substantia gelatinosa (SG) neurons of the trigeminal subnucleus caudalis (Vc) involved in the transmission and modulation of orofacial nociceptive input. The aim of the study is to investigate the direct effect of beta-ionone on SG neurons of the Vc using patch-clamp techniques.
Under conditions of a high chloride pipette solution, beta-ionone-induced inward currents were examined at different concentrations ranging from 1 to 300 μM. Beta-ionone-induced inward currents were bigger at higher concentrations. Next, GABA and glycine were subsequently co-applied together with beta-ionone. Lower concentration (100 μM) of beta-ionone increased the GABA- and Glycine-induced inward currents. Furthermore, the voltage-dependent potassium currents exhibited a significant reduction shortly (within 5 minutes) after exposure to a bath-applied concentration of 300 μM of beta-ionone, similar to tetraethylammonium, a non-specific potassium channel blocker. To test the effect of calcium on beta-ionone-induced block of potassium currents, CaCl2 was replaced with equal molar of ethylene glycol-bis(2-aminoethylether)-N,N,N',N'-tetraacetic acid in the bath solution to create the calcium-free artificial cerebrospinal fluid. The time-course current histogram showed that potassium currents were markedly reduced immediately after the administration of 300 μM beta-ionone in calcium-free artificial cerebrospinal fluid and were restored upon washout.
These findings show that beta-ionone directly effects on the postsynaptic site of SG neurons, enhances the effect of GABA and glycine and blocks potassium channels. In addition, the potassium channel blocking effect by beta-ionone persisted in calcium-free solution, indicating that calcium-activated potassium channels are not involved in the beta-ionone effects. Taken together, these results suggest that beta-ionone can potentially regulate the nociceptive activities of SG neurons of the Vc.

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Keywords: GABA, Glycine, Monoterpenoid, Patch-clamp, Potassium channel

C01-06

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

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MK-801, a non-competitive NMDA receptor antagonist, induces schizophrenia-like symptoms in animal models. Recent studies reported that these cognitive impairments are associated with changes in the activity of Kv3.1 channels in parvalbumin-positive GABAergic interneurons. Therefore, we investigated the effects of MK-801 on Kv3.1 channels expressed in Chinese hamster ovary (CHO) cells, as well as its effects on action potential (AP) induced in human SH-SY5Y neuroblastoma cell-derived neurons that mimic parvalbumin positive GABAergic interneurons. MK-801 caused a concentration-dependent inhibition of Kv3.1, with value of an IC50 of 10.81 μM and a Hill coefficient of 0.89. The blocking potency was stronger at depolarized potentials, showing a voltage-dependent block. The effect of MK-801 on Kv3.1 also showed a use-dependent block that induces progressive inhibition by repeated stimulation at increased frequencies (1 Hz and 2 Hz). Consistent with this, recovery from inactivation of Kv3.1 was also delayed in the presence of MK-801. Also, MK-801 induced a hyperpolarizing shift in the voltage dependence of steady-state inactivation curves of Kv 3.1. These results indicate that MK-801 blocked Kv3.1 expressed in CHO cells in a concentration-, voltage-, and state-dependent manner. Furthermore, MK-801 induced a significant change in the shape of AP of SH-SY5Y cells. Given the importance of Kv3.1 in parvalbumin-positive, fast-spiking GABAergic interneurons, our findings suggest the possibility that MK-801 may affect the firing patterns of action potential in inhibitory neurons, triggering the onset and symptoms of schizophrenia in clinical settings.

Keywords: MK-801, Schizophrenia, Kv3.1 channel, Fast-spiking GABAergic interneuron, Human SH-SY5Y neuroblastoma cells

C01-07

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

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Aberrant Ca^{2+} influx through podocyte Ca2+ channels such as Orai1 and TRPC6 disrupts podocyte cytoskeleton integrity, contributing to injury and proteinuria in chronic kidney disease (CKD). These channels are regulated by STIM1 (stromal interaction molecule 1), an ER Ca^{2+} sensor, through its role in podocyte function and interaction with the renin-angiotensin-aldosterone system (RAAS) remains unclear. This study investigates the protective effects of podocyte-specific STIM1 deletion in a renal fibrosis model and its impact on RAAS-mediated podocyte damage.
Using an adenine-enriched diet, we induced renal fibrosis in wild-type (WT) and podocyte-specific STIM1 knockout (*Nphs2;stim1*$^{fl/fl}$, s1KO) mice. WT mice developed significant renal fibrosis, marked by increased expression of collagen I, IV, and fibronectin, along with decreased slit diaphragm components (podocin, and nephrin) and cytoskeletal proteins (synaptopodin), leading to severe proteinuria. Histological analysis (H&E and Masson's trichrome staining) confirmed extensive fibrosis in WT mice. In contrast, s1KO mice exhibited preserved slit diaphragm integrity and cytoskeletal structure, showing protection against both molecular and histological markers of fibrosis.
In vitro, high doses of Angiotensin II, a key factor in RAAS activation, increased Ca^{2+} influx through TRPC6 in cultured mouse podocytes, while aldosterone treatment did not affect Orai1 or STIM1 expression. These results suggest that STIM1 deficiency protects podocytes from RAAS-mediated Ca^{2+} overload by reducing Ca^{2+} influx through Orai1 and TRPC6, thereby preventing podocyte injury and proteinuria.
In conclusion, STIM1 plays a pivotal role in podocyte injury by regulating Ca^{2+} entry through Orai1 and TRPC6 during RAAS activation. Targeting STIM1-mediated Ca^{2+} signaling may provide a promising therapeutic approach for protecting podocytes and reducing proteinuria in CKD.

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Keywords: Podocyte, Proteinuria, RAAS, STIM1, TRPC6

C01-08

Pannexin-mediated ATP release induces enhancement of ventricular Ca^{2+} transients under shear stress via P2Y1 purinoceptor signaling

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We have previously reported that shear stress increases Ca^{2+} transients in rat ventricular myocytes. Here we examined underlying mechanism for the shear-induced enhancement in Ca^{2+} signaling in field stimulated murine ventricular myocytes using confocal Ca^{2+} imaging. Application of shear stress of 15 dyn/cm^2 using micro-jet apparatus onto single ventricle cells

enhanced Ca^{2+} transient magnitude by ~35% at steady state (15 s), with a small transient increase in diastolic Ca^{2+} level immediately following shear exposure (2 s). Suppression of mitochondrial ROS generation (25 μM mito-TEMPO) eliminated the stimulatory shear effects on Ca^{2+} transients. Inhibitions of either pannexins (800 μM probenecid) or external ATP action (2 U/ml apyrase) abolished the shear-induced Ca^{2+} transient increase. The P2Y1 purinoceptor antagonist (400 nM MRS2179) removed the shear-mediated Ca^{2+} transient increase with rather augmenting the early phase Ca^{2+} signals. Neither antagonism of P2X4 receptors or inhibition of connexin hemichannels did alter the shear-Ca^{2+} response. In P2Y1 purinoceptor knock-out mouse ventricular cells, shear stress failed to induce the stimulatory effects on Ca^{2+} transient but augmented shear induced immediate basal Ca^{2+} increase. Our data suggest that shear stress augments depolarization-induced Ca^{2+} release via P2Y1 receptor-mitochondrial ROS signaling pathway, activated by pannexin-mediated ATP release in an autocrine mode.

Keywords: Shear stress, Ventricular myocytes, Ca^{2+} transients, P2Y1 purinoceptor, Pannexin

C01-09

Differential regulation of current kinetics by beta subunits in N-type calcium channel

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The N-type voltage-gated calcium channel (CaV2.2) regulates synaptic transmission by controlling calcium influx during membrane depolarization. Auxiliary β subunits act as modulators for the gating properties of various calcium channels. However, the differential effects of β2 splice variants on CaV2.2 current kinetics remain unclear. Here, we elucidate how β2a and β2c subunits distinctly modulate CaV2.2 current kinetics. Using whole-cell voltage-clamp in a heterologous system, we analyzed current decay with a double exponential function model ($y = Aexp(-x/\tau_A) + Bexp(-x/\tau_B) + y_0$). During 10-second depolarizing pulses, the current decayed much more slowly in CaV2.2 with β2a compared to CaV2.2 with β2c. Double exponential fitting uncovered β subunit-dependent patterns in amplitude components (A and B) and time constants (τ_A and τ_B). CaV2.2 with β2a showed a dominant slow component ($A \approx 0.88$, $\tau_A \approx 2$ s) and a minor fast component ($B \approx 0.12$, $\tau_B \approx 70$ ms). In contrast, CaV2.2 with β2c displayed a predominant fast component ($A \approx 0.85$, $\tau_A \approx 116$ ms) and a minor slow component ($B \approx 0.15$, $\tau_B \approx 3$ s). We hypothesize that components A and B represent voltage-dependent inactivation and deactivation, respectively, under sustained depolarization. β2a promotes rapid channel deactivation, allowing the current to reach equilibrium between activation and deactivation quickly with slow inactivation. Conversely, β2c induces rapid overall current decay primarily through accelerated inactivation, overshadowing the gradual deactivation process. Our findings demonstrate a significant functional divergence between membrane-anchored (β2a) and cytosolic (β2c) subunits within the β2 family, highlighting the critical role of β subunit localization in fine-tuning channel function. This study will provide novel insights into the molecular basis of calcium signaling in neurons.

Keywords: N-type calcium channels, B subunits, Current decay, Inactivation, Deactivation

C01-10

Role of TREK-2 (KCNK10) K+ channel in differentiation of human epidermal keratinocyte

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Keratinocytes, the predominant cell type in the epidermis, differentiate into corneocytes to form a protective skin barrier. Ion channels, particularly TRPV family Ca^{2+} channels, are believed to play a key role in keratinocyte differentiation. In addition, K^+ channels are thought to facilitate Ca^{2+} influx by providing the necessary electrical driving force. While the expression of the two-pore domain K^+ channel TREK-2 has been suggested, its role in normal human epidermal keratinocyte (NHEK) differentiation remains unexplored. Using immunohistochemistry, we observed increasing expression of TREK-2 in the transitional zone from the basal layer to the upper layers of the human epidermis. TREK-2 expression and the associated voltage-independent K^+ current (ITREK-2) were confirmed in cultured NHEKs during Ca^{2+}-induced differentiation. Inhibition of ITREK-2 by norfluoxetine, a TREK-2 inhibitor, impaired the expression of differentiation markers such as keratin-10 and loricrin. Moreover, TREK-2 activation by ML-335 led to early termination of proliferation, while norfluoxetine promoted prolonged proliferation in cultured NHEKs. These results highlight the crucial role of TREK-2 in coordinating the balance between keratinocyte proliferation and differentiation, thereby contributing to epidermal homeostasis and skin barrier integrity.

Keywords: Keratinocyte differentiation, Epidermal homeostasis, Skin barrier integrity, TREK-2(KCNK10), K^+ channels

C01-11

Asarinin: A Natural TRPV3 Inhibitor Unveiled by In Silico Screening with Therapeutic Potential for Inflammatory Skin Disorders

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Transient receptor potential vanilloid 3 (TRPV3) is a thermosensitive ion channel implicated in various skin disorders. We aimed to identify novel TRPV3 inhibitors from a library of 1,063 natural compounds using in silico molecular docking and to validate their effects in vitro. We performed in silico screening using AutoDock Vina and a unique scoring function, Residue Interaction Similarity (RIS), to identify potential TRPV3 inhibitors. The inhibitory effects of the top hit, asarinin, were validated using patch-clamp, calcium imaging, and cytokine release assays in normal human epidermal keratinocytes (NHEKs). The effects of asarinin on the gain-of-function TRPV3 variants associated with Olmsted syndrome were also investigated. Asarinin, a natural compound from Asarum sieboldii, was identified as a potent TRPV3 inhibitor with an IC50 of 24.7 μM at -100 mV. Asarinin selectively suppressed TRPV3-mediated currents, calcium influx, and cytokine release in NHEKs. Furthermore, asarinin effectively inhibited the constitutive activity of TRPV3 gain-of-function variants (G573S and G573C) and rescued cell death in transfected HEK293T cells. Our study demonstrates the potential of in silico screening in identifying novel TRPV3 inhibitors and reveals asarinin as a promising candidate for treating skin disorders associated with TRPV3 dysfunction, such as Olmsted syndrome. These findings provide a basis for further investigation of asarinin in preclinical and clinical settings.

Keywords: TRPV3, Asarinin, Molecular docking, Olmsted syndrome, Keratinocytes

C01-12

WNK1 suppresses autophagy by inhibiting TRPML1-mediated peri-lysosomal Ca^{2+} dynamics

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Autophagy is a fundamental cellular degradation pathway vital for maintaining cellular homeostasis and adapting to metabolic stress. The TRPML1 lysosomal Ca^{2+} release channel plays a pivotal role in initiating autophagy. WNK(With-No-Lysine [K])- kinases(WNK1-4) are well established ion channel and transporter homeostasis regulators. WNK1, in particular, has been implicated in autophagy inhibition by suppressing the class III phosphoinositide-3-kinase(PI3K) complex. However, the precise mechanisms by which WNK signaling regulates TRPML1 in the context of autophagy remains unclear. This study found that WNK kinases suppressed TRPML1 activity, leading to autophagy inhibition. Using HEK293 or HeLa cells expressing GCaMP3-labelled TRPML1, we observed that the overexpression of WNK1 or 4 significantly reduced TRPML1-mediated peri-lysosomal Ca^{2+} release. This suggest that multiple WNK kinases act as regulators of TRPML1. Notably, the suppression of Ca^{2+} release and the subsequent nuclear translocation of TFEB by WNK1 was rescued by the forced expression of a catalytically inactive mutant of WNK1 (kinase-dead mutant, K233M). This highlights the crucial role of the catalytic activity of WNK1 in inhibiting TRPML. Furthermore, insulin, an endogenous WNK1 activator, also suppressed TRPML1-mediated Ca^{2+} release, reinforcing the link between WNK1 activation and autophagy inhibition. This effect was effectively reversed by pretreatment with WNK463 (a WNK inhibitor) or PI(3,5)P2-(diC16), further supporting the that WNK1 inhibits TRPML1 by suppressing the class III PI3K. In conclusion, our findings reveal a novel role for WNK kinase signaling in the regulation of autophagy, specifically through its inhibition of TRPML1-mediated Ca^{2+} release and lysosomal biogenesis. These insights offer potential therapeutic targets for modulating autophagy in metabolic and degenerative disease. [This study was supported by the National Research Foundation of Korea (RS-2024-00409403 & NRF-2022R1A2C2011079 and the BK21 FOUR program through the NRF under the Ministry of Education)]

Keywords: TFEB, Lysosomal biogenesis, Lysosomal Ca^{2+}

C01-13

Unraveling the molecular reason of opposing effects of α-mangostin and norfluoxetine on TREK-2 at the same binding site

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TWIK-related K^+channel (TREK)-2, expressed in sensory neurons, is involved in setting membrane potential, and its modulations contributes to the generation of nociceptive signals. Although acute and chronic pain is a common symptom experienced by patients with various conditions, most existing analgesics exhibit low efficacy and are associated with adverse effects. For this reason, finding the novel modulator of TREK-2 is of significance for the development of new analgesics. Recent studies have shown that α-Mangostin (α-MG) activates TREK-2, facilitating analgesic effects, yet the underlying molecular mechanisms remain elusive. Intriguingly, even though norfluoxetine (NFx) is known to inhibit TREK-2, α-MG is also observed to share the same binding site with NFx, and this implies that TREK-2 might be modulated in a highly complicated manner. Therefore, we examine the mechanism of how TREK-2 is activated by α-MG using computational methods and patch clamp experiments in the present study. Based on these results, we offer an explanation of how α-MG and NFx exhibit opposing effects at the same binding site of TREK-2. These findings will broaden our understanding of TREK-2 modulation, providing clues for designing novel analgesic drugs.

Keywords: TREK-2, Alpha-mangostin, Ion channel, Modulation, Molecular dynamics

C01-14

Diphenyleneiodonium suppresses cardiac Ca^{2+} signaling and contraction

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Diphenyleneiodonium (DPI) has been widely used as an inhibitor of NADPH oxidase (Nox) to discover its function in cardiac myocytes under various stimuli. However, the effects of DPI itself on Ca^{2+} signaling and contraction in cardiac myocytes under control conditions have not been understood. We investigated the effects of DPI on contraction and Ca^{2+} signaling and their underlying mechanisms using video edge detection, confocal imaging, and whole-cell patch clamp technique in isolated rat cardiac myocytes. Application of DPI suppressed cell shortenings in a concentration-dependent manner (IC50 of ≅0.17 μM) with a maximal inhibition of ~70% at ~100 μM. DPI decreased the magnitude of Ca^{2+} transient and sarcoplasmic reticulum Ca^{2+} content by 20%–30% at 3 μM that is usually used to remove the Nox activity, with no effect on fractional release. There was no significant change in the half-decay time of Ca^{2+} transients by DPI. The L-type Ca^{2+} current (ICa) was decreased concentration-dependently by DPI (IC50 of ≅40.3 μM) with ≅13.1%-inhibition at 3 μM. The frequency of Ca^{2+} sparks was reduced by 3 μM DPI (by ~25%), which was resistant to a brief removal of external Ca^{2+} and Na+. Mitochondrial superoxide level was reduced by DPI at 3–100 μM. Our data suggest that DPI may suppress L-type Ca^{2+} channel and RyR, thereby attenuating Ca^{2+}-induced Ca^{2+} release and contractility in cardiac myocytes, and that such DPI effects may be related to mitochondrial metabolic suppression.

Keywords: Diphenyleneiodonium, Cardiac myocytes, Ca^{2+} release, Contraction, L-type Ca^{2+} current

D01-01

Immature skeletal myotubes are an effective source for improving the terminal differentiation of skeletal muscle

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Transplantation of satellite cells or cultured myoblasts has been used to improve the skeletal muscle regeneration of injured or atrophied adult skeletal muscles. However, some limitations observed result from the limited number of available satellite cells that can be harvested and the efficiency of fusion of cultured myoblasts with mature muscle fibers (i.e., terminal differentiation) upon transplantation. In addition, possible use of immature myotubes in the middle of the terminal differentiation process instead of satellite cells or cultured myoblasts have not been thoroughly investigated. Herein, myoblasts (Mb) or immature myotubes on differentiation day 2 (D2 immature myotubes) or 3 (D3 immature myotubes) were transferred

to plates containing D2 or D3 immature myotubes as host cells. The transferred Mb/immature myotubes on the plates were further codifferentiated with host immature myotubes into mature myotubes in six conditions: Mb-to-D2, D2-to-D2, D3-to-D2, Mb-to-D3, D2-to-D3, and D3-to-D3. Among these six codifferentiation conditions, the D2-to-D3 codifferentiation condition exhibited the most characteristic myotube appearance and the greatest availability of Ca^{2+} for skeletal muscle contraction. Compared with non-codifferentiated control myotubes, D2-to-D3 codifferentiated myotubes presented increases in the expression of myogenic protein and increased myotube width, accompanied by parallel and swirling alignment. These increases correlated with functional increases in the both electrically induced intracellular Ca_{2+} release. These increases were not detected in any of the other codifferentiation conditions. These results suggest that *in vitro*-cultured D2-to-D3 codifferentiated mature myotubes could be a good alternative source of satellite cells or cultured myoblasts for skeletal muscle regeneration.

Keywords: Immature myotube, Codifferentiation, Terminal differentiation

D01-02

Possible mechanism for difference in Ca^{2+}-frequency response between right and left atrial myocytes

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We have previously found that Ca^{2+} transients decrease at increased stimulation frequency in left atrial (LA) myocytes, but not in right atrial (RA) myocytes. To know underlying mechanism for this difference we investigated SERCA2 and PLB protein expression and their subcellular distributions, and frequency-dependent PLB phosphorylation in rat RA and LA myocytes using Western blot and immunocytochemistry. We found that SERCA2 and PLB monomer expressions were higher in RA than in LA myocytes, and that both of them were more abundant in RA myocytes compared to LA myocytes, with peripheral abundance. The expression profile was somewhat consistent with that obtained from total mRNA sequencing in RA and LA tissues from human and rat. Under resting conditions, PLB phosphorylation at both protein kinase A (PKA) site (Ser16) and Ca^{2+}/Calmodulin-dependent kinase (CaMKII) site (Thr17) were higher in RA than in LA myocytes. In addition, gradual increase in the frequency of electrical stimulations from 0- to 3-Hz in isolated rat RA myocytes and LA myocytes increased the level of PLB phosphorylated at Ser16 and that at Thr17, respectively. These results suggest that SR Ca^{2+} uptake may be more effectively enhanced in RA myocytes in response to increased heart rate, and that PKA and CaMKII may be responsible for the frequency-dependent PLB phosphorylation in RA and LA cells, respectively.

Keywords: Right atrial myocytes, Left atrial myocytes, Frequency, SERCA2, PLB phosphorylation

D01-03

Lubiprostone improves distal segment-specific colonic contractions through TRPC4 activation stimulated by EP3 prostanoid receptor

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Prokinetic agents are effective in increasing gastrointestinal (GI) contractility and alleviating constipation, which is often caused by slow intestinal motility. In particular, lubiprostone (LUB), known for activating CLC-2 chloride channels, increases the chloride ion concentration in the GI tract, which supports the retention of water and facilitates stool movement. Despite its therapeutic efficacy, the exact mechanisms underlying its pharmacological action are poorly understood. Here, we investigated whether LUB activates the canonical transient receptor potential cation channel type 4 (TRPC4) through stimulation with E-type prostaglandin receptor (EP) type 3. In isotonic tension recordings using mouse colon strips, we first noted that LUB showed significant contraction in the distal segment rather than in the proximal segment. Using mouse colon tissue, we first observed significant enhanced contractile wave by LUB in the distal segments compared to that in the proximal segments. Among the EP1-4 receptor subtypes, mRNA levels of the EP3 receptor were found to be highly expressed in distal colonic muscular strips and isolated myocytes by quantitative real-time polymerase chain reaction (qRT-PCR), which was attributed to increased contraction. Ultimately, the LUB-stimulated EP3 receptor could be responsible for TRPC4 activation and intracellular calcium increase in the colonic smooth muscle. LUB-induced spontaneous contractions in distal colon muscles were reduced by TRPC4 blocker or EP3 antagonist.

Taken together, our findings suggest that LUB improves mass movement through indirect activation of the TRPC4 channel in the distal colon. The properties of prokinetic agents in this segment-specific manner can provide compelling evidence for a personalized approach to symptom management to aid the defecation reflex.

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Keywords: Lubiprostone, TRPC4 channel, EP receptors, Smooth muscle contraction, Colonic motility

D01-04

Extracts H ameliorate skeletal muscle wasting in High-Fat Diet-induced sarcopenic obesity via activating FNDC5 signaling pathway

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Sarcopenic obesity (SO) combines obesity with muscle loss, presenting significant health risks due to high-fat diet-induced skeletal muscle atrophy driven by inflammation, apoptosis, reduced protein synthesis, increased proteolysis, and mitochondrial dysfunction. This study investigates the effects of Extract H on muscle atrophy in a high-fat diet (HFD)-induced mouse model. C57BL/6J mice were fed either a regular diet, an HFD, or an HFD supplemented with Extract H for eight weeks. HFD-induced muscle atrophy was associated with elevated levels of atrophy-related proteins such as MuRF-1 and Atrogin-1, mediated by the activation of inflammatory pathways, and impaired glucose transport. Our results demonstrate that Extract H significantly reduced inflammatory markers, enhanced protein synthesis, and improved antioxidant defenses. Additionally, Extract H promoted GLUT4 translocation in skeletal muscle, leading to enhanced glucose uptake. Moreover, HFD-induced mitochondrial dysfunction was reversed by treatment with Extract H. In C2C12 myotube cells, palmitic acid-induced reductions in mitochondrial biogenesis were also restored by Extract H treatment. Furthermore, Extract H increased the expression of FNDC5, a myokine known to alleviate obesity and metabolic disorders by reducing inflammation and improving insulin sensitivity, as shown in both in vivo and in vitro studies.

These findings highlight the potential of Extract H as a therapeutic agent for managing sarcopenic obesity and enhancing muscle health in the context of a high-fat diet. Additionally, Extract H acts as an exercise mimetic, offering a promising intervention to counteract HFD-induced muscle atrophy.

Keywords: Sarcopenic obesity, Muscle atrophy, GLUT4, Inflammation, FNDC5

D01-05

αKlotho Mitigates Doxorubicin-Induced Muscle Atrophy by Regulation of Transcriptional Factors, FOXO3a and Myogenin

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As the global population ages, sarcopenia—the progressive loss of muscle mass and strength—has emerged as a critical health challenge. Understanding the molecular mechanisms driving muscle degradation in aging is essential for developing effective treatments. This study explores the potential of αKlotho, a hormone associated with longevity, to protect against muscle atrophy by regulating key transcription factors, FOXO3a and myogenin.
In vitro, differentiated C2C12 myotubes were treated with low concentrations of doxorubicin (Dox) to simulate the muscle wasting observed in sarcopenia. Dox treatment led to increased FOXO3a expression and decreased myogenin levels, impairing muscle differentiation. Co-treatment with αKlotho reversed these effects, inhibiting FOXO3a and restoring myogenin expression, which in turn promoted muscle recovery. Given that FOXO3a acts as a transcription factor for genes such as Atrogin1, MuRF1, and Myostatin—key regulators of protein degradation—these results suggest that αKlotho may reduce protein degradation by modulating FOXO3a activity.
In addition, αKlotho demonstrated protective effects against H2O2-induced oxidative stress in muscle cells. It boosted myogenin levels, which were otherwise reduced by H2O2, and facilitated the nuclear translocation of FOXO3a while reducing its cytosolic presence. This shift in FOXO3a localization suggests that αKlotho not only regulates myogenin expression but also mitigates protein degradation through FOXO3a's transcriptional control of catabolic genes.
Collectively, these findings indicate that αKlotho plays a crucial role in preventing muscle loss in aging-related sarcopenia by targeting the FOXO3a-myogenin pathway. This highlights its therapeutic potential in mitigating muscle atrophy and preserving muscle function in age-related conditions.

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Keywords: αKlotho, FOXO3a, Myogenin, Reactive oxygen species, Sarcopenia

D01-06

The effects of TFAM on Calcium Dynamics in Skeletal Muscle

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Introduction: Mitochondrial transcription factor A (TFAM) is essential for the function of mitochondria which are heavily involved in regulating energy metabolism[1-3], thus, we hypothesize that TFAM is involved in the regulation of calcium (Ca^{2+}) dynamics in the skeletal muscle. This study investigates the impact of TFAM expression on calcium-associated proteins and Ca^{2+} flux between organelles in C2C12 myotubes.
Methods: TFAM was transfected using either an empty vector (EV) or a TFAM-Adenovirus vector. Proteomic analysis of C2C12 cells was performed to identify pathways mostly influenced by TFAM expression using gene set enrichment analysis (GSEA)[4]. The expression of interest genes and proteins involved in these pathways was validated using reverse transcript–quantitative PCR (RT-qPCR) and Western blotting (WB). Cytosolic Ca^{2+} levels, both at baseline and following caffeine treatment, were measured using FURA-2, AM to evaluate intracellular calcium storage and dynamics.
Results: Gene ontology (GO) pathway analysis indicated that TFAM overexpression attenuates mitochondrial respiration whereas enhancing cytoskeletal dynamics, including calcium ion binding pathway. RT-qPCR and WB validation showed that TFAM overexpression increases the expression of genes and proteins involved in calcium release from the sarcoplasmic reticulum (Casq1, Casq2), while decreasing the levels of Ca^{2+}-buffering cytosolic protein parvalbumin (Pvalb).
Conclusion: These findings suggest that TFAM modulates the expression of Ca^{2+}-associated proteins, which may alter Ca^{2+} flux, consequently, mediating organelle communication in skeletal muscle. However, further studies are required to confirm the role of TFAM in regulating calcium dynamics and retrograde signaling between organelles in skeletal muscle.

Keywords: TFAM, Skeletal Muscle, Calcium Dynamics

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D01-07

Compound A enhances PGC-1α in skeletal muscle, modulates kynurenine metabolism, and improves mitochondrial function in chronic kidney disease

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Chronic kidney disease (CKD) has emerged as one of the most prominent causes of death and suffering in the 21st century. Due in part to the rise in risk factors, such as obesity and diabetes mellitus, the number of patients affected by CKD has also been increasing, affecting an estimated 850 million individuals worldwide in 2024. CKD is characterized by impaired kidney function and progressive renal damage, leading to uremic sarcopenia—a condition marked by muscle wasting. Uremic toxins, acting as agonists of the aryl hydrocarbon receptor (AhR), play a pivotal role in promoting muscle wasting and mild cognitive impairment. Despite the prevalence of CKD-associated myopathy, effective treatments remain elusive. In our study, we aimed to identify Compound A, a potential AhR-targeting compound, for mitigating CKD-induced muscle atrophy and neuroinflammation. Our findings demonstrate that Compound A reduces AhR-related gene suppression, reactive oxygen species (ROS), and increases muscle protein synthesis through upregulation of kynurenine aminotransferases (KATs), antioxidant markers, and myotube differentiation in C2C12 myotubes. For the in vivo study, we used 4-month-old C57BL/6J mice, randomly divided into five groups. Chronic kidney disease was induced in mice through an adenine diet, and Compound A was administered daily for 31 days. We observed that Compound A modulates mitochondria-related genes, suppresses neuroinflammation and enhances KAT expression in CKD mice. Then we conclude that Compound A attenuates muscle mitochondrial dysfunction and neuroinflammation due to its effect on KAT expression in skeletal muscle.

Keywords: Chronic Kidney Disease (CKD), Neuroinflammation, Mitochondrial Function

D01-08

Skeletal muscle-specific DKK3 overexpression exacerbates insulin resistance in obese mice

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Dickkopf-related protein 3(DKK3) is a secreted glycoprotein belonging to the Dickkopf family. It is a regulator of the Wnt signaling pathway, which is associated with metabolic diseases such as diabetes, and is also known as a tumor suppressor gene due to its reduced expression in several cancers. DKK3 levels are increased in the plasma and skeletal muscle of the elderly. It has also been shown that overexpression of DKK3 in the muscles of young mice causes muscle atrophy. Therefore, we were interested in investigating the metabolic role of DKK3 overexpression in skeletal muscle, which has yet to be elucidated. We found that DKK3 is increased in the plasma of old mice and at the protein level in mouse muscle. Based on these previous studies, we aimed to explore the mechanisms underlying its effect on insulin resistance in skeletal muscle-specific obese mice.

We produced the skeletal muscle-specific inducible DKK3 overexpressed (SKM-iDKK3 TG) mice by Cre-dependent gene expression using ACTA1-rtTA tetO-cre. Mice harboring DKK3 TG without Cre were used as a control. High-fat diet (HFD) induced obesity in both SKM-iDKK3 TG and control mice. The two groups had similar body weight, fat mass, and muscle weight. The hyperinsulinemic-euglycemic clamp confirmed that whole-body glucose turnover rates and glucose uptake rates in the skeletal muscle were reduced in HFD-fed SKM-iDKK3 TG mice compared with HFD-fed control mice. In addition, the protein levels of phosphorylated Akt (pAkt), pAS160, and glucose transporter 4 were lower in SKM-iDKK3 TG than those in control mice. DKK3 overexpression also significantly increased p-ERK and inflammatory cytokines. WNT signaling markers such as p-GSK3b and non-p-b-catenin and p-ERK were significantly increased in C2C12 myofibers. Inflammatory cytokines and markers of aging were also significantly increased. Overexpression of DKK3 increased WNT signaling and p-ERK, and also increased markers of aging and inflammation.

These results suggest that overexpression of DKK3 in skeletal muscle exacerbates insulin resistance and aggravates aging and inflammation in obese mice. DKK3 may therefore be a therapeutic target for type 2 diabetes.

Keywords: DKK3, Skeletal muscle, Insulin resistance, High-fat diet, Aging

E01-01

Subunit-specific developmental roles of phosphatidylinositol 3-kinase in steroidogenic factor-1- expressing cells

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Purpose: Current study figure out that PI3K, especially its catalytic subunits, plays a functional role in SF-1-expressing organs, including the VMH, adrenal glands, and gonads. Backgroud: Phosphatidylinositol 3-kinase (PI3K) regulates cellular development and energy homeostasis. However, the roles of its subunits in organ development remain largely unknown. **Methods:** We explore the role of PI3K catalytic subunits in SF-1-expressing cells by knockout of both p110α and p110β subunits. **Results:** Although no detectable changes in the formation of the ventromedial hypothalamus, we observed remarkable hypotrophy in the adrenal cortex, testis, and ovary in mice with double-knockout of p110α and p110β in SF-1-expressing cells (p110αβ KOSF-1). In addition, the hormones such as corticosterone and aldosterone were significantly reduced. Furthermore, the absence of these subunits led to a reduction in body weight reduction and survival rate as well as impaired glucose homeostasis in p110αβ KOSF-1 mice. **Conclusion:** The data demonstrate the specific role of PI3K catalytic subunits in the developmental and functional roles of SF-1-expressing organs.

Keywords: Phosphatidylinositol 3-kinase, P110α, P110β, SF-1, Development

E01-02

Primary Cilia in the Hypothalamic Neurons Mediate Metabolic Effects of Butyrate

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The microbiota-derived short-chain fatty acid (SCFA) butyrate is known to act beyond the gut to influence host metabolism, including its central nervous system regulation of appetite and energy homeostasis. However, mechanistic insights into central butyrate metabolic actions are undetermined. Here we showed that butyrate directly modulates primary cilia of the agouti-related peptide (AgRP) and pro-opiomelanocortin (POMC) neurons in the hypothalamus arcuate nuclei to promote its anorexigenic and metabolic effects on glucose homeostasis. Butyrate treatement, either via peripheral or central administration, markedly increased histone acetylation and ciliogenesis in the hypothalamus, suppressing food intake to benefit whole-body metabolism. Disruption of primary cilia in the entire hypothalamus or specifically in the arcuate nuclei, but not in the ventromedial hypothalamus (VMH), abolished butyrate metabolic effects. Mechanistically, deletion of primary cilia impaired cellular expression of the butyrate receptor, GPR41/FFAR3, in the AgRP neurons and eradicated its inhibitory action on these neurons.

Keywords: Short-chain fatty acid, Primary cilia, Hypothalamus, Energy homeostasis

E01-03

Liver receptor homolog-1 regulates methionine cycle via BHMT in liver

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Betaine-homocysteine S-methyltransferase (BHMT), one of the most abundant proteins in the liver, is involved in the regulation of homocysteine metabolism. However, the molecular mechanism of *Bhmt* transcription has not been elucidated. This study projects that BHMT deficiency in liver causes methionine disorder and this mechanism is mediated by liver receptor homolog-1 (LRH-1). During fasting conditions, both *Bhmt* and *Lrh-1* expression is increased in the liver of normal mice, but *Bhmt* expression decreased in LRH-1 liver specific knockout (LKO) mice. In addition, the lipid peroxide content in the liver tissues of LRH-1 LKO mice was increased. Promoter activity analysis confirmed the binding of LRH-1 to a specific site at +131/+137 bp of the mouse *Bhmt* promoter. Results of the study confirm that LRH-1 deficiency is associated with elevated reactive oxygen species (ROS) production, lipid peroxidation, whereas deficiency of BHMT leads to homocysteine accumulation leading to mitochondrial stress in liver. In conclusion, this study suggests that lack of LRH-1-mediated decrease in *Bhmt* expression promotes triglyceride accumulation by increasing ROS levels and induces mitochondrial stress via disrupted methionine cycle.

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Keywords: BHMT, LRH-1, Liver, Methionine cycle, Triglycerides

E01-04

Regulatory Mechanism for Aldehyde Dehydrogenase 1B1 by Liver Receptor Homolog-1 in the Liver

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Ethanol is detoxified in the liver by various enzymes. Previous studies confirm that ethanol intake causes liver lipid accumulation. The LRH-1 is involved in the regulation of lipid and bile acid metabolism, but its role in ethanol metabolism is not yet clear. Therefore, this study aimed to explore the relation between ethanol-induced lipid accumulation and LRH-1. To understand LRH-1 role in liver ethanol metabolism, LRH-1$^{f/f}$ and liver-specific LRH-1$^{f/cre+}$ mice were fed a liquid ethanol diet for three weeks. The results showed that LRH-1$^{f/cre+}$ mice had increased liver weight, neutral fat, and total cholesterol levels. Additionally, markers of liver damage and acetaldehyde levels in serum were higher in the LRH-1$^{f/cre+}$ mice on the ethanol-containing diet. To explore LRH-1 target in ethanol metabolism, RNA-Sequencing analysis was conducted. The results showed that Aldehyde dehydrogenase 1B1 (ALDH1B1) was related to ethanol metabolism in liver. When LRH-1 was deficient, ethanol metabolism genes exhibited a significant decrease in ALDH1B1 expression. Overexpression of LRH-1 in HepG2 cells increased ALDH1B1 expression, and ChIP-Sequencing data confirmed the binding peaks of LRH-1 in the ALDH1B1 promoter. In conclusion, this study confirms that depletion of LRH-1 leads to decreased expression of ALDH1B1, resulting in the accumulation of acetaldehyde and accelerated intrahepatic fat accumulation.

Acknowledgement: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2023R1A2C3003717) and the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (RS-2024-00405900).

Keywords: LRH-1, ALDH1B1, Ethanol metabolism, Acetaldehyde, Liver

E01-05

SREBP-1c deficiency ameliorates liver injury and fibrosis in non-alcoholic steatohepatitis via lipocalin-2

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Enhanced de novo lipogenesis mediated by sterol regulatory element–binding proteins (SREBPs) is thought to be involved in nonalcoholic steatohepatitis (NASH) pathogenesis. In this study, we explored the role of SREBP-1c on NASH and LCN2 gene expression regulation. WT and SREBP-1cKO mice fed with a HFHS diet, CCl4-treated, and with LCN2 overexpression. LCN2 gene expression and secretion increased in CCl4-induced liver fibrosis mice models, and SREBP-1c regulated LCN2 gene transcription. Treatment with holo-LCN2 stimulated intracellular iron accumulation and fibrosis gene expression in mouse HSCs, but this effect was not observed in SREBP-1cKO HSCs, indicating that SREBP-1c-induced LCN2 expression and secretion stimulate HSCs activation through iron accumulation. LCN2 expression was strongly correlated with inflammation and fibrosis in patients with NASH. Our findings indicate that SREBP-1c regulates Lcn2 gene expression, contributing to diet-induced NASH. Reduced Lcn2 expression in SREBP-1cKO mice protects against NASH development. Therefore, the activation of Lcn2 by SREBP-1c establishes new connection between iron and lipid metabolism, affecting inflammation.

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Keywords: SREBP-1c, Non-alcoholic steatohepatitis, Lipocalin-2

E01-06

Regulation of Cystathionine γ-lyase by Liver Receptor Homolog-1 in the Liver

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Liver receptor homolog-1 (LRH-1) is a transcription factor that is extensively expressed and is part of the orphan nuclear receptor family. It is essential for bile acid synthesis and reverse cholesterol transport in both the liver and pancreas. Hydrogen sulfide involved in cell protection, inflammation, vascular function, nerve function and mitochondrial function, is generated through areverse sulfur reaction catalyzed by enzymes like cystathione γ -layse (CTH), cystathione β-synthase, and 3-mecaptopyruvate sulfur transferase. However, the regulatory mechanism governing CTH expression remains unknown. This study aimed to investigate how LHR-1 controls CTH expression and the impact of hydrogen sulfide on the hepatic accumulation of neutral fat. CTH expression was significantly increased by 24-hour fasting in normal mice. To assess hydrogen sulfide activity, mice were measured for hydrogen sulfide production under non-fasting or 24-hour fasting conditions, and it was confirmed that hydrogen sulfide production was significantly reduced in LRH-1 LKO mice than in WT mice. In conclusion, this study reinforces the idea that CTH is a target gene of LRH-1, and that a deficiency of LRH-1 reduces hydrogen sulfide production by suppressing CTH expression. This reduction in hydrogen sulfide impairs fatty acid oxidation, resulting in the accelerated accumulation of triglycerides in the liver.

Acknowledgement: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2023R1A2C3003717).

Keywords: LRH-1, CTH, Hydrogen sulfide, TG accumulation, Liver

E01-07

Isocitrate Dehydrogenase 2 Deficiency Impairs Brown Adipocyte Differentiation through Suppression of LncBate10 Expression

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Brown adipose tissue (BAT) serves as a vital heat-generating organ, playing a key role in the regulation of whole-body energy metabolism through the mediation of thermogenesis. Isocitrate dehydrogenase 2 (IDH2) is an NADP$^+$-dependent enzyme that catalyzes the oxidative decarboxylation of isocitrate to α-ketoglutarate (αKG) within the mitochondrial matrix and is essential for the production of NADPH. Here, we showed that high-fat diet (HFD) feeding resulted in increased weight gain in the IDH2KO mice. Moreover, the levels of nicotinamides like NADP+, NADPH, NAD+, and NADH were significantly decreased in the BAT of the HFD-fed IDH2KO animals, accompanied by decreased mitochondrial function and reduced expression of key genes involved in mitochondrial biogenesis, energy expenditure, and ROS resolution. These data reveal a significant role for IDH2 in limiting ROS-dependent mitochondrial damage when BAT metabolism is normally enhanced to limit weight gain in response to dietary caloric overload. Furthermore, we observed reduced differentiation of brown adipocytes in BAT-specific IDH2 knockout (BKO) mice. RNA-Seq analysis revealed de-

creased levels of the long non-coding RNA BATE10 (LncBate10) in IDH2-deficient BAT. LncBATE10 likely participates in regulating UCP1 expression during brown adipocyte differentiation by influencing PGC-1α function. Therefore, our data suggest that IDH2 deficiency may suppress brown adipocyte differentiation through decreased expression of LncBATE10. The IDH2-αKG-TET2-Nrf2-LncBATE10-PGC-1 pathway in brown adipocyte differentiation could represent a therapeutic target to enhance fat burning and potentially reduce obesity.

Acknowledgement: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2023R1A2C3003717).

Keywords: IDH2, Brown adipose tissue, LncRNA, Brown adipocyte differentiation

F01-01

Heterozygous Apex1 Deficiency Aggravates LPS-Induced Systemic Inflammatory Response in Mice

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The precise role of apurinic/apyrimidinic endonuclease 1/redox factor-1 (Apex1) in regulating systemic inflammation remains largely unexplored. We aimed to investigate the effects of heterozygous Apex1 deficiency on lipopolysaccharide (LPS)-induced systemic inflammation using a murine model. Apex1 heterozygous ($Apex1^{+/-}$) and wild-type ($Apex1^{+/+}$) mice, generated via CRISPR/Cas9, were assessed at 8 weeks of age. Key experiments included transcriptomic profiling, evaluation of inflammatory markers, and hematological analysis. Tissue-specific Apex1 protein levels and markers of oxidative stress (Superoxide, 8-OHdG, and MDA) were measured. Additionally, cytokine/chemokine levels and neutrophil infiltration were evaluated post-LPS treatment. Survival was monitored using Kaplan-Meier analysis. $Apex1^{+/-}$ mice exhibited reduced Apex1 protein levels without significant changes in body weight. Transcriptomic analysis revealed downregulation of antioxidant-related genes, with a corresponding increase in markers of oxidative stress. Neutrophil counts, including splenic $Ly6G^{+}$ neutrophils, were elevated in $Apex1^{+/-}$ mice upon hematological analysis. Post-LPS treatment, inflammatory cytokines (IL-1β, IL-10, TNF-α, MCP-1) were significantly higher in $Apex1^{+/-}$ mice compared to wild-type controls. Survival analysis demonstrated a marked decrease in the survival rate of LPS-treated $Apex1^{+/-}$ mice. Histopathological evaluation revealed exacerbated lung and liver injury, along with increased $Ly6G^{+}$ neutrophil infiltration in $Apex1^{+/-}$ mice post-LPS challenge. Our findings indicate that heterozygous Apex1 deficiency amplifies LPS-induced systemic inflammation, tissue damage, and mortality in mice, underscoring the critical role of Apex1 in controlling inflammatory responses and maintaining physiological balance.

Keywords: APE1/Ref-1, Systemic inflammation, ROS, Oxidative stress

F01-02

Suppression of NF-κB via exosome-based delivery modulates microglia and macrophages to reduce age-related neuroinflammation

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Aging has been implicated as a major cause of neuroinflammation, which leads to several neurodegenerative diseases. Most phenotypic characteristics observed during the aging process result from a low-grade chronic proinflammatory status, characterized by increased infiltration of immune cells and production of proinflammatory cytokines, acute-phase proteins, reactive oxygen species, and autoantibodies. In aged mouse brains, the number of infiltrating immune cells increases, and the key transcription factor for increased chemokines is nuclear factor kappa B (NF-κB). Exosomes are potent therapeutics or drug-delivery vehicles for transferring various materials, including proteins and regulatory genes, to target cells. This study evaluates the therapeutic efficacy of the exosomes loaded with a non-degradable form of IκB, which inhibits the nuclear translocation of NF-κB, in reducing age-related neuroinflammation. Our results demonstrate that exosomes containing IκB significantly affect brain immune cell populations, lower interferon-responsive microglia/macrophages, reduce proinflammatory cytokines, and suppress the interactions between macrophages/microglia and T and B cells in the aged brain. Thus, suppressing NF-κB signaling through exosomal delivery can be considered a novel therapeutic approach to modulate age-related neuroinflammation.

Keywords: Aging, Neuroinflammation, NF-κB, IκB, Exosomes, Single-cell RNA sequencing

F01-03

Increase in PDGFRα expression in the lipopolysaccharide-induced acute lung injury mouse model

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Acute lung injury (ALI) is characterized by severe inflammation and tissue damage, which can often progress to fibrosis. While platelet derived growth factor receptor alpha (PDGFRα) is known for its role in tissue remodeling, its involvement in immune cells such as macrophages during the early stages of lung injury remains less understood. In this study, we investigated the role of PDGFRα-expressing cells in an LPS-induced ALI model, where LPS was administered intratracheally, and experiments were conducted 6 hours post-injection. In LPS-induced ALI mice, we observed elevated levels of inflammatory cytokines, including IL-1β, IL-6, and TNF-α, along with an increased number of inflammatory cells in the bronchoalveolar lavage fluid (BALF). Lung cell analysis from wild-type mice revealed an increase in neutrophils and infiltrating macrophages in the LPS-treated group. Similarly, lung cells from PDGFRαEGFP mice showed a significant increase in neutrophils, macrophages, and particularly infiltrating macrophages following LPS administration. we noted a substantial rise in PDGFRα-expressing

cells in the lung, identified as CD45-negative non-immune cells. However, there was also a marked increase in PDGFRα-expressing infiltrating macrophages. PDGFRα expression in macrophages was confirmed in both lung tissue and BALF, with the majority of these macrophages likely representing the M2 phenotype. Additionally, using the MH-S alveolar macrophage cell line, we demonstrated that LPS induces M1 macrophage polarization, while IL-4 treatment promotes M2 polarization. Notably, M2-polarized macrophages exhibited high levels of PDGFRα expression. These findings indicate that PDGFRα-expressing macrophages may play a dual role in modulating inflammation and contributing to fibrosis in ALI.

Keywords: Acute lung injury, Macrophages, Platelet derived growth factor receptor alpha

F01-04

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

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Despites sesamin possesses various pharmacological properties, its role in promoting apoptosis in activated effector T cells, crucial for managing T cell-mediated disorders like atopic dermatitis (AD), remains unclear. This study investigates sesamin's effects on T-cell-mediated disorders, particularly focusing on the induction of apoptosis in activated T cells via interaction with myeloid cell leukemia 1 (MCL-1). This study employed quantitative PCR, flow cytometry, Western blot, ELISA, pull-down assay and immunoprecipitation to measure the level of mRNA and proteins *in vitro*. *In silico* analysis identified MCL-1 as a target of sesamin. A mouse model induced by house dust mite (HDM) extract and 2,4-dinitrochlorobenzene (DNCB) was used to evaluate the therapeutic effects of sesamin *in vivo*. Sesamin suppressed IL-2 production, CD69 expression and proliferation indicating decreased T cell activation. It was confirmed that sesamin directly interacts with MCL-1, inhibiting its function and interaction with Bak, leading to apoptosis of activated T cells. Oral administration of sesamin in the AD model improved AD symptoms, reduced expression of atopic genes, and moderated systemic immune responses, effects linked to the apoptosis of activated T cells mediated by the modulation of MCL-1. Our findings suggest sesamin has significant therapeutic potential for T-cell-mediated diseases by promoting apoptosis in activated T cells through its interaction with MCL-1. This mechanism not only provides insight into the control of T cell activation but also highlights sesamin as a promising natural compound for treating conditions like atopic dermatitis.

Keywords: Sesamin, T cells, Apoptosis, MCL-1, Atopic dermatitis

F01-05

Polypharmacological Effects of Honokiol on Allergic Rhinitis: Modulating TMEM16A, TRPV1, and Calcium Signaling

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Allergic rhinitis (AR) manifests with symptoms such as sneezing, nasal congestion, and rhinorrhea, each linked to the dysregulation of specific ion channels. For instance, the chloride channel ANO1 contributes to excessive mucosal secretion, TRPV1 contributes to airway hyperresponsiveness, while calcium signaling through CRAC channels induces allergic inflammation. Due to the complex interplay of multiple pathways in AR pathophysiology, a polypharmacological approach targeting multiple ion channels and signaling mechanisms is necessary for effective treatment. In this study, honokiol, a natural compound with potential multi-channel regulatory effects, was evaluated for its therapeutic potential in AR. We conducted ion patch-clamp assays to assess honokiol's inhibitory effects on ANO1, TRPV1, and CRAC currents, along with calcium imaging to examine its impact on intracellular calcium levels in immune cells. Additionally, we investigated honokiol's influence on T cell proliferation and its anti-inflammatory effects in an ovalbumin-induced AR mouse model. Honokiol effectively inhibited ANO1 (IC50: 7.502 μM), TRPV1 (IC50: 4.58 μM), and CRAC (IC50: 7.351 μM) currents. In Jurkat T cells, 10 μM and 30 μM honokiol significantly reduced intracellular calcium influx. Honokiol suppressed T cell proliferation, with 10 μM reducing proliferation by over 50% and 30 μM almost completely inhibiting it. In vivo, honokiol significantly alleviated AR symptoms, reduced serum IgE levels, and decreased eosinophil infiltration in the nasal mucosa, comparable to the effects of standard corticosteroid treatment (mometasone). In conclusion, honokiol's multi-target effects on ion channels and immune modulation suggest its potential as a novel therapeutic option for AR, supporting the need for further investigation into its clinical application.

Keywords: Honokiol, Allergic rhinitis, ANO1, TRPV1, CRAC, Polypharmacology

F01-06

IDH2 Deficiency Triggers Endothelial Inflammation via P66sh-mediated Mitochondrial Oxidative Stress

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Isocitrate dehydrogenase 2 (IDH2) is an essential enzyme in the mitochondrial antioxidant system, which produces nicotinamide adenine dinucleotide phosphate, and thereby defends against oxidative stress. We have shown that IDH2 downregulation results in mitochondrial dysfunction and reactive oxygen species (ROS) generation in mouse endothelial cells. The redox enzyme p66shc is a key factor in regulating the level of ROS in endothelial cells. In this study, we hypothesized that IDH2 knockdown-induced mitochondrial dysfunction stimulates endothelial inflammation, which might be regulated by p66shc-mediated oxidative stress. Our results showed that IDH2 downregulation led to mitochondrial dysfunction by decreasing the expression of mitochondrial oxidative phosphorylation complexes I, II, and IV, reducing oxygen consumption, and depolarizing mitochondrial membrane potential in human umbilical vein endothelial cells (HUVECs). The dysfunction not only increased mitochondrial ROS levels but also activated p66shc expression in HUVECs and IDH2 knockout mice. IDH2 deficiency increased intercellular adhesion molecule (ICAM)-1 expression and mRNA levels of pro-inflammatory cytokines (tumor necrosis factor [TNF]-α, and interleukin [IL]-1β) in HUVECs. The mRNA expression of ICAM-1 in endothelial cells and plasma levels of TNF-α and IL-1β were also markedly elevated in IDH2 knockout mice. However, p66shc knockdown rescued IDH2 deficiency-induced mitochondrial ROS levels, monocyte adhesion, ICAM-1, TNF-α, and IL-1β expression in HUVECs. These findings suggest that IDH2 deficiency induced endothelial inflammation via p66shc-mediated mitochondrial oxidative stress.

Keywords: Endothelial inflammation, IDH2, Mitochondrial dysfunction, P66shc

F01-07

Real-Time Imaging of In Vivo Drug Response Mechanisms within Thymic Tissues

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The CXCR4 antagonist AMD3100 is widely recognized for its role in disrupting the CXCR4-CXCL12 axis, a key mechanism in leukocyte migration and hematopoietic stem cell mobilization. While AMD3100's influence on leukocyte trafficking is well-established, its effects on neutrophil dynamics in specific tissues, such as the thymus, remain less defined. To directly examine the impact of AMD3100 on neutrophil migration, we employed intravital microscopy (IVM) to observe neutrophil behavior in real-time within live mouse thymus tissue.
In this study, mice were divided into two groups. Group 1 (control) received subcutaneous injections of an in vivo buffer, while Group 2 (experimental) received AMD3100. Using IVM with fluorescent labeling, time-lapse Z-stack images were captured at 0-, 45-, and 90-minutes post-injection, allowing for continuous observation of neutrophil migration. A customized chamber was employed to achieve high-resolution imaging of the thymus, situated near the heart.
Results from IVM revealed clear differences between the two groups. In Group 1, neutrophil counts progressively increased over time. In contrast, Group 2 (AMD3100-treated) exhibited a marked peak in neutrophil migration at 45 minutes, followed by a significant reduction by 90 minutes. These findings suggest that AMD3100 alters neutrophil migration dynamics in the thymus, providing real-time evidence of its effects on immune cell behavior in this tissue.
This study demonstrates the value of IVM in visualizing immune cell migration within the thymus, overcoming the challenges posed by its proximity to the heart. By capturing live neutrophil behavior, we gained new insights into thymic immune responses and the pharmacological action of CXCR4 antagonism. Our approach underscores the utility of IVM for advancing our understanding of immune cell dynamics and drug responses in difficult-to-access tissues.

Keywords: Thymus, AMD3100, Neutrophil, Real time imaging, Intravital microscope

F01-08

Gas6-induced AIM suppresses acute lung injury by inhibiting NLRP3 inflammasome activation and inducing autophagy in alveolar macrophages

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Growth arrest-specific protein 6 (Gas6) and apoptosis inhibitor of macrophage (AIM) are crucial proteins that regulate the homeostasis of the immune system and inflammatory disease. The NLRP3 inflammasome is critically implicated in the development of various types of acute lung injury (ALI). Our study explored how Gas6-induced AIM influences the inflammatory response and activation of NLRP3 inflammasome activation in LPS-induced ALI, using both wild type (WT) and AIM–/– mice. We observed that inflammatory cytokine production, neutrophil numbers and protein levels in bronchoalveolar lavage fluid peaked 3 days after LPS treatment, with these responses being mitigated by rGas6 administration. However, these anti-inflammatory effects were absent in AIM–/– mice. In particular, rGas6 administration reduced elevated levels of IL-1β and IL-18, increased caspase-1 activity, and enhanced the formation of apoptosis-associated speck-like protein containing a caspase activation and recruitment domain (ASC) specks in alveolar macrophages at 3 days post-LPS treatment. Furthermore, rGas6 administration promoted autophagy induction and efferocytosis by alveolar macrophages while suppressing reactive oxygen species (ROS) production through AIM production in LPS-induced ALI. However, these effects were not observed in AIM–/– mice. In summary, Gas6-induced AIM production protects against ALI by inhibiting NLRP3 inflammasome activation, promoting autophagy, and reducing oxidative stress.

Acknowledgement: This work was supported by the National Research Foundation of Korea grants funded by the Korean government (MSIT) (2020R1A5A2019210 and 2023R1A2C2003185).

Keywords: Gas6, AIM, Inflammasome, Autophagy, ROS production, Acute lung injury

F01-09

Astrocytic iNOS upregulation contributes to chronic below-level neuropathic pain after spinal cord injury in rats

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Chronic neuropathic pain is a significant complication following spinal cord injury (SCI). Persistent inflammation throughout the spinal cord contributes to the neuropathic pain, but current treatments show limited efficacy. Three types of nitric oxide synthase (NOS) have different role in inflammation and neuronal hyperexcitation. Thus, this study aimed to determine the predominant NOS subtype contributing to neuropathic pain following spinal contusion.
We examined the effects of intrathecal administration of various NOS inhibitors on mechanical hypersensitivity in a rat model of moderate spinal contusion injury. We used N(G)-Nitro-L-arginine methyl ester hydrochloride (L-NAME), 1400W, Aminoguanidine, Nω-Propyl-L-arginine hydrochloride (NPLA), and N5-(1-iminoethyl)-L-ornithine (L-NIO) in this study. Protein expression and cellular localization of spinal NOS subtypes were analyzed in sham and SCI rats.
The non-selective NOS inhibitor L-NAME significantly reduced paw hypersensitivity in a dose-dependent manner, but motor deficits appeared in the highest dose (30 μM). Selective iNOS inhibitors (1400W and Aminoguanidine) effectively reduced mechanical hypersensitivity without motor side effects. The nNOS inhibitor NPLA showed limited efficacy, while the eNOS inhibitor L-NIO had no effect. Protein expression of iNOS revealed a two-fold increase in the L4-5 spinal segment of SCI rats compared to sham controls. The iNOS-immunoreactivity was colocalized with GFAP positive cells in the superficial laminae of the L4-5 spinal segment after SCI, and 1400W reduced hyper-reactivity of iNOS and GFAP.
These findings suggest that iNOS, among the three NOS subtypes, is involved in below-level neuropathic pain following thoracic spinal cord contusion in rats. The specific blockade of iNOS activity may have a potential as a therapeutic intervention for spinal contusion-induced neuropathic pain with minimal risk of side effects.

Keywords: Spinal cord injury, Neuropathic pain, INOS, 1400w

G01-01

Identification of potent bioactive compound from Artemisia princeps for breast cancer therapy

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Breast cancer (BC) is the most common cancer in women worldwide, and is characterized by its histological and molecular heterogeneity. Among the

various BC subtypes, triple-negative BC (TNBC) is the most challenging subtype due to its lack of effective molecular targets and the presence of cancer stem cells (CSCs), which contribute to both recurrence and resistance to conventional breast cancer treatments, ultimately leading to therapeutic failure and increased mortality. Despite the availability of hormone therapies and targeted treatments, patients continue to experience early and late relapses, thus there is a demand for new cytotoxic and selective treatment strategies for these patients. In this study, we investigated the effects of protocatechualdehyde (PCA), a potent bioactive compound derived from *Artemisia princeps*, on both CSCs and non-CSCs in breast cancer cells. PCA inhibited breast cancer cell proliferation and mammosphere formation in a dose-dependent manner. This compound reduced the $CD44^{high}$ /$CD24^{low}$ subpopulation, ALDH-expressing cell population, and the expression levels of self-renewal-related genes such as Nanog, Sox2, and Oct4. Moreover, PCA preferentially reduced protein levels of AKT, pAKT and SOX2. Our findings support the novel utilization of PCA for breast cancer therapy via the AKT/SOX2 signaling pathway. PCA inhibited AKT signaling by reducing AKT and SOX2 protein expression, a CSC survival factor. These findings suggested that PCA held significant therapeutic potential for BC.

Keywords: Breast cancer, Anti-cancer effect, Cancer stem cell, AKT, SOX2

G01-02

Mitochondrial methionyl-tRNA formyltransferase participates in integrated stress response

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Mitochondrial methionyl-tRNA formyltransferase (MTFMT) is required for the initiation of mitochondrial protein translation, and its product, N-formylmethionine, is linked to the cellular stress and proteostasis. However, molecular mechanisms for MTFMT involved in integrated stress response (ISR) has not been clearly elucidated. We introduced MTFMT-deficiency models using siRNA or CRISPR-Cas9 system in HK-2 cells, an immortalized human kidney tubular cell line. Genetic suppression of MTFMT led to decreased protein levels of complex I and IV components but increased copy number of mitochondrial DNA. MTFMT deficiency reduced mitochondrial respiratory activities, NAD+/NADH ratio, and ATP synthesis and augmented mitochondrial electrical gradient and oxidative stress. We further investigated the role of MTFMT in stress response, focusing on its interaction with four stress-activated kinases: PERK, GCN2, HRI, and PKR. Different stresses sensitive to each kinase increased cytosolic localization of MTFMT, while reducing mitochondrial expression of MTFMT. Knockdown of any stress-activated kinases resulted in upregulation of MTFMT. Notably, overexpressing cytosolic MTFMT by introducing E. coli MTFMT elevated the phosphorylation of eIF2α, ATF4, and CHOP, indicating the activation of ISR. Conversely, knockdown or knockout of MTFMT abrogated the ISR, such as upregulation of ATF4 and GRP78 (BiP) upon thapsigargin or amino acid deprivation. The absence of MTFMT not only induced more serious stress, but also led cells more susceptible to death. Taken all together, we suggest that MTFMT plays crucial roles in cellular functions under normal or stress conditions, particularly, to protect from noxious insults by activating stress responses.

Keywords: MTFMT, Mitochondrial translation, Stress response, ISR

G01-03

Paeonia japonica inhibits tumor growth in the mouse CT-26 colon tumor model

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Paeonia japonica has been used as a traditional medicine to treat a variety of ailments, including liver disease. However, the inhibitory effect of *Paeonia japonica* on colon cancer has not been fully understood. The purpose of this study was to evaluate the effect of *Paeonia japonica* on colon cancer. To find a possible explanation for the anticancer effect of *Paeonia japonica*, we evaluated the effect of *Paeonia japonica* on the levels of proliferation and apoptosis in tumor cell line CT-26. In addition, the CT-26-iRFP cell line was used in vitro study whether *Paeonia japonica* has the effect of treating cancer. After that $5*10^3$ CT-26 cells were injected into the flank of mice for in vivo experiments. Mice were randomly divided into groups receiving *Paeonia japonica* (100 mg/kg) as a positive control or PBS as a negative control. We evaluated the effect of *Paeonia japonica* on colon cancer, measuring tumor reduction in mice. The results showed that mice treated with *Paeonia japonica* exhibited measurable clinical signs, including tumor shrinkage. Additionally, *Paeonia japonica* suppressed the expression levels of pERK/ERK and pAKT/AKT in tumors. Overall, the results of this study suggest that *Paeonia japonica* may help treat colon cancer.

Keywords: *Paeonia japonica*, Colon cancer, CT-26, Anticancer

G01-04

Treatment of EGFR-mediated tumors via lysosome acidification

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Hypoxia is a hallmark of solid tumors and occurs in various cancers, including colon cancer. This hypoxic condition promotes cancer cell survival, invasion, and metastasis, while also increasing treatment resistance. It has been observed that hypoxia enhances the activity of RTKs like EGFR, while reducing lysosomal acidification.
The lysosome is a membrane-enclosed organelle that functions as an essential part of the cell's digestive system. This organelle contains over 60 types of hydrolases that can break down biological polymers such as proteins, carbohydrates, lipids, and nucleic acids. These enzymes require an acidic pH for optimal function, achieved by using ATP hydrolysis to pump protons against their electrochemical gradient into the lysosome by the vacuolar H+ ATPase (V-ATPase). The primary function of lysosomes is to digest extracellular material that has been internalized by endocytosis and intracellular components that have been sequestered by autophagy. They recycle the unwanted cellular material as energy, providing a nutrient source for maintaining cellular homeostasis. Lysosomal activity affects the tumor microenvironment, making the tumor cells use energy more efficiently, and it is known to be increased compared to neighboring normal tissues. However, recent studies have shown that increased lysosomal activity can lead to downregulation of Receptor tyrosine kinase (RTK) activity in cancer cells. We hypothesized that lysosomal acidification in cancer cells optimizes hydrolase activity, promote RTK degradation, and thus suppressing tumor malignancy. We induced lysosomal acidification by overexpressing V-ATPase subunits ATP6V1a and ATP6V1B2 in DLD-1 cells and analyzed its effects on tumor suppression through molecular biological assays both in vitro and in vivo. Our results demonstrated that lysosomal acidification promoted RTKs degradation, inhibited downstream signaling pathways RAS-Raf-MEK-ERK and PI3K-AKT, and reduced the growth and migration of cancer cells. Additionally, co-treatment with Osimertinib, an irreversible EGFR tyrosine kinase inhibitor, further inhibited cancer cell growth and increased apoptosis. In vivo experiments also showed significant tumor growth in-

hibition. Targeting lysosomes may be a new approach to overcoming EGFR-mediated cancers.

Keywords: Lysosome acidification, RTK, EGFR, Colon cancer, Hypoxia

G01-05

Mitochondrial Ca^{2+}-regulating gene dynamics as key drivers of the transition from MASLD to MASH

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Not all patients with metabolic liver diseases progress to metabolic dysfunction-associated steatohepatitis (MASH); some remain with metabolic dysfunction-associated steatotic liver disease (MASLD). While the role of mitochondria in lipid metabolism and fibrosis, hallmarks of both MASLD and MASH, is well established, the dynamic regulation of mitochondrial Ca^{2+} during the progression of hepatic metabolic disorders remains unclear. We hypothesized that mitochondrial Ca^{2+} handling plays a pivotal role in the transition of MASLD to MASH. Differential expression (DE) analysis and subsequent meta-analysis of public transcriptome datasets revealed that genes regulating mitochondrial Ca^{2+} uptake exhibit distinct expression patterns in MASLD and MASH. In early disease stages, the expression of the mitochondrial Ca^{2+} uniporter (MCU) increases, while the overall MCU complex and mitochondrial-associated membranes (MAMs) show a declining trend. However, as the disease progresses and fibrosis sets in, MCU further escalates, while other mitochondrial genes exhibit inverse trends compared to the early stages. This indicates a critical role for mitochondrial Ca^{2+} uptake in progressing metabolic liver disorders. Moreover, the correlation between MCU complex and fibrosis markers becomes progressively stronger in control, MASLD, and MASH conditions. Mendelian randomization analysis revealed a significant causal relationship between increased MCU expression and hepatic fibrosis but not fatty liver disease, indicating the centrality of MCU in fibrogenesis. In conclusion, this study highlights the differential regulation of mitochondrial Ca^{2+} uptake genes during the progression of hepatic metabolic disease. Specifically, MCU emerges as a critical factor in the transition from fatty liver to fibrosis, positioning mitochondrial metabolism as a crucial driver of hepatic disease progression.

Acknowledgement: This study was supported by the National Research Foundation of Korea (RS-2024-00409403 & NRF-2022R1A2C2011079 and the BK21 FOUR program through the NRF under the Ministry of Education).

Keywords: Mitochondria, Ca^{2+} signaling, Metabolic liver disorder

H01-01

Sweating Patterns on the Dorsal and Palmar Hands under Heat Stress

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The hands of the human play an important role in body heat exchange. However, studies on segmental differences in hand sweating are not sufficient. The purpose of this study was to examine sweating patterns on both the palmar and dorsal surfaces of the hands, including sweat rate, skin moisture level, and activated sweat gland density (ASGD) in a hot and humid environment. Twenty-five healthy Korean males (24 ± 3.2 y in age, 177.6 ± 5.1 cm in height, 78.6 ± 12.6 kg in weight, 24.8 ± 3.3 kg/m^2 in BMI, 495 ± 43 cm^2 in hand surface area, 0.35 ± 0.05 L in hand volume) participated in the following two trials: dorsal (1) and palmar sweating measurements (2). Local sweat rate, skin hydration, and ASGD were measured on the 13 sites of the hand. A trial consisted of 10-min rest and 60-min passive heating (leg immersion in 42°C water) at an air temperature of 33°C with 60%RH. The results showed that significantly higher sweating was observed on the dorsal regions compared to the palm for all the hand regions (all *P*s < 0.001), except for the ASGD in the interdigital space, indicating the same value during dorsal and palmar measurements. Dorsal regions (66.7%) showed significant relationships between sudomotor responses and morphological parameters. The interdigital space on the hand emerged as a notably important area in the context of sweating patterns. The obtained sweating maps of the dorsum and palm can serve as a visual guide to critical hand regions for assessing regional skin sweating.

Keywords: Sweat gland, Morphology, Local sweat rate, Activated sweat gland density, Skin hydration

H01-02

Relationships with morphological variables, cardiovascular fitness during exercise, and thermophysiological responses under passive heat stress according to Sasang typology

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The present study explored relationships for the Sasang constitutional types between morphological characteristics, cardiovascular fitness during exercise, and thermophysiological responses under passive heat stress. 24 healthy males participated in this study. A questionnaire (QSCCII+) classified the 24 males into 4 Tae-Eum (TE), 5 So-Yang (SY), 15 So-Eum (SE), but no male with Tae-Yang (TY). Morphological characteristics (height, weight, body surface area, total body fat, and body mass index), cardiovascular fitness during exercise (maximum oxygen consumption [VO_{2max}] and maximum heart rate) and thermophysiological responses during passive heat stress test (rectal temperature, total sweat rate, thermal sensation, and thermal comfort) were recorded. The results showed that the TE group had smaller standardized VO_{2max} (ml/kg/min) than the SE and SY group ($P<0.05$), but unstandardized VO2max (ml/min) showed the opposite tendency (TE > SE). There were differences in thermoregulatory behavior to cold stress between the TE and SY groups ($P<0.05$). However, no differences among the three constitutional types in core body temperature, total sweat rate, and subjective perception were found during the passive heat stress. Irrespective of the Sasang types, heavier and fatter subjects showed lower maximum rectal temperature under the passive heat stress ($P<0.05$). These results indicated that the Sasang constitutional types reflect the level of cardiovascular fitness during exercise rather than thermo-physiological responses during the passive heat stress. Further studies with a sufficient number of subjects including TY individuals during both heat and cold stress tests are required in order to verify the present findings.

Keywords: Sasang constitutional medicine, Physical characteristics, Total sweat rate, Self-identified heat tolerance, Heat waves

H01-03

Neurotoxicity of polystyrene in human induced pluripotent stem cell-derived neuron via *Hes* signaling pathway change

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Polystyrene (PS), a type of nanoplastics (NPs) widely used in commercial and industrial fields, is a mixture of styrene monomers. It accumulates in

the human body through respiration or ingestion, induces changes in transcription factors in various organs, and potentially poses a risk to human health. However, research on the exact mechanism is insufficient. In this study, we analyzed the neurotoxicity that appears when PS is treated to human-induced pluripotent stem cell-derived neuron through morphological and physiological changes and aimed to elucidate the mechanism. We treated 30 nm PS, which is a size that can move through the blood-brain barrier and placenta, at 50, 100, and 150 ug/ml for 24 hours, and analyzed the morphological changes of neurons, immunostaining, qPCR, reactive oxygen species (ROS) assay, and changes in neuronal electrophysiological function. As PS was treated, changes in the length of axons and dendrites of neurons and changes in cell body size were observed as the concentration increased. This was also confirmed when observing Nestin and Map2 markers through immunostaining. To confirm at the molecular level, qPCR was performed, and it was confirmed that early neural development markers (*Sox2* and *Pax6*) were significantly decreased, and late neural development markers (*Map2* and *Tuj1*) were significantly increased. Additionally, we confirmed that the transcription factors *Hes1* and *Hes5*, which regulate neurodevelopment, were significantly reduced. Significant changes in ROS and neuro-electrophysiological function were also observed following PS treatment. The findings demonstrated that PS exerted neurotoxic effects on neurons, negatively impacting neurodevelopmental signaling pathways, particularly the regulation of *Hes* transcription factors. These insights may provide a foundational basis for the future development of neuroprotective agents that specifically target this signaling pathway.

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Keywords: Neurotoxicity, Nanoplastic, Polystyrene, *Hes* signaling pathway, IPSC-derived neuron

H01-04

Impact of gestational and lactational low-level cadmium exposure on neurodevelopment

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Cadmium (Cd), a widespread environmental pollutant, is commonly encountered through diet and smoking. Cd can pass from mother to fetus via the placenta and to infants through breast milk, posing potential risks to neurodevelopment. Although high Cd exposure has been linked to neurodevelopmental disorders like ADHD, the effects of low-level exposure remain underexplored. This study investigates the effect of low-level Cd exposure during pregnancy and lactation on neurodevelopment in mice. Prenatal exposure to Cd reduced synaptic excitability in primary cultured neurons and disrupted neuronal morphological maturation. In postnatal day 28 (PND 28) mice, Cd exposure led to a significant reduction in hippocampal neuron populations without evidence of overt toxicity. Additionally, Cd impaired cell proliferation and hindered neuronal differentiation in the dentate gyrus. Analysis of gene expression indicated increased levels of proinflammatory cytokines, microglial markers, and glutamate-related proteins in response to Cd exposure. Enhanced expression of GLT-1 and GFAP was observed in brain tissue. In an in vitro model, Cd-treated neurons displayed increased mGluR5 and GLT-1 levels alongside altered synaptic protein patterns. Pharmacological inhibition of mGluR5 or GLT-1 partially reversed these synaptic alterations. These findings suggest that low-level Cd exposure may interfere with neurodevelopment by affecting synaptic activity and neurogenesis, potentially mediated through dysregulation of mGluR5 and GLT-1 pathways. (This work was supported by the National Research Foundation of Korea (NRF) funded by the Korean government (MSIT) (NRF-2019M3C7A1031455 and NRF-2022R1F1A1075083).)

Keywords: Cadmium, Neurodevelopment, Synapse development, Glutamate receptor, Glutamate transporter

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

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In the context of Republic of Korea's increasing multicultural family demographic, largely attributed to the rise in marriage migration, the nation has recognized a growing need for suitable medical and mental health care services tailored to these families' unique challenges. Adolescents from multicultural families are particularly prone to skin diseases such as allergies and atopic dermatitis due to dietary habits like selective eating and high consumption of instant food, leading to nutritional imbalance. These physical health issues frequently coexist with mental health struggles, such as depression, which are intensified by severe symptoms including pruritus and skin dryness, alongside heightened stress levels. But current mental health services for multicultural families predominantly comprise social adaptation programs, with a focus on female marriage immigrants. This research thus aims to evaluate the potential benefits and necessity of incorporating music therapy into mental health services to address depression and stress in multicultural family adolescents suffering from atopic dermatitis. The study's comprehensive measurement approach encompassed both physiological and psychological aspects linked to depression and stress. Physiological metrics included axon reflex-mediated sweating, active sweating gland density (ASGD), and active single sweat gland output (ASSGO), while psychological assessments were conducted using the Patient Health Questionnaire-9 and the Daily Hassles Questionnaire to monitor variations in depression and stress. The findings revealed that participants in the music therapy group showed statistically significant enhancements in autonomic nervous system disorders (quantitative sudomotor axon reflex function test), a key indicator often compromised by atopic conditions, depression, and stress. Additionally, significant positive shifts were observed in the psychological assessments. These study results underscore the imperative for integrating music therapy into mental health care practices, aimed at mitigating symptom aggravation, and managing depression and stress in multicultural family adolescents afflicted with atopic dermatitis.

Keywords: ASGD, ASSGO, Depression, Music therapy, Atopic dermatitis

H01-06

Effects of dance movement therapy on anxiety of juvenile delinquents in a detention center: Role of dopamine and body temperature in anxiety

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Anxiety levels were exacerbated among adolescents amid the COVID-19 pandemic. Agitation and stress of juvenile delinquents (JD) could be considerably higher than those of general adolescents due to their restricted status of liberty and social isolation in the juvenile detention center in Korea. The aim of this research is to discern the psychophysiological impacts of dance movement therapy (DMT) as a form of psychotherapeutic physical activity on improving anxiety symptoms among JD. A total of all females 55

adolescents participated in this study, including general adolescents control group (n=30) and JD group (n=25). For 8 weeks consisting of 24 sessions, JD group was subjected to DMT interventions. Before and after intervention assessments of psychological anxiety levels were conducted using the Beck Anxiety Inventory (BAI), while physiological factors including mean body temperature (mTb) and blood dopamine (DA) levels were also measured. Subsequent to the implementation of DMT, a noteworthy reduction in BAI scores (10%) was observed within the JD group, alongside a significant elevation in mTb (0.11±0.07℃) and blood DA levels (30%). Furthermore, inverse associations were identified between BAI scores and mTb, whereas positive correlations were evident between mTb and DA levels. Conversely, negative correlations emerged between BAI scores and DA levels. Although it is difficult to generalize the results of this study, these findings collectively underscore the efficacy of DMT as a non-pharmacological intervention for mitigating anxiety symptoms among JD subjected to the constraints of physical confinement in a stressful and restricted environment during the COVID-19 pandemic.

Keywords: Anxiety, Dance movement therapy, Juvenile delinquents, Dopamine, Body temperature

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H01-07

Impact of GIM Guided Imagery and Music using Ambient music on heart rate variability and plasma cortisol

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This study evaluated the effects of ambient music on human's emotional and physiological changes and confirmed the therapeutic usefulness of ambient music based on the effects. In order to verify the heart rate variability and cortisol changes of 42 study subjects with GIM Guided Imagery and Music using ambient music, before and after neurotransmitter's degree of change was compared and analyzed by hormone analysis through body blood test. As a result of music therapy between the two groups, autonomic nervous system control ability, mental stress, fatigability, average heart rate, and cortisol showed significant differences between the two groups in the measurement stage T#2. In all measurement stages, autonomic nervous system control ability, mental stress and fatigability were strongly correlated with the alteration of cortisol. In particular, high correlation coefficient between autonomic nervous system control ability and fatigability proves a strong correlation between them. It was confirmed that guided imagery technique using ambient music based on electronic music is effective in reducing stress. Moreover, it can be actively used in the development of basic data for various music therapy studies on electronic music and multi-purpose music therapy programs in the future.

Keywords: Music therapy, Ambient music, Guided imagery and music therapy, Heart rate variability, Cortisol

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H01-08

The acclimatization of Haenyeo to a cold environment and occupational characteristics evaluated by fibroblast growth factor 21 levels

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Haenyeo is a woman who has the job of collecting seafood in the Jeju Sea at an average temperature of 13 – 14 °C. The purpose of this study was to examine the cold acclimatization and occupational characteristics of Haenyeo through biomarkers such as fibroblast growth factor 21 and irisin related to heat generation in the body. A group of 25 Haenyeo and 30 general public group participants with similar ages and body mass indexes were randomly selected. In the cold-loading experiment, an automated climate chamber was set to 5 °C and both feet were immersed in a 15 °C water tank for 30 minutes. Tympanic temperature (Tty) and skin temperature (Tsk) were measured, and the mean body temperature (mTb) was calculated. Blood samples were collected before and immediately after the examination. Orexin, irisin and, FGF21 levels were analyzed. FGF21 levels were elevated after cold stimulation from 17.28±9.24 to 26.41±14.07 pg/ml (Haenyeo group, $P < 0.001$) and 13.61±8.44 to 15.93±10.27 pg/ml (control group, $P < 0.001$). Our experimental results suggest that Haenyeo were superior in heat generation compared to the control group in conditions of chronic low-temperature exposure. This study increases the empirical reliability of the global agenda on climate change and suggests that it is necessary to establish a clinical foundation in the field.

Keywords: Haenyeo, Elderly women diver, Brown adipose tissue (BAT), Orexin, Irisin, Cold acclimatization

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I01-01

TRPML3 regulates type III unconventional protein secretion of MIF

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The intracellular Ca^{2+} channel TRPML3 regulates various membrane trafficking events, including endocytosis and autophagy; however, its role in other types of membrane dynamics remains unclear. In this study, we demonstrate that TRPML3 also regulates type III unconventional protein secretion (UcPS) pathways: TMED10-Channeled UcPS (THU) and secretory autophagy. TRPML3 interacted with TMED10 and the pro-inflammatory cytokine MIF that is secreted via an undefined UcPS mechanism. MIF interacted with TMED10 and its secretion was increased by TMED10 overexpression. Notably, TMED10 knockdown also enhanced MIF secretion, which is blocked by autophagy inhibition. MIF colocalized with LC3 and its secretion was increased upon autophagy induction. Importantly, overexpression of wild-type TRPML3 increased, whereas that of dominant-negative TRPML3 decreased MIF secretion. Taken together, our findings establish MIF as a novel substrate of THU and secretory autophagy and highlight the role of TRPML3 in regulating type III UcPS.

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Keywords: TRPML3, Unconventional protein secretion, MIF, TMED10, Secretory autophagy

I01-02

The cholesterol-binding protein STARD3NL negatively regulates autophagy through interaction with TRPML3

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TRPML3 is a lipid-regulated channel that releases Ca^{2+} from the phagophore to facilitate autophagosome formation as a downstream effector of PI3P. Although various lipids, including cholesterol, are implicated in autophagy, the molecular mechanism by which lipids regulate autophagy remains elusive. Here, we report that the cholesterol-binding protein STARD3NL acts as a negative regulator of autophagy in a manner similar to cholesterol. Overexpression of STARD3NL decreased, while its knockdown increased autophagic flux. Upon induction of autophagy, STARD3NL, which is normally expressed in late endosomes, was translocated to the phagophore and trans-Golgi network. STARD3NL interacted with the phagophore Ca^{2+} channel TRPML3, and this interaction was enhanced by autophagy induction. Importantly, TRPML3 activation rescued autophagy defects induced by either cholesterol or STARD3NL overexpression, implying a specific relationship between cholesterol and TRPML3. These findings suggest that cholesterol and its binding protein STARD3NL negatively regulate autophagy, perhaps by inhibiting the lipid-regulated channel TRPML3 during the early stage of autophagy.

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Keywords: TRPML3, Cholesterol, STARD3NL, Autophagy

I01-03

The scramblase ATG9A regulates TRPML3 activation by PI3P in autophagy

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TRPML3 functions downstream of PI3P in the phagophore to provide Ca^{2+} for autophagosome formation. TRPML3 binds to PI3P in both the cytosolic and luminal leaflets, which induces Ca^{2+} release via TRPML3 upon autophagy induction to increase autophagy. Since ATG9A serves as a scramblase to transport PI3P from the cytosolic to the luminal leaflet of the phagophore, we hypothesized that TRPML3 may interact with ATG9A to be activated by PI3P of both leaflets in autophagy. We found that TRPML3 interacts with ATG9A at its N-terminus, and the interaction is required for not only TRPML3 activation but also autophagosome formation upon autophagy induction. Lipid delivery experiments revealed that the TRPML3-ATG9A interaction allows PI3P to be supplied to the luminal leaflet for TRPML3 activation in autophagy. Using ATG9A mutants lacking scramblase function, we confirmed that ATG9A-mediated PI3P translocation is responsible for TRPML3 activation by PI3P in autophagy. These findings suggest that TRPML3 is activated by PI3P translocation through interaction with ATG9A to increase autophagy.

Acknowledgement: RS-2024-00355756

Keywords: TRPML3, ATG9A, Scramblase, PI3P, Autophagy

I01-04

Ulinastastin Attenuates Vascular Damage in IDH2-Deficient Endothelial Cells via TGF-β/MMP7/SDS2 signaling pathway

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Syndecan-2 (SDC2), a glycocalyx protein, is highly expressed in endothelial cells and upregulated during inflammation. In our previous study, we have shown that mitochondrial dysfunction in isocitrate dehydrogenase 2 (IDH2)-deficient endothelial cells leads to an increase in inflammation induction. Therefore, we aimed to explore the effect of SDC2 expression in IDH2-deficient endothelial cells. We demonstrated that IDH2 knockdown led to an increase in SDC2, matrix metalloproteinase 7 (MMP7), and TGF-β expression in human umbilical vein endothelial cells (HUVECs). SDS2 level was decreased by MMP7 inhibitor treatment, suggesting that MMP7 affected SDC2 expression via TGF-β pathway in IDH2-deficient HUVECs. Furthermore, Ulinastatin (UTI) reversed the changes induced by IDH2 deficiency in both HUVECs and aorta of mice respectively. These results showed that UTI attenuated vascular endothelial cell damage caused by downregulation of IDH2 via the TGF-β/MMP7 signaling pathway.

Key word: Ulinastatin, IDH2, SDS2, Endothelial cells, Vascular damage

I01-05

Downregulation of CTCF ameliorates tau-induced deficits in *Drosophila melanogaster*

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Tauopathies, such as Alzheimer's disease (AD), are neurodegenerative diseases characterized by the deposition of neurofibrillary tangles comprising hyperphosphorylated tau protein in the human brain. Given that abnormal epigenetic alterations in CTCF insulator configuration have been documented in AD patients, we investigated the roles of CTCF insulator in tauopathies. We examined whether loss-of-function alleles of CTCF can affect tau-induced neurotoxicity using transgenic flies via UAS-Gal4 binary system. Here, we found that loss-of-function alleles of CTCF ameliorates locomotion defects and reduced lifespan. Intriguingly, loss-of-function allele of CTCF restored tau-induced heterochromatin loosening; it repressed abnormal overexpression of heterochromatic genes and transposable elements. Moreover, loss-of-function allele of CTCF restored aberrant insulator-mediated epigenetic alterations and reduced phosphorylated tau. These results suggest that downregulation of CTCF expression may be a potential therapeutic target in neurodegenerative diseases; they also provide new insights regarding the roles of insulator proteins in tauopathies.

Keywords: *Drosophila melanogaster*, Tauopathy, CTCF, Insulator, Heterochromatin, Transposable elements

I01-06

Neddylation fine-tunes bone homeostasis by seesawing between the differentiation of osteoblasts and osteoclasts

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Postmenopausal osteoporosis, the most prevalent type of osteoporosis in women, arises from an imbalance in osteoblast and osteoclast function. Recent studies have extensively investigated the post-translational modifications (PTMs) of Runt-related transcription factor 2 (Runx2), the key transcription factor required for osteoblast differentiation. They have also investigated the PTMs of the nuclear factor of activated T-cells calcineurin-dependent 1 (NFATc1), which is vital for osteoclast differentiation. However, the role of neddylation, a crucial PTM regulated by the NEDD8 conjugation pathway, has not been explored. Here, we demonstrated that neddylation plays a pivotal role in the differentiation of both osteoblasts and osteoclasts, notably influencing Runx2 and NFATc1. Inhibiting the neddylation of Runx2 increased its stability and promoted osteoblast differentiation. Conversely, blocking neddylation reduced the stability of NFATc1 by promoting its degradation through ubiquitin-dependent proteasomal pathways, resulting in decreased osteoclast differentiation. Furthermore, the neddylation inhibitor MLN4924 enhanced bone mineral density (BMD) indices and bone formation markers while reducing bone resorption markers in mice with induced osteoporosis. Our findings suggest that inhibiting neddylation could be a potential treatment for postmenopausal osteoporosis, as neddylation appears to play a crucial role in the differentiation of osteoblasts and osteoclasts.

Acknowledgement: Jooseung Lee, Min Young Lee, Geon Ho Moon, and Jun Bum Park received scholarships from the BK21-plus education program of the National Research Foundation of Korea.

Keywords: Neddylation, Post-translational modification, Runx2, NFATc1, Osteoblast, Osteoclast, Postmenopausal osteoporosis

A02-01

Transcriptomic changes by classical fear conditioning in the cerebellum

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Transcriptional changes are essential for long-term synaptic plasticity and memory. Despite growing evidence that the cerebellum is critically involved in classical fear conditioning, changes in gene expressions in the cerebellum following fear learning remain poorly understood. Here, we used spatial and single nucleus sequencing (snRNA-seq) approaches to investigate molecular mechanisms associated with fear learning in the cerebellum, especially in deep cerebellar nuclei (DCN). We found that, like other fear-related brain regions, DCN also showed dynamic changes in pathways related to memory processing such as translation and synapse structure regulation. Furthermore, cell-type specific transcriptional changes were found in DCN after fear conditioning paradigm, suggesting the role of specific cell types in fear memory processing. Together, these findings highlight that the cerebellum, especially the DCN, is an active fear-processing region that undergoes various transcriptional changes by fear conditioning. Our data might shed light elucidating the molecular mechanism how the cerebellum modulates non-motor learning.

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A02-02

Astrocyte-Driven Modulation of Place Cell Activity in the Hippocampus

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Hippocampal place cells are crucial for encoding spatial information and forming the cognitive map. While astrocytes are known to modulate neuronal activity and synaptic transmission, their role in shaping place cell properties and spatial coding remains unclear. We hypothesized that astrocyte activity in the hippocampus plays a key role in modulating place cell function. To test this, we used a mouse model with hM3Dq-expressing astrocytes and GCaMP6f-expressing pyramidal neurons to modulate astrocyte activity and monitor calcium activity in place cells using miniaturized microscopy. During exploration of a familiar arena, astrocyte Gq activation led to a reduction in spatial information scores in non-place cells, as well as decreased place cell stability and proportion, while average firing rates remained unchanged. In contrast, during exploration of a novel arena, astrocyte activation caused a significant decrease in both place cell propor-

tion and spatial information, along with reduced place cell stability, but average firing rates were unaffected. These results highlight the critical role of astrocytes in maintaining precise place coding in the hippocampus, particularly in novel environments where spatial representations are forming. Additionally, we found that astrocyte Gq activation impaired object place recognition in mice, emphasizing the broader influence of astrocytes on spatial cognition and memory processes.Taken together, our study sheds light on the intricate interplay between astrocyte activity and hippocampal place cell properties, emphasizing the importance of astrocytes in spatial cognition.

Keywords: Place cell,s Astrocytes, Miniscope, DREADD

Acknowledgement: This study was supported by grants from National Research Foundation of Korea(NRF) grant funded by the Korea government (800-20240198).

A02-03

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

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Shp2, a SRC homology 2 (SH2) domain–containing non-receptor protein tyrosine phosphatase, regulates synaptic plasticity and associated learning and memory behaviors through posttranslational modification. While the role of Shp2 in regulating synaptic plasticity in mGluR-dependent long-term depression (LTD) has recently been reported, the relationship between Shp2 and N-methyl-D-aspartate receptor (NMDAR)-dependent LTD is not fully understood. We investigated the role of Shp2 in NMDA receptor-dependent long-term depression (NMDAR LTD) by recording depressed local synaptic plasticity at Schaffer collateral (SC)-hippocampal dorsal CA1 synapses. Inhibition of Shp2 was achieved with both active site-directed and allosteric inhibitors to assess its involvement in NMDAR LTD. Interestingly, Shp2 regulates NMDAR LTD with its potential involvement in the SRC homology domain, but not with its active site. Furthermore, Shp2 is engaged in post-synapse, rather than pre-synapse mediating NMDAR LTD. Our findings propose that protein tyrosine phosphatase, specifically Shp2, might be a regulatory factor of NMDAR LTD through its posttranslational modification, suggesting a novel signaling pathway during NMDAR LTD.

Acknowledgement: This work was supported by grants to Y.-S.L (NRF-2022M3E5E8018049) from the National Research Foundation of Korea.

Keywords: Shp2, NMDAR LTD, Synaptic plasticity, Posttranslational modification

References

Lee, S., et al. (2024). "SHP2 regulates GluA2 tyrosine phosphorylation required for AMPA receptor endocytosis and mGluR-LTD." Proceedings of the National Academy of Sciences 121(18): e2316819121.

A02-04

Receptive field difference across cell subtypes of S1B L2/3

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The body receives various external stimuli through somatosensation and relays this information to the primary somatosensory cortex. Notably, the spatial organization of peripheral receptors is preserved in the brain, forming the somatosensory homunculus. In mice, the primary somatosensory barrel cortex (S1B) processes whisker sensory information through inputs relayed from the trigeminal ganglion (TG) in the brainstem to two distinct thalamic nuclei, which then project to the S1B. In layer 4, pyramidal neurons predominantly receive input from the VPM, which forms a cluster of the barrel column. The dendritic and axonal segments of layer 2/3 (L2/3) pyramidal cells from different columns overlap extensively, and the axonal architecture of L2/3 cells differs significantly from that of L4 cells. In layer 2/3, vasoactive intestinal peptide (VIP) and somatostatin (SST) interneurons form local circuits with pyramidal (PYR) cells to regulate sensory processing. Although these differences in morphology and spatial distribution suggest distinct functional roles for pyramidal cells and interneurons, their specific contributions remain poorly understood. We hypothesized that S1B layer 2/3 PYR, VIP, and SST cells exhibit different types of receptive fields. For this study, we employed in vivo two-photon calcium imaging on awake mouse to investigate the receptive field properties of S1B L2/3 neurons across different cell types. We found that the receptive fields of excitatory neurons in S1B are segmented by stimulus location, while the receptive fields of SST and VIP inhibitory neurons in S1B are more dispersed.

Keywords: Primary somatosensory cortex, Barrel cortex, Interneuron, Receptive field, Two-photon microscope

A02-05

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

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Fear conditioning is mediated by a brain-wide distributed neuronal network, which requires intricate neural communication between different brain regions. The amygdala is involved in fear conditioning by strengthening cortico-amygdala synapses. Within this same system, the cerebellum is also known to be recruited in response to fear conditioning. However, its interaction with the post-circuitry remains unknown. Here, we identify a population of neurons in the reticulotegmental nucleus (RtTg) projections to the fastigial nucleus (FN), and the FN is involved in long-term auditory fear memory processing but not in long-term contextual fear memory processing in the cerebellum. Moreover, we recorded the cerebellar cortical activity during the fear learning and consolidation. We found that gamma power in the cerebellar cortex (CTX) is potentiated during fear memory consolidation. Furthermore, the gamma power at fear memory consolidation positively correlated with fear memory. These results suggest that FN is involved only in auditory fear, and fear learning reorganizes cerebellar cortical activity.

Keywords: Fear, Cerebellum, Plasticity, Brain wave

A02-06

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

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The cerebellum is a brain region which receives and integrates diverse sensory information, and subsequently contributes to a function of error prediction for learning and memory. This fundamental cerebellar principle makes the cerebellum perform its motor coordination functions as well as non-motor functions such as classical fear conditioning and social behavior. Even though several cerebellar output pathways have been suggested to affect fear learning and memory, however, how neural activities in the cerebellum and its postsynaptic target regions are affected by fear conditioning remains elusive. Here, using a multi-site in-vivo tetrode recording technique, our study shows changes in neural activities of the deep cerebellar nuclei, the lateral parabrachial nucleus, and the central amygdala after auditory fear conditioning. We found that there were distinct neuronal population showing their excitation or suppression aligned with conditioned tone delivery or freezing behavior in each brain region. Our study supplements the previous findings that the cerebellar output networks are engaged in classical fear conditioning.

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Keywords: Deep cerebellar nuclei (DCN), Lateral parabrachial nucleus (lPBN), Central amygdala (CeA), Classical fear conditioning, Multi-site in-vivo tetrode recording

A02-07

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

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Social memory encoding individual identities can be generalized to represent abstract information such as familiarity. Episodic memory involves multiple complementary systems: the cortex is crucial for storing abstract memory, whereas the hippocampus retains detailed memory. However, the precise locus for processing generalized social memory remains unclear. Here, we explore the role of nucleus accumbens shell (NAcSh)-projecting prefrontal infralimbic (IL) neurons ($IL^{\rightarrow NAcSh}$) in encoding social familiarity in male mice by utilizing *in vivo* calcium imaging, optogenetic, and chemogenetic manipulation with activity-dependent tagging. We discovered that inactivating $IL^{\rightarrow NAcSh}$ neurons activated by a familiar conspecific impaired subsequent social recognition, indicated by increased interaction with other familiar conspecifics including littermates. Furthermore, inactivation of the hippocampal ventral CA1 (vCA1) not only impaired social recognition but also disrupted the neural representation of social familiarity in the IL. These findings demonstrate that generalized social memory is represented by NAcSh-projecting IL neurons, with support from vCA1, highlighting the intricate cortical-hippocampal interactions underlying social recognition.

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Keywords: Prefrontal cortex, Neural circuit, Social identity, Complementary learning

A02-08

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

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Epilepsy is one of the most common neurological disorders, often leading to significant neuronal death and cognitive impairments. Despite its widespread impact, effective treatments remain limited. Clinically, epilepsy is characterized by two or more unexplained seizures within a 24-hour period or chronic seizures. These seizures and related neurological conditions are often caused by abnormal cellular energy metabolism and inadequate energy supply through blood vessels. C1q/TNF-Related Protein 9 (CTRP9) is a protein similar to adiponectin, known for its anti-inflammatory and pro-angiogenic effects, primarily mediated through the activation of the AMP-activated protein kinase (AMPK) pathway. Although CTRP9 has been extensively studied in cardiovascular diseases, its role in neurological disorders, beyond global cerebral ischemia (GCI), remains largely unexplored. This study aimed to investigate the effects of CTRP9 in an epilepsy model. Neuronal excitotoxicity was induced using pilocarpine and L-glutamic acid, followed by treatment with 2 μg/ml CTRP9. Additionally, in a pilocarpine-induced epilepsy model in vivo, CTRP9 was administered intravenously at a dose of 1 mg/kg. Brain tissue was collected at various time points for histological and biochemical analyses. Our findings showed that CTRP9 treatment reduced neuronal death by decreasing glial cell activation and lowering the expression of pro-inflammatory factors. Furthermore, post-seizure CTRP9 treatment enhanced angiogenesis and improved pericyte function, indicating its potential as a therapeutic agent for epilepsy. These results suggest that CTRP9 may offer neuroprotective effects in epilepsy through its anti-inflammatory and angiogenic properties, as well as by supporting energy metabolism and promoting endothelial repair, particularly through pericyte-mediated angiogenesis. Further basic and clinical research is needed to explore CTRP9's potential as a novel treatment strategy for epilepsy.

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Keywords: Epilepsy, CTRP9, Anti-inflammation, Blood brain barrier, Angiogenesis

A02-09

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

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Multiple sclerosis (MS) is an autoimmune disease characterized by axon demyelination, often leading to sensory disorders such as mechanical allodynia. Mechanical allodynia is a condition in which non-painful stimuli are recognized as pain, and it is one of the main causes of reduced quality of life in MS patients. Recent studies have suggested that Schwan cells play a key role in remyelination and peripheral nerve repair, and that transient receptor potential vanilloid 1 (TRPV1) channel in Schwann cells may serve as potential therapeutic targets. Furthermore, several components of bee venom (BV) from *Apis mellifera*, including melittin and phospholipase A2, interact with TRPV1 to modulate the neuroimmune response and reduce the production of inflammatory cytokines and could alleviate the symptoms of MS. However, there is no direct evidence that the pathways related to alleviating MS-induced allodynia by BV. Therefore, we aimed to study the pathway associated with the therapeutic effect of BV on mechanical allodynia in multiple sclerosis model.
In 6-week-old ICR mice, we induced MS by oral administration of 12mg cuprizone in 1% CMC 200μl for 5 weeks, and then injected BV once a day at a dose of 0.05 and 0.5mg/kg into the peri-sciatic nerve area on the right side of the mice from the 4th week. Once a week, we performed Rota-rod and CatWalk tests to evaluate motor function and the von Frey test to determine mechanical allodynia. After 5 weeks, we stained the brain and sciatic nerves of the mice to examine myelin basic protein (MBP) expression and G-ratio. Consequently, we confirmed cuprizone-induced allodynia and a decrease in MBP expression, and an increase in the G-ratio of the sciatic nerve, which are characteristics of MS. However, significant therapeutic effect was not observed in the concentration of BV used in this study yet.
We thought bee venom doses may not be suitable to produce its effect in the study. Further studies will need to find the concentration that shows the therapeutic effect of cuprizone-induced allodynia without causing side effects. This study demonstrates that bee venom modulates Schwann cell activity through its interaction with TRPV1 to alleviate mechanical allodynia in multiple sclerosis, providing bee venom as a novel adjuvant therapeutic strategy for neurodegenerative diseases.

Keywords: Bee venom, Multiple sclerosis, TRPV1, Schwann cell, Mechanical allodynia

A02-10

Orexin-A regulates GABA in cultured mice astrocytes

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Astrocytes, the most abundant type of glial cell in the brain, provide metabolic and trophic support to neurons and regulate synaptic activity under normal physiological conditions. In addition, recent research suggests that astrocytes play a neuroprotective role through astrocyte-neuron interactions, including metabolic support and the secretion of neuroprotective factors. The orexin-1 receptor (OR1), which can act on orexin-A (OXA), commonly reported to have a neuroprotective role, exists in astrocytes. However, research on the mechanism for its neuroprotective role is still lacking. Therefore, we aimed to elucidate the mechanism by which OXA plays a neuroprotective role in astrocytes. Primary cell culture from the cerebral cortex of 2-day-old ICR mice was performed and we found that LPS treatment upregulated OXA expression time-dependently and peaked at 48hr after the LPS treatment. After Calbryte520-AM (a calcium indicator) staining, we determined the expression of OXA that could reduce the calcium increase induced by LPS and subsequently performed experiments at a concentration of 10 nM. Astrocytes can be activated by responding to the neuronal injuries and diseases. Activated astrocytes become migratory through a process called astrogliosis. We investigated the effect of OXA on astrocyte migration by using LPS to induce astrocytic damage through neuro-inflammation. Results showed that OXA inhibited migration and western blot and staining analyses revealed that OXA mediated an increase in the expression of GABA Transporters 1 and 3 (GAT1 and GAT3) which is known to modulate the production of GABA. We confirmed that increased GABA reduces the phosphorylation of MAPK (Mitogen-activated protein kinase) pathways, specifically ERK and P38, suggesting that the effect of OXA on migration is linked to this pathway. In conclusion, when treating astrocytes with LPS, OXA inhibits cell migration through the OXA-OR1-GABA-MAPK signaling pathway. The effect of OXA prevents abnormal migration of astrocytes induced by LPS, suggesting a neuroprotective effect. Our study contributes to understanding the molecular mechanisms underlying OXA neuroprotective effects and could lead to new therapeutic strategies for inflammation-related pain or diseases.

Keywords: Astrocyte, Orexin-A, LPS, GABA, GAT

A02-11

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

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Menopause is characterized by a gradual decline in ovarian function while maintaining residual ovarian tissue. The decrease in estrogen caused by menopause affects emotional changes, the sensory nervous system, and leads to related diseases. Although the ovariectomy (OVX) model is commonly used in studies related to estrogen reduction, it does not retain residual ovarian tissue, as the ovaries are completely removed. As a result, while general menopause, with residual ovarian tissue, impacts the sensory nervous system due to hormonal changes, we concluded that the surgical menopause model may not be suitable for studying sensory changes associated with menopause. VCD (4-vinylcyclohexene) model, which chemically induces menopause, is physiologically more appropriate for studying sensory nervous system changes related to menopause because it retains residual ovarian tissue, similar to natural menopause, and can still produce hormones like androstenedione. Although several studies have compared OVX and VCD, there is a lack of research on the precise differences and mechanisms involved. Therefore, our research aims to explore the emotional and sensory changes caused by residual ovarian tissue and to elucidate the underlying mechanisms.
Female ICR mice were injected intraperitoneally with 160mg/kg of VCD for 15 days to induce follicular depletion, and the OVX model was used as a surgical menopause model. In the forced swimming test, the VCD model had a shorter immobility time than the OVX model, and in the pain nociception test using diluted 5% formalin, pain behavior was reduced in the 2nd phase compared to the OVX model. As a result, we confirmed the emotional and pain differences between the VCD model and the OVX model, and we con-

cluded that it might be due to the hormonal effects induced by the residual ovarian tissue existing in the VCD. Therefore, we can suggest that the VCD model is a menopause model similar to human menopause. This is expected to help conduct more accurate research on emotional and pain changes in human menopause and to help study treatment methods.

Keywords: 4-vinylcyclohexene, Ovariectomy, Pain, Estrogen, Mice

A02-12

Indexing changes in soma-glial microcontact associated with pain severity

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Satellite glial cells (SGCs), which surround primary sensory neurons in the dorsal root ganglion (DRG), play a key role in peripheral nerve injury and pain modulation (Hanani, 2005; Pannese, 2010). Recent studies have emphasized their involvement in regulating pain thresholds (Jasmin et al., 2010; Kim et al., 2016). Under conditions such as neuropathy or inflammation, SGCs undergo structural and functional alterations that influence communication between DRG neurons and SGCs (Cherkas et al., 2004; Hanani, 2005; Warwick and Hanani, 2013).

This research investigates specific structural changes in SGCs during pain, using Transmission Electron Microscope (TEM) imagery. We also explored cell-specific genetic changes by analyzing GEO data (GSE154659), revealing significant gene expression shifts in a pain model. The findings suggest that monitoring SGC morphological alterations could serve as a novel indicator for pain.

Our study uncovered distinct structural modifications in SGCs under pain conditions, as seen in TEM images. Specifically, an increase in the gap between neurons and SGCs and changes in SGC shape were consistently observed across all pain models, indicating these alterations are characteristic of neuropathic pain. We then focused on gene expression changes in each neuropathic model, particularly in genes involved in neuron-SGC interactions. By reanalyzing GEO data (GSE154659), we observed a general decline in adhesion molecule expression in neurons affected by nerve injury. Additionally, specific neuronal clusters exhibited changes, suggesting their active role in pain processing. These structural and genetic changes were strongly associated with pain.

In conclusion, our research highlights diverse structural changes in SGCs during neuronal injury that leads to pain. The increased distance between neurons and SGCs suggests significant alterations in their interactions, potentially serving as a marker for pain. Moreover, a specific DRG neuron cluster was found to be involved in this process, with decreased expression of genes crucial for maintaining neuron-SGC structure. These findings point to potential targets for pain modulation and propose a novel morphological marker for pain while identifying key genes and neuronal clusters implicated in these changes.

Keywords: Pain, Satellite glial cells, Dorsal root ganglion, SnRNA-seq

A02-13

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

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Neuropathic pain, which occurs due to nerve damage or dysfunction, is a serious disease that reduces the quality of life. Recently, modulating brain activities involved in pain has been proposed as an alternative to pain treatments. Our previous study reported that electrical stimulation of the insular cortex (IC) alleviates neuropathic pain and affects synaptic plasticity. However, the detailed mechanisms of pain modulation by insular cortex stimulation (ICS) are not fully understood. This study aimed to determine the mechanisms of pain-modulation induced by ICS in neuropathic pain. We investigated changes in mechanical allodynia using optogenetic and ICS methods to modulate synaptic changes in a neuropathy model of rats. Synaptic changes were assessed by measuring expression levels of glutamate receptors (AMPAR, NR2A, and NR2B). At postoperative days (POD) 7 and 14, optogenetic inhibition of neurons in the IC, specifically inhibition of CaMKIIα-positive neurons, resulted in the attenuation of mechanical allodynia, while optogenetic activation of GABAergic neurons in the IC also showed an antinociceptive effect. 30 minutes of daily optogenetic stimulation of the IC from POD7 to POD14 did not show any pain modulation effect. Repetitive ICS combined with optogenetic activation of neurons resulted in pain-like behavior. Furthermore, repetitive ICS combined with optogenetic activation of CaMKIIα-positive neurons showed significantly reduced antinociceptive effect. In the Western blot analysis, changes in the expression levels of AMPAR and NR2B after repetitive trials of ICS combined with optogenetic excitation of neurons showed similar values to those in the neuropathic pain group. These results indicate that the inhibition of excitatory neurons or the activation of inhibitory neurons could modulate pain under neuropathic pain conditions. Additionally, repetitive optogenetic activation of excitatory neurons counteracted the antinociceptive effect of ICS, accompanied by changes in synaptic plasticity, revealing the pain modulation mechanisms of ICS in a neuropathic pain model.

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Keywords: Neuropathic pain, Insular cortex stimulation, AMPAR, NR2B, Neural plasticity

A02-14

Neurotoxin mediated neuronal dysfunction regulated by lysosomal function

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Neurotoxins encompass diverse groups of drugs that have detrimental effects on the neuronal system, leading to cognitive and neurological impairments. These toxins can disrupt intracellular signaling and homeostasis. Lysosomes are crucial organelles responsible for waste disposal and the supply of essential materials. The connection between lysosomal homeostasis and neurological dysfunction remains poorly understood. In this study, we investigated how to alleviate neurodegeneration through the management of lysosomal function. Some neurotoxins are known to affect lysosomal ion influx or efflux. After treating N2A cells with hydroperoxide, a known neurotoxin, we observed a decrease in cell proliferation. When

blocking the lysosomal ion exchange, it protected N2A cell viability against the damaging effects of hydroperoxide. For intracellular signaling, hydroperoxide increased AKT phosphorylation, but this effect was diminished after regulating lysosomal ion exchange. Hydroperoxide also increased the level of p-raptor protein, a key component of mTORC1, which plays a fundamental role in lysosomes. However, this change did not affect the total raptor protein level. When we induced starvation in the cells and added hydroperoxide, cell viability decreased, and this was accompanied by an increase in AKT phosphorylation and p-raptor levels, but those were attenuated by lysosome regulation. LC3, a specific marker for autophagy, was accelerated in response to hydroperoxide treatment but was also disrupted by the control of lysosomal ion exchange. Thus, the regulation of lysosomal activity can prevent neurodegeneration and impact intracellular signaling pathways affected by hydroperoxide

Keywords: Neuron, Ion channel, Lysosome

A02-15

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

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Compared to other neuromodulation techniques, magnetic brain stimulation utilizing nanomaterials has garnered considerable interest in recent years as it is wireless, minimally invasive, and capable of precisely regulating a specific neural circuit without substantial attenuation. Previous studies using magnetothermal brain stimulation (MTS) have demonstrated that this technique could induce neural excitation and silence of the targeted brain region, thereby inducing motor behavior in awake rodents. However, whether MTS utilizing nanomaterials can restore synaptic plasticity in the adult cortex remains to be determined. Furthermore, MTS usually necessitates genetic alteration by introducing viruses that carry transient receptor potential (TRP) channel proteins on the neuronal membranes to regulate the specific brain area. Nevertheless, using viruses to generate exogenous channel proteins can present a substantial regulatory barrier to clinical implementation.
This study aimed to determine whether MTS via nanomaterials reactivates synaptic plasticity in the adult mouse cortex through the innate TRP channels. We administered MTS centered on the targeted brain region after injecting the nanoparticles into the barrel cortex of the adult mice. A single application of MTS enhanced the neuronal activity of the barrel cortex, as indicated by increased c-fos expression. Furthermore, a long-term MTS for three days increased the amplitude of the field potential of layer 4 of the barrel cortex induced by electrical whisker stimulation. Ex vivo slice patch clamp recording showed that the potency elicited by thalamocortical input was increased following the long-term MTS while the excitation-inhibition balance was preserved. In addition, the proportion of GluN2B-NMDAR current was elevated in MTS mice, and Ro 25-6981, a selective GluN2B-NMDAR antagonist, blocked the synaptic plasticity induced by MTS. Finally, a reward-based texture discrimination behavior test demonstrated that MTS enhanced texture discrimination ability. This study was the first to show that MTS can induce cortical synaptic plasticity and facilitate functional improvement without using exogenously produced channel proteins in the adult cortex.

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Keywords: Neuromodulation, Magnetic stimulation, Synaptic plasticity, Barrel cortex

B02-01

Convergence of gustatory and visceral input on parabrachial neurons

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The parabrachial nucleus (PbN) in the pons receives visceral information from the nucleus of the solitary tract (NST) in the medulla. In rodent, the PbN also receives gustatory information from the NST and transfers the information to the rostral gustatory centers. The dorsal motor nucleus of the vagus (DMV) in the medulla not only sends visceral efferents but also receive visceral afferents, mainly via the NST. Some neurons in the DMV were retrogradely labeled after injection of HRP into the PbN, suggesting that visceral afferent information is transmitted from the DMV to the PbN. In the present study, we investigated whether taste-responsive neurons in the PbN can be activated by electrical stimulation of the DMV. Extracellular single- unit activities were recorded from the PbN of the urethane-anesthetized hamster. Recordings were made in the PbN while taste solutions were applied to the tongue. After identifying taste-responsiveness of a PbN neuron, neuronal firing was recorded again while electrically stimulating the DMV. A total of 80 gustatory neurons were recorded in the PbN. Seventy-eight cells orthodromically responded to ipsilateral DMV stimulation. Contralateral DMV stimulation also activated 39 PbN taste-responsive neurons and inhibited 7. These data show that some PbN neurons convergently receive input from both the gustatory NST and the DMV in the medulla.

Keywords: Neuron, Recording, Stimulation, Taste, Pons

B02-02

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

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Long term depression (LTD) at parallel fiber-to-Purkinje cell (PF-PC) synapses is essential for driving a proper optokinetic response (OKR). There have been numerous studies about the relation between synaptic LTD and intrinsic PC LTD after cerebellar motor learning. Moreover, it has been suggested that memory is acquired in the cerebellar cortex and is transferred to the vestibular nucleus for the memory consolidation phase. However, the synaptic mechanism occurred at PF-PC has not been completely identified yet. Until now, Purkinje cells have long been the major focus for the cerebellar motor learning, as their depressed activity is the main driving force for OKR gain-UP. On the other hand, although they also participate in the cerebellar learning circuit, the role of PFs, which are the axons of granule cells (GC), has remained obscure. In addition, defining the site of presynaptic plasticity occurrence is also necessary. To be specific, GC soma may act as a primary stage for signal modification, or it is also possible that PFs uniquely integrate and modify the inputs. Moreover, it also remains unidentified that how presynaptic activity affects postsynaptic activity, in this case, how GC activity affects PC activity. Therefore, in this study, we take advantage of patch clamp recording to unravel the synaptic mechanism at PF-PC synapse after OKR training and GC manipulation to demonstrate the effect of GC activity on behavioral result. Likewise, we observe distinct changes in training-dependent synaptic plasticity at three time points (right after, 1hour, and 24 hours) and the significant role of GCs during OKR for proper expression of learning. This study validates the function of GC transmission during the cerebellar motor learning and clarifies the direction of the train-

ing-dependent synaptic plasticity.

B02-03

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

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CALHM (Calcium Homeostasis Modulator) is a large-pore nonselective ion channel family. We have demonstrated that CALHM1 showed very slow activation at high depolarization of membrane and exhibits temperature and extracellular pH sensitivity (Jeon et al., 2021; Kwon et al., 2023). In murine B lymphocyte, we reported that Calhm2 is responsible for the CALHM-like currents ($I_{Calhm\text{-}L}$) (Choi et al. 2024). Microglia are the primary immune cells of the central nervous system, responsible for maintaining homeostasis, clearing debris, and mediating immune responses through phagocytosis and the release of signaling molecules. Similar to mouse B cells (Choi et al., 2024), microglial BV2 cells also exhibited $I_{Calhm\text{-}L}$. RT-PCR results indicated that Calhm2 and Calhm6 are expressed throughout the mouse brain, while Calhm2 is specifically expressed in microglial cell-line cells, BV2. To find out the physiological role of Calhm2 in microglia cells, we made Calhm2-knockout BV2 using CRISPR-Cas9 lentivirus. The $I_{Calhm\text{-}L}$ was not observed in the *Calhm2*-knockout BV2. The ATP release from BV2 was attenuated. Further study aiming to elucidate the characteristics and physiological functions of the Calhm2 in primary microglia is required.

Keywords: Calcium homeostasis modulator, Calhm2, Microglia

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B02-04

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 $GABA_A$ 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 $GAGA_A$ current

B02-05

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

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STING, a pivotal immune regulator, has emerged as a contributor to nociception, yet its role in chronic pains remain still unknown. Here, we demonstrate that STING plays a dual role in normal and neuropathic pain. STING maintains type I interferon (IFN I) level restraining pain sensitivity in normal and sham control, while activated STING/IRF3 signaling increases the expression of GABA transporter 1 (GAT1) in the spinal cord (SC), thus, generating paclitaxel (PTX)-induced peripheral neuropathy. Genetic interference of STING ($STING^{-/-}$ mice) attenuated PTX-induced mechanical hypersensitivity with attenuated PTX-induced GAT1 increase, preventing PTX-induced increase in tonic $GABA_A$ inhibition of the spinal dorsal horn neurons. STING regulates GAT expression through a TANK-binding kinase 1 (TBK1) - interferon regulatory factor 3 (IRF3) signaling pathway, with IRF3 as a crucial transcription factor. Silencing neuronal STING, as opposed to its astrocytic counterpart, effectively restrained the PTX-induced mechanical hypersensitivity and GAT1 increase in the SC. Pharmacological inhibition of STING (H-151) efficiently diminished TBK1/IRF3/GAT1 signaling pathway to alleviate PTX-induced mechanical hypersensitivity. Our findings show that STING-IRF3 serves a dual role: suppressing physiological nociception through IFN I and acting as a transcriptional regulator of GAT1, contributing to chemotherapy-induced neuropathic pain.

Keywords: GATs, Neuropathic pain, STING-IRF3 pathway, Tonic $GAGA_A$ current

B02-06

Protective effect of tomatidine in isoproterenol-induced cardiac hypertrophy model

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The purpose of this study is to investigate the protective effect of Tomatidine (Toma) on Isoproterenol (ISO)-induced cardiac hypertrophy. In cell experiments, cardiac hypertrophy was confirmed by the increased levels of Brain Natriuretic Peptide (BNP) protein, and a decrease in BNP expression was observed in the Toma-treated group. In the cytotoxicity test, ISO was

applied to AC16 cells, and it was confirmed that no cytotoxicity occurred in any group when treated with Toma. However, in the Reactive Oxygen Species (ROS) assay, it was confirmed that Toma reduced ISO-induced ROS in a concentration-dependent manner. In animal experiments, cardiac function was measured in vivo using tissue analysis, echocardiography, and electrophysiology in a cardiac hypertrophy mouse model. It was confirmed that the group induced with isoproterenol had larger heart sizes, and there was a significant difference in the heart weight to tibia length ratio. Additionally, H&E staining showed that myocyte cross-sectional area increased in ISO-treated mice, but this was alleviated in the Toma-treated group. In echocardiography, the ejection fraction (EF) and fractional shortening (FS) showed a significant difference between the normal and ISO groups, and this difference was mitigated with Toma treatment. Furthermore, cardiomyocytes were isolated from the ISO-induced cardiac hypertrophy mouse model, and action potential (AP) and patch-clamp technique. The results showed that the ISO group had longer action potential duration (APD) and greater calcium influx than the normal group. The increase in calcium levels is thought to be due to heart failure caused during animal modeling. These results indicate that Toma has a ROS-inhibiting effect on cardiac hypertrophy and modulates calcium channels. Therefore, it is suggested that Toma may have potential utility in treating cardiac hypertrophy.

Keywords: Tomatidine, Isoproterenol, Cardiac hypertrophy, Electrophysiology

B02-07

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

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The second-generation atypical antipsychotic paliperidone is widely used to treat schizophrenia. In this study, we investigated the inhibitory effect of paliperidone on voltage-dependent K^+ (Kv) channels using rabbit coronary arterial smooth muscle cells. Paliperidone inhibited Kv current in a dose-dependent manner with an IC50 of 16.43 ± 2.26 μM and a Hill coefficient of 0.72 ± 0.10. Although paliperidone effectively reduced the Kv currents, the drug did not significantly affect the steady-state activation or inactivation curves. Administration of train depolarizing pulses (1 and 2 Hz) slowly augmented the inhibition of the Kv current in the presence of paliperidone. Moreover, paliperidone increased the recovery time from channel inactivation, suggesting that paliperidone inhibited the Kv current in a use (state)-dependent manner. Pretreatment with DPO-1, a Kv1.5 subtype inhibitor effectively decreased the inhibitory effect of paliperidone. However, pretreatment with a Kv2.1 or Kv7 inhibitor did not affect the paliperidone effect. From these results, we conclude that paliperidone inhibits Kv channels (primarily Kv1.5 subtype) in a dose- and use (state)-dependent manner without affecting gating properties of channel.

Keywords: Paliperidone, Voltage-dependent K^+ channel, Coronary arterial smooth muscle, Use-dependent, Kv1.5 subtype

B02-08

The second-generation antipsychotic lurasidone inhibits the voltage-dependent K+ channels in coronary arterial smooth muscle cells

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The second-generation antipsychotic lurasidone, which is an antagonist of the 5-HT2A and D2 receptors, used to treat mania, schizophrenia, and bipolar disorder. To date, the effect of lurasidone on the voltage-dependent K+ (Kv) channels has yet been revealed. Here, we identify that lurasidone induces the inhibition of Kv channels in rabbit coronary arterial smooth muscle cells in a concentration-dependent manner with an IC50 of 1.88 ± 0.19 μM and a Hill coefficient of 0.96 ± 0.11. Although lurasidone (3 μM) did not change the steady-state activation kinetics, it shifted the inactivation curve to a negative potential, suggesting that the lurasidone interacted with the voltage sensors of Kv channels. Application of train pulses (1 or 2 Hz) in the presence of lurasidone effectively augmented inhibition of Kv current. Furthermore, the recovery time from channel inactivation was also increased in the presence of lurasidone suggesting that the inhibitory effect of lurasidone is use (state)-dependent. Inhibitory effect of lurasidone was reduced by pretreatment with a Kv 1.5 subtype inhibitor. However, lurasidone effect on Kv channels was not significantly changed after pretreatment with a Kv 2.1 or a Kv7 subtype inhibitor. Based on these results, we conclude that lurasidone inhibits Kv channels (mainly the Kv1.5 subtype) in a concentration- and use (state)-dependent manner by changing the steady-state inactivation curve.

Keywords: Lurasidone, Voltage-dependent K^+ channel, Electrophysiology, Coronary arterial smooth muscle cell

B02-09

Unique responses of fixed stoichiometric TRPC1-TRPC5 concatemer to G proteins

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Transient receptor potential canonical (TRPC)5 channel is a nonselective cation channel that plays a significant role in membrane depolarization and calcium influx. TRPC5 not only forms homotetramers itself but also heterotetramers with TRPC1. However, accurately testing and confirming these heterotetrameric channels at specific ratios has proven challenging. Therefore, creating heteromeric concatemers of TRPC5 and TRPC1 with a fixed stoichiometry of 1:1 becomes essential. This study aims to meticulously identify and reaffirm the properties of TRPC5 homomers and heteromers with a 1:1 fixed stoichiometry, to determine the optimal ratio for the TRPC1/5 heterotetramer. Overall characteristics were consistent with the previous studies, but several specific features were different. The TRPC1-TRPC5 concatemer is activated by Englerin A, but neither carbachol nor constitutively active Gαi protein can trigger its activation. However, carbachol can activate the TRPC1-TRPC5 concatemer when internal GTPγS is present. Meanwhile, the TRPC5-TRPC5 concatemer is responsive to both carbachol and Englerin A. In conclusion, we provide evidence that TRPC1-TRPC5 heteromeric concatemer with fixed stoichiometry need specific condition to respond to carbachol whereas TRPC5-TRPC5 homomeric concatemer responds physiologically to carbachol. Additional research may be necessary to ascertain the optimal stoichiometry for the TRPC1-TRPC5 concatemer to enhance its electrophysiological properties.

Keywords: TRPC5, TRPC1, Heteromer, Homomer, Concatemer, G protein, Englerin A, GTPγS

B02-10

Blockade of voltage-gated K^+ channels of rabbit coronary arterial smooth muscle cells by the antipsychotic drug zotepine

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Zotepine, a second-generation antipsychotic, demonstrates significant

efficacy by antagonizing D2 and 5-HT2A receptors. Although clinical investigations have shown that administration of zotepine is associated with an increased prevalence of hyperglycemia and a heightened risk of cardiovascular diseases, the side effects of zotepine on voltage-gated K+ (Kv) channels have not yet been established. Zotepine suppresses the vascular Kv channels in rabbit coronary arterial smooth muscle cells in a concentration-dependent manner, with an IC50 of 5.3 ± 0.4 μM and a Hill coefficient of 1.6 ± 0.2. The decay rate of inactivation was significantly accelerated by zotepine. The application of zotepine (10 μM) shifted the steady-state inactivation curve in a negative direction. The application of train pulses at 1 and 2 Hz was resulted in a progressive increase in the blockage of Kv currents by zotepine. Furthermore, zotepine prolonged the recovery time from inactivation. Although pretreatment with the Kv2.1 subtype inhibitor stromatoxin-1 and the Kv7 subtype inhibitor linopirdine did not alter the degree of zotepine-induced inhibition of Kv currents, pretreatment with the Kv1.5 channel inhibitor DPO-1 decreased the inhibitory effects of zotepine on Kv currents. Zotepine also induced membrane depolarization. From these results, we conclude that zotepine inhibits Kv currents (mainly Kv1.5 subtype) in dose-, time-, and use (state)-dependent manners by changing of steady-state inactivation curve.

Keywords: Zotepine, Voltage-gated K^+ channel, Electrophysiology, Coronary arterial smooth muscle cell

B02-11

Inhibition of voltage-dependent K+ channels in rabbit coronary arterial smooth muscle cells by the atypical antipsychotic agent sertindole

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The regulation of membrane potential and the contractility of vascular smooth muscle cells (VSMCs) by voltage-dependent K^+ (Kv) potassium channels are well-established. In this study, native VSMCs from rabbit coronary arteries were used to investigate the inhibitory effect of sertindole, an atypical antipsychotic agent, on Kv channels. Sertindole induced dose-dependent inhibition of Kv channels, with an IC_{50} of 3.13 ± 0.72 μM. Although sertindole did not cause a change in the steady-state activation curve, it did lead to a negative shift in the steady-state inactivation curve. The application of 1- or 2-Hz train pulses failed to alter the sertindole-induced inhibition of Kv channels, suggesting use-independent effects of the drug. The inhibitory response to sertindole was significantly diminished by pretreatment with a Kv1.5 inhibitor but not by Kv2.1 and Kv7 subtype inhibitors. These findings demonstrate the sertindole dose-dependent and use-independent inhibition of vascular Kv channels (mainly the Kv1.5 subtype) through a mechanism that involves altering steady-state inactivation curves. Therefore, the use of sertindole as an antipsychotic drug may have adverse effects on the cardiovascular system.

Keywords: Sertindole, Voltage-dependent K^+ channel, Electrophysiology, Coronary arterial smooth muscle cell

B02-12

Second-generation antipsychotic quetiapine blocks voltage-dependent potassium channels in coronary arterial smooth muscle cells

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Voltage-dependent K^+ (Kv) channels play an important role in restoring the membrane potential to its resting state, thereby maintaining vascular tone. In this study, native smooth muscle cells from rabbit coronary arteries were used to investigate the inhibitory effect of quetiapine, an atypical antipsychotic agent, on Kv channels. Quetiapine showed a concentration-dependent inhibition of Kv channels, with an IC_{50} of 47.98 ± 9.46 μM. Although quetiapine (50 μM) did not alter the steady-state activation curve, it caused a negative shift in the steady-state inactivation curve. The application of 1 and 2 Hz train steps in the presence of quetiapine significantly increased the inhibition of Kv current. Moreover, the recovery time constants from inactivation were prolonged in the presence of quetiapine, suggesting that its inhibitory action on Kv channels is use (state)-dependent. The inhibitory effects of quetiapine were not significantly affected by pretreatment with Kv1.5, Kv2.1, and Kv7 subtype inhibitors. Based on these findings, we conclude that quetiapine inhibits Kv channels in both a concentration- and use (state)-dependent manner. Given the physiological significance of Kv channels, caution is advised in the use of quetiapine as an antipsychotic due to its potential side effects on cardiovascular Kv channels.

Keywords: Quetiapine, Voltage-dependent K^+ channel, Electrophysiology, Coronary arterial smooth muscle cell

B02-13

Inhibitory mechanisms of aripiprazole on voltage-gated potassium channels in rabbit coronary arterial smooth muscle cells

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Aripiprazole, a third-generation antipsychotic, has been widely used to treat schizophrenia. In this study, we evaluated the effect of aripiprazole on voltage-gated potassium (Kv) channels in rabbit coronary arterial smooth muscle cells using the patch clamp technique. Aripiprazole reduced the Kv current in a concentration-dependent manner with a half-maximal inhibitory concentration of 0.89 ± 0.20 μM and a Hill coefficient of 1.30 ± 0.25. The inhibitory effect of aripiprazole on Kv channels was voltage-dependent, and an additional aripiprazole-induced decrease in the Kv current was observed in the voltage range of full channel activation. The decay rate of Kv channel inactivation was accelerated by aripiprazole. Aripiprazole shifted the steady-state activation curve to the right and the inactivation curve to the left. Application of a repetitive train of pulses (1 and 2 Hz) promoted inhibition of the Kv current by aripiprazole. Furthermore, the recovery time constant from inactivation increased in the presence of aripiprazole. Pretreatment of Kv1.5 subtype inhibitor reduced the inhibitory effect of aripiprazole. However, pretreatment with Kv 7 and Kv2.1 subtype inhibitors did not change the degree of aripiprazole-induced inhibition of the Kv current. We conclude that aripiprazole inhibits Kv channels in a concentration-, voltage-, time-, and use (state)-dependent manner by affecting the gating properties of the channels.

Keywords: Aripiprazole, Voltage-gated K^+ channels, Use-dependent, Time-dependent, Voltage-dependent

B02-14

Cryo-EM Structure-Based Investigation of Stoichiometry and Ion Permeability of TRPC1/C4 heteromer

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TRPC1, the first member of the TRP family discovered in humans, is expressed in nearly all human tissues. TRPC1 proteins are known to form heteromeric channels with TRPC4, TRPC5, and other TRP channels, resulting in unique characteristics and functions. In particular, TRPC1/4/5 heteromers are predominantly found in gastrointestinal (GI) smooth muscle and brain tissues, where they are associated with GI motility, epilepsy, and Huntington's disease. One of the key features of TRPC1/4/5 heteromers is their lower calcium permeability compared to TRPC4/5 homomers. However, understanding the intrinsic biophysical mechanisms underlying this feature has been challenging due to the lack of structural data. Here, we present the Cryo-EM structure of the TRPC1/C4 heteromer, along with the ion permeability-determining motifs and the intramolecular mechanism in the pore region. The TRPC1/C4 heteromer exhibits a 1:3 stoichiometry. Utilizing FRET and whole-cell patch-clamp recordings in mammalian cells, we have validated this stoichiometry *in vivo* and confirmed its functionality. Additionally, we elucidate the pharmacological mechanism underlying the potent antagonism of TRPC1/4/5 channels with supporting structural and functional data. The most notable difference between the TRPC1/C4 heteromer and the TRPC4 homomer was observed in the pore region, where the pore contour was asymmetrical. Through the use of chimeras and single amino acid mutants, we pinpointed the pore residues responsible for calcium and monovalent cation permeabilities. These findings will expand our understanding of the biophysical properties and pathophysiological role of TRPC1-containing heteromers, as well as other heteromers in the TRP and non-TRP channel families.

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Keywords: TRPC, Heteromer, Cryo-EM, Calcium, Structure-function

C02-01

DPP-4 inhibitor antidiabetic anagliptin relaxes the rabbit aorta via activation of SERCA pump and Kv channels

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We investigated the vasorelaxant effects of anagliptin, an DPP-4 antidiabetic drug, using phenylephrine (Phe)-induced pre-contracted aortic rings of rabbits. Anagliptin relaxed the aorta in a concentration-dependent manner. Application of classical voltage-gated K^+ (Kv) channel inhibitors tetraethylammonium and 4-aminopyridine effectively reduced the vasorelaxant effect of anagliptin, whereas application of the ATP-sensitive K^+ (K_{ATP}) channel inhibitor glibenclamide, the large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel inhibitor paxilline, and the inwardly rectifying K^+ (Kir) channel inhibitor Ba^{2+} and did not alter the vasorelaxant effect of anagliptin. Moreover, the anagliptin effect was significantly reduced by application of the sarco/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) pump inhibitors thapsigargin and cyclopiazonic acid. However, adenylyl cyclase inhibitor SQ 22536, PKA inhibitor KT 5720, guanylyl cyclase inhibitor ODQ, and PKG inhibitor KT 5823 did not reduce the vasorelaxant effect of anagliptin. Similarly, the vasorelaxant effect of anagliptin was independent of the endothelium. From these results, we conclude that anagliptin induced vasorelaxation in rabbit aortic smooth muscle via activation of Kv channels and the SERCA pump regardless of other vascular K^+ channels, cAMP/PKA- or cGMP/PKG-related signaling pathways, and the endothelium.

Keywords: Anagliptin, Voltage-gated K^+ channel, SERCA pump, Aorta, Vasorelaxation

C02-02

The antidiabetic drug teneligliptin induces vasodilation via activation of PKG, Kv channels, and SERCA pumps in aortic smooth muscle

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Diabetes mellitus (DM) is a metabolic disease closely related to cardiovascular disease. The dipeptidyl peptidase-4 inhibitor teneligliptin is used to treat DM and has recently been shown to have a cardiovascular protective effect against diseases such as hypertension and heart failure. The present study demonstrates the vasodilatory effect of teneligliptin using aortic rings pre-contracted with phenylephrine. Teneligliptin induced a vasodilatory effect in a dose-dependent manner, with and without endothelium. In addition, pretreatment with the nitric oxide synthase inhibitor L-NAME and small-conductance Ca^{2+}-activated K^+ channel inhibitor apamin did not alter the teneligliptin-induced vasodilatory effect. Although the adenylyl cyclase inhibitor SQ 22536 and protein kinase A (PKA) inhibitor KT 5720 did not modulate the vasodilatory effect of teneligliptin, the guanylyl cyclase inhibitor ODQ and protein kinase G (PKG) inhibitor KT 5823 effectively reduced the effect of teneligliptin. Similarly, pretreatment with the voltage-dependent K^+ (Kv) channel inhibitor 4-aminopyridine (4-AP) also reduced teneligliptin-induced vasodilation. However, pretreatment with the inward rectifier K^+ (Kir) channel inhibitor Ba^{2+}, large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel inhibitor paxilline, and ATP-sensitive K^+ (K_{ATP}) channel inhibitor glibenclamide did not alter the vasodilatory effect of teneligliptin. Our data suggest that Kv7.X, but not Kv1.5 or Kv2.1, is one of the major Kv subtypes involved in teneligliptin-induced vasodilation. Furthermore, pretreatment with the sarcoplasmic/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) pump inhibitor thapsigargin and CPA inhibited the vasodilation induced by teneligliptin. Our results suggest that teneligliptin-induced vasodilation occurs via activation of PKG, SERCA pumps and Kv channels, but not the PKA signaling pathway, other K^+ channels, or endothelium.

Keywords: Teneligliptin, Vasorelaxation, Voltage-dependent K^+ channel, SERCA pump, Aorta

C02-03

Vasorelaxant mechanisms of ipragliflozin by activating a Kv channel, the SERCA pump, and the PKA signaling pathway in rabbit femoral artery

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We explored the vasodilatory effects of ipragliflozin, a sodium–glucose cotransporter-2 inhibitor, on rabbit femoral arterial rings. Ipragliflozin dilated phenylephrine-induced pre-contracted rings in a dose-dependent manner. Pre-treatment with the ATP-sensitive K^+ channel inhibitor glibenclamide, the inwardly rectifying K^+ channel inhibitor Ba^{2+}, or the Ca^{2+}-sensitive K^+ channel inhibitor paxilline did not influence the vasodilatory effect. However, the voltage-dependent K^+ (Kv) channel inhibitor 4-aminopyridine reduced the vasodilatory effect. Specifically, the vasodilatory response to ipragliflozin was significantly attenuated by pretreatment with the Kv7.X channel inhibitors linopirdine and XE991, the sarcoplasmic/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) pump inhibitors thapsigargin and cyclopiazonic acid, and the cAMP/PKA-associated signaling pathway inhibitors SQ22536 and KT5720. Neither the cGMP/PKG-associated signaling pathway nor the endothelium was involved in ipragliflozin-induced vasodilation. We conclude that ipragliflozin induced vasodilation of rabbit femoral arteries by activating Kv channels (principally the Kv7.X channel), the SERCA pump, and the cAMP/PKA-associated signaling pathway independent of other K^+ (ATP-sensitive K^+, inwardly rectifying K^+, and Ca^{2+}-sensitive K^+) channels, cGMP/PKG-associated signaling, and the endothelium.

Keywords: Ipragliflozin, Femoral artery, Vasodilation, Kv channel, SERCA pump

D02-01

Effects of H2S on Cardiac Mitochondrial Function in STZ-Induced Type 1 Diabetic Rats

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Background: Hydrogen sulfide (H2S) is produced from cystathionine gamma-lyase (CSE), cystathionine beta-synthase (CBS), and 3-mercaptopyruvate thiotransferase (MPST).
Objective: To investigate the effects of H2S on mitochondrial function in type 1 diabetic rat hearts.
Methods & Results: Diabetes was induced by peritoneal injection of streptozotocin (STZ, 55mg/kg) in SD male rats, confirmed increased glucose level by oral glucose tolerance tests (OGTT) . We observed reduced H2S protein enzyme (MPST), unchanged CBS protein level and reduced its activity (Elisa assay) in DM cardiac mitochondria whereas CSE was absent. H2S in the plasma and cardiac mitochondria were elevated and mitochondrial functions was reduced (reactive oxygen species (ROS) was increased; mitochondrial membrane potential (MMP) and oxygen consumption rate (OCR) were reduced). Protein expressions of complex I-V (immunoblotting), sulfhydration of these proteins (modified biotin switch S-sulfhydration assay) were analyzed. After NaHS treatment, the activities of mitochondrial complexes I, II, III, and V were significantly increased, while complex IV activity was reduced in both groups. In contrast, after treatment with inhibitors (propargylglycine, a CSE inhibitor; hydroxylamine, a CBS inhibitor; and indole-3-methylthiol, a MPST inhibitor), the activities of mitochondrial complexes I-V were significantly reduced in both groups. H2S donor (NaHS) reduced complex IV-sulfhydration and its activity, increased complex V-sulfhydration and its activity. In contrast, inhibitors of H2S producing enzymes (HA, PAG, I3MT) reduced the activities and sulfhydration of mitochondrial complexes. Furthermore, inhibitors of H2S producing enzymes exacerbated mitochondrial dysfunction (increased ROS, reduced MMP, and decreased OCR).
Conclusion: H2S and the post-transcription of mitochondrial complexes are essential in maintaining mitochondrial function. Regulation of H2S level and downstream signaling play important parts in diabetic cardiac protection.

D02-02

Enhanced Brugada Syndrome Phenotype Driven by Increased Transient Outward K+ Current Due to SCN5A-p.A385T/R504T Mutations

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Brugada syndrome (BrS) is an inherited cardiac channelopathy that significantly increases the risk of ventricular tachycardia and fibrillation, leading to sudden cardiac death. Characteristically, the BrS ECG shows ST-segment elevation primarily in the right precordial leads (V1-V3), attributed to either loss-of-function (LOF) variants affecting Na+ current (I_{Na}) or gain-of-function (GOF) variants affecting transient outward currents (I_{to}). The missense mutations p.A385T/R504T in SCN5A are associated with BrS. The reduction in INa requires co-expression of the β-subunit *SCN1B* along with A385T/R504T. To gain further insights into the mechanisms underlying the BrS phenotype, we employed whole-cell patch-clamp techniques using patient-derived induced pluripotent stem cell-cardiomyocytes (iPSC-CMs/BrS) and a heterologous expression system. Specifically, we co-transfected SCN5A with Ito-related genes (*KCNA4, KCND2, KCND3*) and the auxiliary subunit *KChIP2*, with or without *SCN1B*. The iPSC-CMs/BrS recapitulated the accentuated phase-1 notch in the action potential. *KCNA4* and *KCND2* displayed increased Ito in the presence of *SCN1B*, while *KCND3* required co-expression with *SCN1B* for similar effects. Additionally, when *KCND3* was co-expressed with *SCN5A*-p.A385T/R504T and *SCN1B*, a significant reduction in INa was observed, suggesting a regulatory interaction between INa and Ito channels in BrS.
These findings demonstrate that SCN5A mutations not only reduce INa but also increase Ito activity, contributing to the Brugada syndrome phenotype. The interaction between these ion channels may play a crucial role in the electrophysiological abnormalities seen in BrS, and pharmacological targeting of Ito could provide a potential therapeutic approach for managing this condition.

Keywords: Brugada syndrome, SCN5A, Transient outward potassium current, Arrhythmia

D02-03

Finasteride prevents neointimal hyperplasia and affects vascular smooth muscle cells proliferation, migration, and apoptosis.

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Vascular smooth muscle cells (VSMCs) play a key role in the regulation of blood pressure and vascular tone. However, normal functions of VSMCs is disrupted by factors that cause inflammation and oxidative damage to cardiovascular system, such as hypertension, diabetes, hyperlipidemia, and smoking. In this process, VSMCs undergo phenotype switching from con-

tractile to synthetic, and synthetic VSMCs exhibit increased migration and proliferation activity. This is part of the repair process, but if excessive, it can lead to neointimal hyperplasia, which narrows the vessel lumen, causing stenosis.
Although the relationship of T and DHT to cardiovascular disease (CVD) remains controversial, T and DHT out of the ideal physiologic range in older men and patients receiving hormone therapy are thought to be a risk factor for CVD. However, studies on the benefits or side effects of anti-androgenic drugs on the cardiovascular system are limited compared to androgens. Therefore, here we investigated the effects of finasteride, a competitive inhibitor of 5α-reductase, on the cardiovascular system and VSMCs.
The effect of finasteride on arterial vascular remodeling was evaluated by inducing neointimal hyperplasia in the left carotid artery of male rats with balloon catheter injury. Following subcutaneous administration of finasteride for 2 weeks, the rats were sacrificed and the arteries were histologically analyzed. In addition, the proliferation, migration, apoptosis and cellular response to finasteride were investigated using primary cultured VSMCs separated from male and female rat thoracic aorta.
As a result, Finasteride can effectively inhibit neointima formation, preventing the narrowing of the blood vessel lumen. Proliferation of primary VSMCs was inhibited by finasteride in both males and females, while migration was inhibited in males but not in females. However, this does not seem to be androgen hormone-dependent response, as finasteride's action was not abolished when VSMCs were co-treated with T and DHT. Furthermore, finasteride induced apoptosis in male and female VSMCs in a concentration-dependent manner. For the first time, we tested the effect of finasteride in neointimal hyperplasia. These results propose a novel cardiovascular action of finasteride and suggest that it can be used as a therapeutic agent to prevent neointimal hyperplasia.

Keywords: Neointima, Vascular smooth muscle, Finasteride, Androgen, Cardiovascular disease

D02-04

The Role of Sex Hormones in Modulating Cardiac Health Under Normal Physiological Conditions: Insights from the UK Biobank.

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Sex hormones, such as estrogen and testosterone, significantly influence cardiovascular function and inflammation, with notable differences between males and females. This may be caused by C-reactive protein (CRP), which is a key inflammatory marker linked to cardiovascular health. However, the specific correlations among CRP, estrogen, and testosterone, and their impact on cardiac function under normal physiological conditions, remain unclear. Understanding these interactions is crucial for developing sex-specific strategies in cardiovascular disease management. Utilizing data from the UK Biobank, we explored the correlations between CRP, sex hormones, cardiac function indicators and death rate in a large population cohort. Our findings reveal distinct sex-specific patterns: in females, CRP levels negatively correlate with estradiol and the estradiol/testosterone ratio, while positively correlating with testosterone. In contrast, in males, CRP shows a positive correlation with estradiol and a negative correlation with testosterone and the estradiol/testosterone ratio. These hormone-CRP correlations extend to cardiac function, where estrogen affects more cardiac indicators in females than in males. Testosterone uniformly influences cardiac function in both sexes but with notable differences in ECG parameters. CRP levels are positively correlated with mortality in both males and females; there is a negative correlation between estrogen levels and death in females, but a negative correlation between androgen levels and death in males. The study highlights the differential regulatory effects of estrogen and testosterone on cardiac health, emphasizing the importance of considering sex hormones in developing gender-specific therapeutic strategies for cardiovascular disease management. These insights enhance our understanding of how sex hormones influence cardiac health under normal physiological conditions.

Keywords: CRP, Sex hormones, ECG, Cardiac function, UK biobank

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D02-05

Mutations in KCNE1 promote cardiac alternans in Long QT Syndrome Type 5 rabbits

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Long QT syndrome type 5 (LQT5) is caused by mutations in KCNE1, an accessory subunit of the slowly activating delayed rectifier K^+ channel (IKs). We hypothesized that mutations in KCNE1 alter multiple K^+ channels in LQT5 to cause alternans and thereby arrhythmias.
We investigated the mechanisms of alternans in transgenic LQT5 rabbits (G52R-KCNE1 mutation) using ex-vivo optical mapping, voltage clamp, and computer simulation. Alternans readily appears in LQT5 at significantly longer cycle lengths (CL=207 ms) than in littermate control (CL=176 ms). LQT5 alternans starts in the CL range where the slope of the APD restitution curve is < 1 (n=9/11 LQT5). Moreover, there is a unique inverse relationship between the plateau Vm and APD, i.e., the action potential with elevated plateau Vm is associated with a short APD during alternans. Previous voltage clamp data showed that the IKs deactivation kinetics is accelerated and the transient outward K^+ current (Ito) is enhanced in LQT5 myocytes.
In this study, computer modeling shows that IKs remodeling is responsible for APD prolongation while Ito remodeling potentiates alternans in the LQT5 setting. Decreased plateau Vm by Ito enhances negative Ca2+ →Vm coupling by accelerating Ca2+-dependent inactivation of L-type Ca2+ channels during the plateau phase but enhances positive Ca2+→Vm coupling by increasing Na+ / Ca2+ exchange current during the late repolarization phase. This results in the coexistence of Vm- Ca2+ discordant (phase 2) and concordant (phase 3) alternans in LQT5. In conclusion, KCNE1 mutations in LQT5 alter multiple K+ channels, leading to APD prolongation and Ito-mediated alternans.

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Keywords: Long QT syndrome, Arrhythmia, Alternans, KNCE1

D02-06

Short term effects of furosemide on the target organ damage in Angiotensin II-induced hypertensive rats

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Objective: Target organ damage by uncontrolled hypertension underlies risk factors to organ failure or death. Diuretics are first-line prescription to lower the blood pressure. We aimed to observe the effects of furosemide(50mg/kg/d) on cardiovascular systems using a rat hypertensive model induced by angiotensin II(800ng/kg/min).
Methods: Angiotensin II was inserted subcutaneously through osmotic minipumps in rats. Following the establishment of high blood pressure, furosemide was administered by oral gavage for three weeks from the second week. Pathological changes in multiple organs (heart, kidney, skin, and aorta) were observed by H&E and immunohistochemistry. Western blotting was performed to detect biomarkers relate to inflammation and in handling parameters.
Results: Blood pressure was significantly increased by Angiotensin II and furosemide didn't lower blood pressure. Significant adventitia hyperplasia of the aorta, coronary arteries, and renal arteries were observed in Angiotensin II-rats. Furosemide did not alleviate the above changes. Instead, plaque-like protrusions appear in the aortic intima, and some of the small coronary arteries and renal arteries were completely occluded. Immunohistochemistry experiments showed that intensity of eNOS staining was reduced in the heart and skin of the hypertensive rats and furosemide exacerbated the effects. Unexpectedly, the expressions of TNF-α and NFκB proteins in the heart and kidney tissues of Angiotensin II-rats were lower than that of sham group. Furosemide further decreased these parameters in the heart tissue. The ratio of apoptosis-related factors bcl-2 and bax proteins in the heart of Angiotensin II-rats was slightly lower than that in the sham group, furosemide did not change the trend. There was no significant difference in the expression of apoptosis-related proteins in the kidney. The protein expression of sodium-calcium exchanger (NCX) and Na/K pump showed tendency of increment in Angiotensin II-rats and furosemide increased the NCX and Na/K pump proteins significantly in both the heart and kidney.
Conclusion: Acute furosemide is shown to worsen target organ damage. Longer term effects need to be examined thoroughly.

D02-07

Transcriptional Landscape of hiPSC-derived Cardiomyocytes in Hypertrophic Cardiomyopathy: Insights from Comparative Analysis of GSE89714

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Heart disease poses a significant global health challenge, ranking as one of the leading causes of morbidity and mortality. To elucidate the underlying mechanisms, develop novel therapeutic strategies, and enhance drug discovery, researchers have increasingly turned to innovative methodologies. Patient-specific induced pluripotent stem cells (iPSCs) have paved the way for highly personalized cardiac models, facilitating the study of disease mechanisms, drug screening, and the formulation of tailored treatment approaches. Here, we focus on hypertrophic cardiomyopathy (HCM), a prevalent heritable heart condition affecting approximately 1 in 200 to 500 individuals, irrespective of age or sex. HCM is characterized by thickened cardiac tissue, leading to reduced chamber size, impaired relaxation, arrhythmias, and an increased risk of sudden cardiac death. Mutations in genes such as MYH7, MYBPC3, and others are primarily responsible for this disease. Previously, we derived iPSC lines from an HCM family, including a 4-month-old boy with double heterozygous mutations in the sarcomeric β-myosin heavy chain (MYH7-R723C) and muscle LIM protein (MLP-W4R), who presented with severe asymmetric septal hypertrophy. Our findings indicated that double heterozygous iPSC-derived cardiomyocytes (iPSC-CMs) exhibited significant enlargement compared to controls, recapitulating key HCM phenotypes. Furthermore, these mutations led to the upregulation of HCM-associated genes such as ANF and BNP, as well as prolonged twitch events with delayed relaxation in both two-dimensional (2D) and three-dimensional engineered heart tissues (3D-EHTs). Pharmacological interventions were shown to rescue biomechanical and cellular defects in this double mutant HCM model. In the current study, we performed gene expression profiling of iPSC-CMs harboring the MYH7-R723C/MLP-W4R mutations to identify novel HCM markers and explore potential therapeutic targets. Utilizing Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, we investigated dysregulated signaling pathways in HCM patients. Our results revealed several pathways intricately linked to cardiac hypertrophy, with notable upregulation of genes including NFKBIL1, DDAH2, PRRC2A, MTA2, KAT2A, FABP2, and SLC19A1. Comparative analysis with the GSE89714 dataset from the GEO database confirmed the relevance of these genes in the context of human cardiac tissues affected by HCM. This research enhances our understanding of HCM pathogenesis and identifies promising therapeutic targets for further investigation. We believe that these findings will significantly support the development of novel, customized drugs for HCM patients, ultimately improving therapeutic interventions and patient outcomes.

Keywords: IPSC, Hypertrophic cardiomyopathy, RNA Sequencing, Disease modeling

D02-08

CRIF1 Deficiency Improved Homocysteine Production by Disrupting Dihydrofolate Reductase Expression in Vascular Endothelial Cells

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Elevated plasma homocysteine levels can induce vascular endothelial dysfunction; however, the mechanisms regulating homocysteine metabolism in impaired endothelial cells are currently unclear. In this study, we deleted the essential mitoribosomal gene CR6 interacting factor 1 (CRIF1) in human umbilical vein endothelial cells (HUVECs) and mice to induce endothelial cell dysfunction; then, we monitored homocysteine accumulation. We found that CRIF1 downregulation caused significant increases in intracellular and plasma concentrations of homocysteine, which were associated with decreased levels of folate cycle intermediates such as 5-methyltetrahydrofolate (MTHF) and tetrahydrofolate (THF). Moreover, dihydrofolate reductase (DHFR), a key enzyme in folate-mediated metabolism, exhibited impaired activity and decreased protein expression in CRIF1 knockdown endothelial cells. Supplementation with folic acid did not restore DHFR expression levels or MTHF and homocysteine concentrations in endothelial cells with a CRIF1 deletion or DHFR knockdown. However, the overexpression of DHFR in CRIF1 knockdown endothelial cells resulted in decreased accumulation of homocysteine. Taken together, our findings suggest that CRIF1-deleted endothelial cells accumulated more homocysteine, compared with control cells; this was primarily mediated by the disruption of DHFR expression.

Keywords: CR6 interacting factor 1, Dihydrofolate reductase, Folic acid, Homocysteine.

E02-01

TRPC6 as a Defining Marker of Adipogenic Pericytes Driving Adipose Tissue Function and Systemic Metabolism

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Adipose tissues contain a heterogeneous population of multi-potent stromal vascular fraction cells (SVCs), which exhibit varying potency and function. These cells play a critical role in maintaining fat tissue homeostasis, directly affecting systemic metabolism. In the recent years, SVCs have also gained attention for their applications in cosmetic surgery and regenerative medicine. In this study, we identified transient receptor potential channel superfamily canonical member 6 (TRPC6) as a key regulator of adipogenesis in adipose tissue precursor cells. TRPC6 deficiency in mice resulted in an unhealthy obese phenotype characterized by adipose tissue hypertrophy. TRPC6-deficient mice exhibited suppressed browning of white adipose tissue (WAT) and increased whitening of brown fat. Additionally, WAT in these mice showed reduced differentiation capacity, impaired mitochondrial biogenesis, and decreased cAMP signaling. In vitro differentiation of SVCs demonstrated that TRPC6 is essential for adipogenesis by regulating cAMP signaling pathways. Notably, our in-depth analysis of adipose tissue cell populations revealed that TRPC6 is highly expressed in the SVC population, particularly in perivascular cells. Pericytes, a subset of these cells, are proposed to be an alternative source of adipocytes with a high tendency toward beige-like characteristics. Furthermore, TRPC6 expression was found to correlate with CD34, a marker associated with adipocyte progenitor cells known for high lipid turnover. Taken together, our findings suggest that TRPC6 is not only a marker but also a crucial regulator of adipogenic pericyte populations, contributing to the formation of beige adipocytes and potentially enhancing adipose tissue metabolism. This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and RS-2024-00409403) and BK21 FOUR program through the NRF under the Ministry of Education.

Keywords: TRPC6, Pericyte, Adipose tissue, Adipogenesis, Beige adipocytes

E02-02

Unraveling the Molecular Pathways of Obesity-Driven Insulin Resistance: The Role of NEDD4-2 in Regulating Calcium Homeostasis

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Insulin resistance is a key metabolic disorder characterized by reduced responsiveness to insulin, often associated with ectopic lipid accumulation and increased intracellular calcium (Ca^{2+}) levels in peripheral tissues. Obesity and high-fat diets have been shown to elevate intracellular Ca^{2+} concentrations, which inhibit the translocation of PH domain-containing proteins like AKT, PLCδ, and IRS to the plasma membrane, leading to metabolic dysfunction. Despite this, the molecular mechanisms driving disruptions in intracellular Ca^{2+} homeostasis remain unclear. This study aimed to investigate the role of NEDD4-2 (NEDD4L), a HECT-type ubiquitin ligase, in the regulation of Ca^{2+} channels and transporters under obesity-induced conditions. We used immunoprecipitation and proximity ligation assays (PLA) to detect interactions between NEDD4-2 and PMCA2, a plasma membrane Ca^{2+} ATPase, and assessed NEDD4-2's activity in regulating Ca^{2+} homeostasis. Our results showed that obesity significantly reduced the phosphorylation of NEDD4-2 and the expression of PMCA2, which is critical for maintaining Ca^{2+} balance. Overexpression of NEDD4-2 in HepG2 cells further reduced PMCA2 levels and elevated intracellular Ca^{2+}. We confirmed that NEDD4-2 directly interacts with PMCA2, contributing to the disruption of Ca^{2+} homeostasis in obesity. This interaction appears to occur through Ca^{2+}-mediated membrane association via the C2 domain and the hydrolysis of target proteins via the WW domain. These processes exacerbate metabolic disturbances and promote insulin resistance. In conclusion, our findings underscore the significant role of NEDD4-2 in obesity-induced Ca^{2+} dysregulation and insulin resistance, positioning NEDD4-2 as a potential therapeutic target for addressing the metabolic consequences of obesity.

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Keywords: Insulin resistance, Intracellular calcium, NEDD4-2

E02-03

Pharmacological Approaches to Insulin Resistance: The Impact of Angiotensin II Receptor Blockers on Intracellular Ca^{2+} Dysregulation

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Insulin resistance is strongly associated with increased intracellular calcium levels, a condition worsened by lipid accumulation and hyperglycemia-induced cellular stress. Our initial findings reveal that in obesity, dysregulated intracellular calcium impedes the translocation of critical signaling proteins, such as AKT, PLCδ, and IRS, to the cell membrane. This study aimed to explore pharmacological interventions that enhance insulin sensitivity by directly addressing intracellular calcium overload. We tested nine angiotensin-II-receptor blockers (ARBs), typically used for lowering blood pressure, to assess their ability to counteract insulin resistance induced by palmitic acid (PA). Using calcium indicators, we measured the activity of calcium channels, calcium ATPase, and endoplasmic reticulum calcium levels in PA-treated HepG2 cells, evaluating overall calcium balance within the cell. Furthermore, the effects of ARBs on insulin resistance, liver fat accumulation, and inflammation were examined in a high-fat diet mouse model, with a focus on insulin signaling pathways in the liver and muscle tissues. Our results demonstrated that certain ARBs effectively mitigated the harmful effects of PA, such as calcium overload and lipid accumulation, by restoring proper calcium entry via store-operated calcium channels (SOC). This led to improved insulin sensitivity, as evidenced by enhanced AKT membrane translocation and phosphorylation in PA-treated HepG2 cells. In mice, ARBs reduced insulin resistance, liver fat, and inflammation by modulating calcium dysregulation caused by obesity, replenishing endoplasmic reticulum calcium stores, and improving insulin signaling in the liver and muscle after feeding. Notably, candesartan emerged as particularly effective, reversing calcium depletion and alleviating endoplasmic reticulum stress, offering a novel approach to restoring cellular homeostasis. These findings highlight the potential clinical application of ARBs in treating insulin resistance by correcting intracellular calcium dysregulation, providing a new therapeutic avenue for combating metabolic disorders associated with insulin resistance.

Acknowledgement: This study was supported by grants from the Mid-career Researcher Program (2022R1A2C2092700; B.-C.O. and RS-2024-00354120129820768701 01; O.-H.K), the Medical Research Center (No. NRF-2021R1A5A2030333) of the National Research Foundation (NRF) funded by the Korean government.

Keywords: Insulin resistance, Calcium, ARB, Insulin signaling

E02-04

Alterations in Adipose Tissue and Adipokines in Heterozygous APE1/Ref-1 Deficient Mice

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The role of apurinic/apyrimidinic endonuclease 1/redox factor-1 (APE1/Ref-1) in adipose tissue remains poorly understood. This study investigates adipose tissue dysfunction in heterozygous APE1/Ref-1 deficiency (APE1/Ref-1$^{+/-}$) mice, focusing on changes in adipocyte physiology, oxidative stress, adipokine regulation, and adipose tissue distribution. APE1/Ref-1 mRNA and protein levels in white adipose tissue (WAT) were measured in APE1/Ref-1$^{+/-}$ mice, compared to their wild-type (APE1/Ref-1$^{+/+}$) controls. Oxidative stress was assessed by evaluating reactive oxygen species (ROS) levels. Histological and immunohistochemical analyses were conducted to observe adipocyte size and macrophage infiltration of WAT. Adipokine expression was measured, and micro-magnetic resonance imaging (MRI) was used to quantify abdominal fat volumes. APE1/Ref-1$^{+/-}$ mice exhibited significant reductions in APE1/Ref-1 mRNA and protein levels in WAT and liver tissue. These mice also showed elevated ROS levels, suggesting a regulatory role for APE1/Ref-1 in oxidative stress in WAT and liver. Histological and immunohistochemical analyses revealed hypertrophic adipocytes and macrophage infiltration in WAT, while Oil Red O staining demonstrated enhanced ectopic fat deposition in the liver of APE1/Ref-1$^{+/-}$ mice. These mice also displayed altered adipokine expression, with decreased adiponectin and increased leptin levels in the WAT, along with corresponding alterations in plasma levels. Despite no significant changes in overall body weight, microMRI assessments demonstrated a significant increase in visceral and subcutaneous abdominal fat volumes in APE1/Ref-1$^{+/-}$ mice.APE1/Ref-1 is crucial in adipokine regulation and mitigating oxidative stress. These findings suggest its involvement in adipose tissue dysfunction, highlighting its potential impact on abdominal fat distribution and its implications for obesity and oxidative stress-related conditions.

Keywords: Abdominal fat distribution, Adipokine expression, Adipose tissue dysfunction, APE1, Ref-1, Oxidative stress

F02-01

Mechanical Stimulation-Induced ATP Release: A Key Mediator of Paracrine Signaling in MCC13 Cells

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Merkel cells, located in the basal epidermis of the skin, serve an important role as a mechanoreceptors and form touch dome structures essential for tactile perception. These cells contribute to somatosensory processes by releasing a variety of neurotransmitters. Despite their importance, there is still debate regarding the neurotransmitters involved in Merkel cell function. Here, we investigated the function of MCC13 cells, a human Merkel cell carcinoma line, in response to mechanical stimulation using fluorescence imaging. Our results revealed a significant increase in intracellular calcium ($[Ca^{2+}]_i$) level upon mechanical stimulation in MCC13 cells, initiating a paracrine response that elevates $[Ca^{2+}]_i$ in neighboring cells. To elucidate the underlying signaling mechanisms, we explored the calcium responses of MCC13 cells to various neurotransmitters. ATP treatment induced an elevation in $[Ca^{2+}]_i$ levels, while serotonin and norepinephrine did not, suggesting the absence of their receptors in MCC13 cells. Furthermore, our findings showed that mechanical stimuli induce the release of ATP, resulting in a paracrine effect on neighboring MCC13 cells via P2X receptors. The release of ATP upon mechanical stimulation was mediated through the exocytosis pathway of ATP vesicles. To confirm whether MCC13 cells release serotonin and/or norepinephrine during mechanical stimulation, we used chlorpromazine (CPZ), generating inward bending of the cell membrane, to mimic mechanical stimulation. CPZ increased $[Ca^{2+}]_i$ and decreased $[ATP]_i$ levels in MCC13 cells, similar to mechanical stimulation. ELISA analysis confirmed the release of serotonin and norepinephrine in MCC13 cells following CPZ treatment. These findings indicate that mechanical stimulation elicits co-release of serotonin, norepinephrine, and ATP, with ATP playing a paracrine action in human Merkel cells. They also offer a new perspective on the intricate communication network between Merkel cells during mechanical stimulation, suggesting an emerging role for Merkel cells in somatosensory processes.

Keywords: Merkel cells, Mechanical stimulation, ATP release, Paracrine signaling, Neurotransmitter secretion

F02-02

Genetic suppression of mitochondrial Ca^{2+} uniporter prevents podocyte ferroptosis and glomerulosclerosis

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Mitochondrial Ca^{2+} uniporter (MCU) is the main route of Ca^{2+} uptake into the mitochondrial matrix, participating in Ca^{2+} homeostasis and metabolic regulation. However, genetic ablation of MCU have not been resulted in any obvious disease phenotypes, raising doubt about its critical role in physiology and pathophysiology. In this study, we investigated the pathologic implication of MCU in renal fibrosis, focusing on its role in ferroptosis, a form of regulated cell death associated with Fe^{2+}-dependent lipid peroxidation. Using *in vitro* experiments with differentiated human podocytes, we demonstrated that silencing of MCU protects against TGF-β-induced epithelial-mesenchymal transition (EMT) and fibrotic changes. Moreover, MCU knockdown suppressed lipid peroxidation and ferroptotic cell death by erastin- or adriamycin, indicating its involvement in the process of ferroptosis. To further evaluate the therapeutic potential of MCU inhibition in fibrosis associated with ferroptosis, we applied adriamycin-induced glomerulosclerosis model to tamoxifen-inducible whole-body MCU knockout mice. Wild-type mice treated with adriamycin developed marked albuminuria within 2 weeks, along with destructive alterations in glomerular filtration barrier. Consistent with our *in vitro* results, glomerulosclerotic changes with foot process effacement in podocytes by adriamycin were significantly attenuated in MCU knockout mice. Albuminuria with deteriorated kidney functions in adriamycin-induced nephropathy were also prevented by genetic deletion of MCU, highlighting a protective effect of MCU inhibition against renal fibrosis. Our findings suggest that MCU act as a pathogenic mediator of podocyte ferroptosis and glomerulosclerosis, positioning it a novel and promising therapeutic target for the treatment of chronic kidney diseases.

Keywords: Ferroptosis, Mitochondrial Ca^{2+} uniporter (MCU), Glomerulosclerosis, Chronic kidney disease

F02-03

c-Jun N-terminal kinase as a therapeutic target for glomerulosclerosis in chronic kidney diseases

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Transforming growth factor-β (TGF-β) is a key player in the development of fibrotic kidney diseases. Non-canonical TGF-β signaling, including the activation of ERK and subsequent upregulation of mTOR and NOX4, contribute to epithelial-mesenchymal transition (EMT) and renal fibrosis. However, the pathogenic roles of other mitogen-activated kinases (MAPKs), such as p38 MAPK and c-Jun N-terminal kinase (JNK), in glomerular and tubular diseases remains unclear. In this study, we investigated the therapeutic potential of JNK inhibitors in immortalized human podocytes and Adriamycin-induced glomerulosclerosis model. TGF-β increased mesenchymal markers (collagen, α-SMA) and reduced epithelial markers (ZO-1, cadherin), changes that were prevented by SP600125, a pan-JNK inhibitors, not by SB203580, a p38 MAPK inhibitor. Furthermore, inhibition of JNK blocked the expression and secretion of endogenous TGF-β, implying an autocrine action, triggered by exogenous TGF-β. Notably, among JNK subtypes, knockdown of JNK3 provided the most effective protection against TGF-β-induced EMT and fibrosis. In vitro studies using a selective JNK inhibitors demonstrated significant suppression of oxidative stress, EMT, fibrosis, and morphologic derangement of podocytes. In an animal model of focal sclerosing glomerulosclerosis, we developed an Adriamycin-induced nephropathy mouse, and treated with JNK inhibitor, which protected against renal fibrosis, podocyte damage and albuminuria induced by Adriamycin. These results suggest that JNK inhibition offers a more targeted and effective therapeutic strategy for combating TGF-β-induced fibrosis and protecting kidney function, surpassing the therapeutic efficacy of general JNK inhibition. Therefore, JNK could be a novel and promising therapeutic target for the treatment of chronic kidney diseases.

Keywords: Renal fibrosis, TGF-Beta signaling, C-Jun N-terminal kinase 3 (JNK3), Glomerulosclerosis, Chronic kidney disease

G02-01

Oxidative stress and inflammatory responses induced by fine particulate matter in bone marrow-derived macrophages

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Fine particulate matter (FPM), typically particles smaller than 2.5 micrometers (PM2.5), is a significant environmental pollutant that poses serious health risks due to its ability to penetrate deep into the lungs and enter the bloodstream. Macrophages, which are crucial immune cells, play a vital role in host defense and inflammation. This study aimed to investigate the effects of FPM on bone marrow-derived macrophages (BMMs). BMMs were exposed to various concentrations of FPM, and the levels of reactive oxygen species (ROS) were measured using a fluorescent probe. To measure ROS levels in BMMs, we used the DCFH-DA fluorescent probe, which detects intracellular ROS through fluorescence intensity. Additionally, an enzyme-linked immunosorbent assay (ELISA) was performed to quantify the expression of pro-inflammatory cytokines. Our results demonstrated that exposure of FPM is sufficient to induce ROS generation in BMM cells. Furthermore, a dose-dependent increase in pro-inflammatory cytokine secretion, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), was observed in response to FPM exposure. These findings suggest that FPM exposure can induce oxidative stress and inflammatory responses in macrophages, highlighting the potential role of oxidative stress in FPM-related health issues. Future research should explore the molecular mechanisms underlying FPM-induced oxidative stress and inflammation in macrophages, as well as potential therapeutic interventions that could mitigate these effects in the context of environmental pollution-related diseases.

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Keywords: Bone marrow-derived macrophages, Fine particulate matter, Inflammation, Oxidative stress, Reactive oxygen species

H02-01

The Role of Ei24 in Modulating Calcium Homeostasis Through Interaction with STIM1 and CRAC Channel

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Store-operated calcium entry (SOCE) is essential for maintaining Ca^{2+} homeostasis by triggering Ca^{2+} influx when endoplasmic reticulum (ER) Ca^{2+} stores are depleted. This process is mediated by stromal interaction molecules 1 (STIM1), which functions as an ER Ca^{2+} sensor, and Orai1, which forms Ca^{2+} release-activated Ca^{2+} (CRAC) channels in the plasma membrane. Ei24, a component of the mitochondria-associated membrane (MAM) complex, has been shown to interact directly with ER Ca^{2+} channels. However, its potential role in modulating plasma membrane channels like CRAC remains unclear. This study explores the role of Ei24 in regulating SOCE through its interaction with STIM1. Ei24 overexpression reduced CRAC channel current density. Furthermore, Ei24-deficient HeLa cells exhibited a marked increase in SOCE, an effect that was reversed by reintroducing Ei24. Co-immunoprecipitation confirmed a physical interaction between STIM1 and Ei24 at the CRAC activation domain (CAD). Additionally, fluorescence recovery after photobleaching (FRAP) assays demonstrated that Ei24 overexpression slowed the mobilization kinetics of STIM1.These findings underscore the critical role of Ei24 in regulating the Ca^{2+} sensor STIM1 and fine-tuning SOCE function, providing valuable insights into Ca2+ homeostasis mechanisms.

Acknowledgement: This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and RS-2024-00409403, and BK21 FOUR program through the NRF under the Ministry of Education).

Keywords: ER-PM contact site, Orai1, CAD domain, Mitochondria-associated membrane

H02-02

Combining CYP2J2 inhibition with immune checkpoint blockade for enhanced liver cancer therapy

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Immune checkpoint blockade represents a cutting-edge approach in cancer immunotherapy, focusing on the regulation of critical immune pathways in the immune system, specifically targeting checkpoints that usually suppress immune responses to prevent autoimmunity. In liver cancer, immune checkpoint blockade has shown great promise as a therapeutic strategy. Traditional therapies for liver cancer have been largely ineffective due to the complexity of the disease and the immune-suppressive nature of the liver environment. However, immune checkpoint inhibitors have opened new possibilities by reactivating the immune system, enabling it to recog-

nize and eliminate liver tumor cells. Beyond immune checkpoint inhibitors, targeting molecular pathway such as cyp2j2, which is overexpressed in various cancers, including liver cancer, offers an additional therapeutic avenue. In our research, we discovered that silencing cyp2j2 led to an increase in cd274 expression in liver cancer cells. Furthermore, in an orthotopic mouse model, cyp2j2 deletion resulted in significant tumor suppression, which was linked to decreased CD8+ T cell activity. These findings suggest that the combination of cyp2j2 inhibition with immune checkpoint blockade could yield synergistic effects in liver cancer treatment. This dual approach has the potential to not only reduce tumor-promoting signals but also amplify immune activation, thereby enhancing the efficacy of liver cancer therapy.

Keywords: CYP2J2, Immunotherapy, Cd274, Liver cancer

H02-03

Activation of TMEM16E scramblase induces ligand-independent growth factor receptor signaling and macropinocytosis for membrane restructuring.

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The calcium-dependent phospholipid scramblase TMEM16E mediates ion transport and lipid translocation across the plasma membrane. TMEM16E also contributes to protection of membrane structure by facilitating cellular repair signaling. Our research reveals that activation of TMEM16E scramblase promotes macropinocytosis, a critical response for preserving plasma membrane integrity. The scramblase externalizes phosphatidylserine that is normally associated with resting growth factor receptors. We demonstrate that TMEM16E can interact with and signal through growth factor receptors, including epidermal growth factor receptor, even without their ligands. This interaction stimulates downstream phosphoinositide 3-kinase, PI(3,4,5)P3 production, and macropinocytosis, resulting in internalization of annexin V bound to the membrane, processes sensitive to amiloride inhibition. Although TMEM16E is also internalized during this event, it returns to the plasma membrane. TMEM16E-driven macropinocytosis is proposed to restore membrane integrity after perturbation, which might explain pathologies in conditions like muscular dystrophies and neurologic disorders where TMEM16E functionality is compromised.

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Keywords: TMEM16E, Phospholipid scramblase, Macropinocytosis, Growth factor receptor, Membrane restructuring

H02-04

Collagen triple helix repeat containing 1 as a key regulator of esophageal cancer progression

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Collagen triple-helix repeat-containing 1 (CTHRC1) is frequently overexpressed in a variety of cancers, including breast, liver, pancreatic, and colorectal cancers. Its overexpression is strongly associated with aggressive tumor phenotypes, such as enhanced tumor invasion, increased metastatic potential, and poor patient prognosis. Studies have demonstrated that elevated CTHRC1 levels contribute to heightened cancer cell invasiveness and worsened clinical outcomes. In this study, we sought to explore the functional role of CTHRC1 in esophageal cancer. Consistent with findings in other cancer types, our results show that CTHRC1 overexpression is significantly correlated with lower survival rates in esophageal cancer patients. Silencing of CTHRC1 led to increased expression of key markers associated with epithelial-mesenchymal transition (EMT), including vimentin, twist, as well as elevated levels of matrix metalloproteinase 9 and urokinase plasminogen activator, both of which are critical for cancer cell invasion and metastasis. Further studies are required to elucidate the specific molecular mechanisms by which CTHRC1 promotes esophageal cancer cell proliferation and metastasis, particularly the signaling pathways involved. Our findings suggest that CTHRC1 plays a pivotal role in regulating the growth and metastatic behavior of esophageal cancer, making it a potential therapeutic target for intervention.

Keywords: Esophageal cancer, CTHRC1, Proliferation, Metastasis

H02-05

Suppression of p21-activated kinase -4 enhances CD274 downregulation in liver cancer

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CD274 plays a pivotal role in the immune checkpoint system, where it binds to the programmed death 1 receptor on T cells. This interaction suppresses T cells activity, reducing inflammation and preventing autoimmunity. However, cancer cells often exploit this pathway to evade immune detection, facilitating tumor progression. p21-activated kinase -4 is a protein kinase involved in critical cellular functions such as cell morphology, motility, proliferation, and survival. Its expression in the liver has been investigated in both normal and cancerous tissues. In healthy liver cells, p21-activated kinase -4 is expressed at relatively low levels, contributing to routine cellular processes like migration, survival, and cytoskeletal maintenance. In contrast, p21-activated kinase-4 is often upregulated in liver cancer, where it plays a role in promoting tumorigenesis. This study examines the relationship between CD274 expression and p21-activated kinase -4 regulation in liver cancer. Our findings reveal that p21-activated kinase -4 is positively correlated with CD274 expression and modulates the CD8+ T cell activity, suggesting a potential regulatory mechanism. These results underscore the need for further investigation into how 21-activated kinase -4 influences CD274 expression and its role in immune evasion during liver tumorigenesis at the cellular level.

Keywords: P21-activated kinase -4, CD274, Immunotherapy

H02-06

Senicapoc suppresses TGF-b1-induced metastasis in head and neck squamous cell carcinoma (HNSCC) by blocking KCa3.1 channels

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Head and neck squamous cell carcinoma (HNSCC) metastasis significantly worsen patient prognosis. The intermediate conductance calcium-activated potassium channel (KCa3.1, KCNN4) has been implicated in the metastasis of various human cancers. Senicapoc, a selective KCa3.1 inhibitor, is orally available, is orally available and has demonstrated safety and tolerability in phase I and II clinical trials. This study investigates the role of KCa3.1 in HNSCC metastasis and proposes senicapoc as a repurposed drug for preventing cancer metastasis. KCa3.1 expression and physiological functions were detected in two HNSCC cell lines using western blotting and patch clamp recording. We demonstrate that silencing KCa3.1 suppresses

TGF-β1-induced metastasis in HNSCC cells utilizing transwell and wound healing assays. Furthermore, KCa3.1 downregulation increased E-cadherin expression while decreased N-cadherin and Snail expression. Conversely, KCa3.1 overexpression enhanced cancer cell mobility, decreased E-cadherin, and increased N-cadherin and Snail expression. Senicapoc significantly impaired HNSCC migration and invasion by blocking KCa3.1 channels in a dose-dependent manner. The role of KCa3.1 in TGF-β1-induced metastasis in HNSCC and the effectiveness of senicapoc were confirmed in 3D cell culture using spheroid assays. In conclusion, our findings suggest that KCa3.1 plays a crucial role in HNSCC metastasis and senicapoc represents a promising candidate for its prevention.

Keywords: HNSCC, KCNN4, Senicapoc, Metastasis, TGF-β1

H02-07

The role of recombinant human bmp-2 in colorectal cancer suppression and its safety in surgical applications

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Colorectal cancer originates in the colon or rectum, both of which are parts of the large intestine. The disease typically begins as small benign growths known as polyps, which can gradually evolve into cancer. Colorectal cancer is the third most common cancer affecting both men and women, but early detection through screening can dramatically enhance treatment success. Abnormal BMP signaling, particularly involving BMP-2, has been associated with colorectal cancer development. BMP-2 is recognized for its potential tumor-suppressing effects in colorectal cancer. Recombinant human bone morphogenetic protein-2 (rhBMP-2), a synthetic version of BMP-2, is widely used in orthopedic and spinal surgeries to facilitate bone healing and fusion. Despite its benefits, concerns have arisen regarding its application in humans, especially in surgical contexts. In this study, we aimed to evaluate the safety of rhBMP-2 in human orthopedic and spinal surgeries. Our results showed that rhBMP-2 not only suppressed the proliferation of colorectal cancer cells but also induced apoptosis. Furthermore, rhBMP-2 elevated the expression levels of MST1, MST2, Sav1, and phosphorylated YAP, which are key components of the Hippo signaling pathway. These findings suggest that rhBMP-2 inhibits CRC cell growth and prevents the activation of YAP function, indicating that rhBMP-2 can be safely applied in huma surgeries without promoting cancer cell proliferation.

Keywords: RhBMP-2, Colorectal cancer, Hippo signaling pathway

H02-08

Discovery of a novel natural compound, vitekwangin B, with ANO1 protein reduction properties and anticancer potential

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Background: Prostate cancer and non-small cell lung cancer (NSCLC) present significant challenges in the development of effective therapeutic strategies. Hormone therapies for prostate cancer target androgen receptors and prostate-specific antigen markers. However, treatment options for prostatic small-cell neuroendocrine carcinoma are limited. NSCLC, on the other hand, is primarily treated with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors but exhibits resistance. This study explored a novel therapeutic approach by investigating the potential anticancer properties of vitekwangin B, a natural compound derived from Vitex trifolia.
Methods: Vitekwangin B was chromatographically isolated from the fruits of V. trifolia. ANO1 protein levels in prostate cancer and NSCLC cells were verified and evaluated again after vitekwangin B treatment.
Results: Vitekwangin B did not inhibit anoctamin1 (ANO1) channel function but significantly reduced ANO1 protein levels. These results demonstrate that vitekwangin B effectively inhibited cancer cell viability and induced apoptosis in prostate cancer and NSCLC cells. Moreover, it exhibited minimal toxicity to liver cells and did not affect hERG channel activity, making it a promising candidate for further development as an anticancer drug.
Conclusion: Vitekwangin B may offer a new direction for cancer therapy by targeting ANO1 protein, potentially improving treatment outcomes in patients with prostate cancer and NSCLC. Further research is needed to explore its full potential and overcome existing drug resistance challenges.

Keywords: Anoctamin 1, Apoptosis, Lung cancer, Prostate cancer, Protein reduction, Vitekwangin B

H02-09

Potentiating doxorubicin efficacy in colorectal cancer through inhibition of the Akt/GSK3β/mTOR-SREBP1 pathway via HDAC inhibition

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Doxorubicin, an anthracycline antibiotic, is a widely used chemotherapeutic agent that functions by intercalating into DNA and inhibiting topoisomerase II, leading to DNA damage and subsequent cell death. However, its application in colorectal cancer (CRC) is hampered by the development of resistance and significant toxicity. Panobinostat, a histone deacetylase inhibitor (HDACi), has demonstrated potential in overcoming doxorubicin resistance in CRC by modulating key cellular pathways. Colorectal cancer is the third most common cancer globally and the second leading cause of cancer-related mortality. This study investigated the efficacy of combining panobinostat with doxorubicin in CRC cells. The combination therapy significantly reduced cell viability, induced apoptosis, and downregulated the p-Akt/GSK-3β/mTOR signaling pathway, along with decreased expression of c-Myc and SREBP-1. In vivo, the combined treatment suppressed tumor growth more effectively than either agent alone. These findings indicate that panobinostat enhances doxorubicin's anticancer effects, suggesting a synergistic therapeutic strategy for colorectal cancer.

Keywords: Doxorubicin, Panobinostat, Cell death, Colorectal cancer cells

H02-10

Phosphate impacts mitochondrial stress and Ca2+-based filtration in podocytes

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Dysregulated intracellular Ca^{2+} signaling in podocytes disrupts the actin cytoskeleton and impairs the slit diaphragm, leading to proteinuria, an early indicator of kidney disease. While the role of *Trpc5/6* channels in this process is well-established, recent evidence suggests that Orai1-mediated store-operated Ca^{2+} entry (SOCE) also plays a role in maintaining Ca^{2+}-dependent filtration and protecting podocyte damage. In diabetic nephropathy, elevated podocyte Ca^{2+} levels are linked to increased reactive oxygen species (ROS), which are also elevated in chronic kidney disease (CKD). Hyperphosphatemia contributes to kidney damage, but the specific mechanisms by which excess inorganic phosphate (Pi) affects SOCE-mediated Ca^{2+}

signaling, podocyte actin dynamics, and filtration, leading to proteinuria in CKD, are not fully understood. Our research demonstrates that Pi enhances mitochondrial Ca^{2+} uptake and depolarizes mitochondrial membrane potential, potentially producing mitochondrial ROS. Furthermore, Pi promoted Akt-dependent exocytosis of Orai1 channels, increasing their surface expression. This dysregulation in cytosolic Ca^{2+} or ROS could damage the actin cytoskeleton and reduce synaptopodin expression, impairing podocyte structure and increasing albumin leakage. Notably, inhibiting Orai1 with GSK7975A partially restored the actin cytoskeleton and prevented synaptopodin breakdown. In vivo, podocyte-specific Orai1-deletion (Nphs2;Orai-$1^{fl/fl}$) in mice administered with Pi resulted in less albuminuria compared to wild-type mice. Short-term Pi exposure also increased GDF15 expression, a mitochondrial stress marker that may counteract ROS and Ca^{2+} dysregulation. However, prolonged Pi exposure caused irreversible damage to the actin cytoskeleton, compromising podocyte health and slit diaphragm function, ultimately leading to proteinuria. In summary, our findings emphasize the complex effects of Pi on podocyte function, particularly in relation to Ca^{2+} regulation and filtration integrity.

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Keywords: SOCE, STIM1, Orai1, Ca^{2+} signaling, Actin cytoskeleton, Proteinuria, ROS

H02-11

Mechanistic elucidation of Genistein targeting lung cancer through network pharmacology and molecular dynamics simulation studies

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Food supplements as an adjuvant therapy have become beneficial for many chronic disorders, including cancer. Genistein, a natural isoflavone enriched in soybeans, has gained potential interest as an anti-cancerous agent in various cancers, primarily by modulating apoptosis, the cell cycle, angiogenesis, and inhibiting metastasis. However, the exact effects and when genistein is beneficial against cancer still need clarification. With this regard, network pharmacology and in-silico approaches were followed to unravel molecule mechanisms of genistein with its corresponding targets considering lung, prostate, and breast cancer. Based on network pharmacology and degree score, genistein may significantly interact with the following hub genes: EGFR, ESR1, STAT3, AKT1, CASP3, CDK1, SRC, etc. Since EGFR and ESR1 are more common in later stages of non-small cell lung cancer progression than in earlier ones, genistein may be more effective in targeting these proteins in advanced stages than in earlier ones, except stage II. Identical findings are observed in breast cancer, with ESR1 involvement more prevalent than other hub genes at all stages of breast cancer. In prostate cancer, the proteins AKT1, ESR1, and EGFR stand out most prominently in the advanced stages. In addition, molecular docking and dynamics simulation analysis confirmed significant binding affinity to these critical targets, essential regulators of molecular and cellular processes linked with several cancers. Thus, the current system pharmacology and in silico data exhibited genistein might modulate lung cancer pathobiology significantly, suggesting its therapeutic applicability for preventing and treating lung cancer.

Keywords: MD simulation, Cancer, Lung cancer

H02-12

The Effect of MLN4924 inhibition on IκB-α expression in Renal cell cancer

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Inhibition of the protein neddylation process by the small-molecule inhibitor MLN4924 has been recently indicated as a promising direction for cancer treatment. However, the knowledge of all biological consequences of MLN4924 for cancer cells is still incomplete. Here, we report that MLN4924, similar to TNF-α, induced phosphorylation of inhibitor of nuclear factor kappa B-alpha (IκB-α). Using Cycloheximide chase assay, we found that MLN4924 downregulated protein stability and promoted proteasomal degradation of IκB-α at the mRNA and protein levels. Moreover, through an inhibitors study, it was revealed that phosphorylation of IkB by MLN4924 was caused by the PI3K (IκBα phosphorylation at Tyr42) pathway. We also show that IκB-α is conjugated by Nedd8. Taken together, our findings identified MLN4924 as a suppressor of IkBa in renal cell carcinoma, suggesting that inhibition of neddylation might be a new therapeutic strategy to prevent proliferation, control of apoptosis, promotion of angiogenesis, and stimulation of invasion/metastasis in Renal cell carcinoma patients.

Keywords: NF-kappa-B inhibitor alpha, Renal cancer, Neddylation

H02-13

Fulvic acid inhibits differentiation of 3T3-L1 adipocytes through activating Ca^{2+} / CaMKII / AMPK pathway

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The risk of developing type 2 diabetes in obesity is as high as 80-85%. Various metabolic syndromes are also increased in obesity. Fulvic acid obtained from organic soil was found to alleviate the mean back-fat thickness of pigs when it was supplied together with meals. However, the mechanism for the anti-fat accumulation effect of fulvic acid remains unclear. Therefore, we used 3T3-L1 adipocytes to explore the mechanism of fulvic acid. During the differentiation period on day 2 to 8 of 3T3-L1 cells, intracellular lipid accumulation was reduced by fulvic acid treatment compared to the control without the treatment. Accordingly, the protein expression of Peroxisome proliferator-activated receptor gamma (PPARγ) and CCAAT/enhancer-binding protein alpha (C/EBPα), Sterol regulatory element-binding protein 1 (SREBP1c) which are related to differentiation to mature adipocytes, was weaker in 3T3-L1 cells treated with fulvic acid. In addition, the expression of Fatty acid-binding protein 4 (FABP4) and cluster of differentiation 36 (CD36) which are proteins associated with cellular lipid uptake was less in fulvic acid-treated 3T3-L1 cells than in the control cells. Moreover, fulvic acid increased intracellular Ca^{2+} secretion, enhanced the protein expression of Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) and thus AMP-activated protein kinase (AMPK). Therefore, the Ca^{2+} / CaMKII / AMPK pathway in adipocytes could be a therapeutic target against obesity.

Keywords: 3T3-L1 adipocytes, Fulvic acid, CaMKII, AMPK, Obesity, Ca^{2+}

H02-14

Conditioned medium from reprogramed cancer-associated fibroblasts by apoptotic cancer cells inhibits tumor growth in mice via WISP-1 signaling

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Cancer-associated fibroblasts (CAFs) and apoptotic cancer cells significantly influence cancer progression and metastasis within the tumor microenvironment (TME). In this study, we evaluated the in vivo anti-tumor growth effects of paracrine factors secreted by CAFs exposed to apoptotic cancer cells. CAF-conditioned media (CM) or CM from CAFs exposed to apoptotic 344SQ cells (ApoSQ-CAF CM) was administered intratumorally into syngeneic immunocompetent mice following 344SQ cell injection. Mice treated with either undiluted or 50% diluted ApoSQ-CAF CM showed a marked reduction in lung tumor nodules and metastatic spread compared to those receiving CAF CM (either undiluted or 50% diluted). Notably, undiluted ApoSQ-CAF CM was more effective than the 50% diluted version, resulting in greater reductions in tumor volume and metastasis rate. This effect was observed alongside the downregulation of proliferative and anti-apoptotic markers, while simultaneously boosting the activation of phosphorylated STAT1 and pro-apoptotic markers in isolated CD326+ tumor cells from primary tumors. However, these anti-tumor growth effects observed with ApoSQ-CAF CM were diminished when WISP-1 was immunodepleted from the CM. Notably, intratumoral injection of recombinant WISP-1 (rWISP-1) replicated the effects observed with ApoSQ-CAF CM. These findings suggest that utilizing CM from CAFs exposed to apoptotic lung cancer cells may provide a promising therapeutic strategy to inhibit tumor growth.

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Keywords: Apoptotic cells, CAFs, Tumor growth, RWISP-1

H02-15

Interaction between cancer-associated fibroblasts and apoptotic cancer cells suppresses lung cancer cell growth through WISP-1-integrin αvβ3-STAT1 signaling pathway

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Cell death within the tumor microenvironment (TME) significantly influences tumor-specific immunity, ultimately shaping the overall immune balance. Cancer-associated fibroblasts (CAFs) play a crucial role in tumor progression through paracrine mechanisms. Our previous study revealed that reprogramming of CAFs by apoptotic cancer cells suppresses tumor volume and lung metastasis, primarily through WISP-1 production. Here, we investigated the mechanisms underlying this effect, focusing on how reprogrammed CAFs inhibit tumor growth. We found that treatment with conditioned medium (CM) from CAFs exposed to apoptotic lung cancer cells led to increased phosphorylation of STAT1 and enhanced expression of its downstream targets, such as phosphorylated p53, p53 and p21 in lung cancer cells, including 344SQ and A549. STAT1 specific siRNAs or the pharmacologic inhibitor fludarabine attenuated the antiproliferative and pro-apoptotic effects of this CM. Furthermore, recombinant WISP-1 (rWISP-1) treatment dose- dependently inhibited lung cancer cell proliferation and enhanced apoptosis. Using anti-integrin αv and β3 antibodies or siRNA targeting αv or β3, we demonstrated that WISP-1 signals through the integrin αvβ3-STAT1 pathway to suppress proliferation and promote apoptosis. Co-immunoprecipitation assays confirmed the direct interaction between WISP-1 and integrin αvβ3 in these cells. These findings suggest that CM from apoptotic cancer cell-exposed CAFs could represent a promising therapeutic strategy for targeting tumor cell growth.

Acknowledgement: This work was supported by the National Research Foundation of Korea grants funded by the Korean government (MSIT) (2020R1A5A2019210).

Keywords: CAFs, Apoptotic lung cancer cells, Tumor growth, WISP-1-integrin αvβ3- STAT1

I02-01

Regular exercise increases in NAD+ levels in the skeletal muscle and the brain of aging mice

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Nicotinamide adenine dinucleotide (NAD+) is an essential coenzyme in all living cells and is involved in neurogenesis, inflammation, the immune system, and DNA repair. The level of intracellular NAD+ reportedly decreases with age in tissues and organs, including the brain. This systemic decrease in NAD+ levels during aging is partly due to decreased nicotinamide phosphoribosyltransferase (NAMPT), the rate-limiting enzyme in the major NAD+ biosynthetic pathway in mammals. Furthermore, brain-specific NAMPT knockdown in young and aged mice reportedly reduces hippocampal NAD+ levels and contributes to the development of cognitive impairment. Additionally, the preventive effect of regular exercise against age-related cognitive decline is widely known. However, no research on the relationship between hippocampal NAD+, especially NAMPT levels, and improved cognitive function due to exercise has been published. Here, we aimed to determine whether regular exercise increases NAD+ levels in the hippocampus and prevents cognitive decline. Twenty-month-old female C57BL/6J mice were divided into four groups: (1) the SAL group (saline [SAL] only), (2) FK group (FK866 [FK; a NAMPT inhibitor] only), (3) SAL + Ex group (SAL + regular voluntary exercise [Ex]), and (4) FK + Ex group. All mice were intraperitoneally injected three times a week for four weeks, specifically before exercise in the SAL + Ex and FK + Ex groups. We revealed that regular exercise improved working and long-term memory in aged mice. NAMPT and BDNF mRNA expression in the hippocampus, and NAD+ levels increased in the whole brain and soleus in an age-related manner. Our results suggest that the prevention of cognitive decline and improvement of cognitive function in aged mice via regular exercise are associated with increased NAD+ levels via increased NAMPT levels in the hippocampus.

Keywords: NAD, Aging, Cognitive function, Regular exercise

J02-01

Distributed processing for value-based choice by prelimbic circuits targeting anterior-posterior dorsal striatal subregions in male mice

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Fronto-striatal circuits have been extensively implicated in the cognitive control of behavioral output for both social and appetitive rewards. The functional diversity of prefrontal cortical populations is strongly dependent

on their synaptic targets, with control of motor output in part mediated by connectivity to dorsal striatum. Despite evidence for functional diversity along the anterior-posterior axis of the dorsomedial striatum (DMS), it is unclear how distinct fronto-striatal sub-circuits support neural computations essential for value-based choice. Here we identify prefrontal populations targeting distinct DMS subregions and characterize their functional roles in male mice. We first performed neural circuit tracing to reveal segregated prefrontal populations defined by anterior/posterior dorsomedial striatal target. The parallel nature of these pathways was evident both from afferent input biases and unique local synaptic connectivity within striatum. We probed the functional relevance of these parallel circuits via in vivo calcium imaging and temporally precise causal manipulations during a feedback-based 2-alternative choice task. Single-photon imaging revealed circuit-specific representations of task-relevant information with prelimbic neurons targeting anterior DMS (PL::A-DMS) robustly modulated during choices and in response to negative outcomes, while prelimbic neurons targeting posterior DMS (PL::P-DMS) encoded internal representations of value and positive outcomes contingent on prior choice. Consistent with this distributed coding, optogenetic inhibition of PL::A-DMS circuits strongly impacted choice monitoring and responses to negative outcomes while perturbation of PL::P-DMS signals impaired task engagement and strategies following positive outcomes. Together our data uncover novel PL populations engaged in distributed processing for value-based choice.

Keywords: Striatum, Value-based decision making, Prelimbic cortex, In-vivo calcium imaging, Optogenetics

K02-01

Impact of thermotherapy-induced orexin and dopamine changes on metabolic health in postmenopausal obese women

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The aim of this study is to evaluate the efficacy of thermotherapy as an alternative to exercise in improving metabolic health in postmenopausal obese women by investigating its effects on circulating orexin, dopamine, and various related physiological markers involved in thermoregulation and metabolic control. A total of 53 postmenopausal obese women were divided into two groups: a control group (n=26) with no thermotherapy and a thermotherapy group (n=27) that received 24 times of thermotherapy (warm water half-body bath, 42 ± 0.5°C for 60 minutes) over a 4-week period. Both groups were assessed before and after thermotherapy for orexin, dopamine, body temperature, basal metabolic rate (BMR), adiponectin, high-sensitivity C-reactive protein (hsCRP), and obesity indicators. Significant changes were observed in the thermotherapy group compared to the control group, including a significant increase in circulating orexin, dopamine, body temperature, BMR, and adiponectin, alongside significant reductions in hsCRP and obesity indicators (body fat %, BMI, waist circumference). These findings demonstrate that thermotherapy elicits physiological effects similar to exercise by enhancing orexin and dopamine activation, promoting thermogenesis, and increasing energy metabolism, thus contributing to reductions in inflammation and obesity. Therefore, thermotherapy can be proposed as an effective alternative to exercise for enhancing metabolic health in postmenopausal obese women, particularly in cases where physical or environmental limitations hinder regular exercise.

Keywords: Thermotherapy, Postmenoposal obese women, Orexin, Dopamine; body temperature, Metabolisim

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L02-01

How do blood pressure medications affect the autonomic nervous system in hypertensive patients? – Using QSART

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The number of people with hypertension worldwide has increased to 1.3 billion, and it is estimated that 28% of the adult population aged 20 or older in Korea, or about 12.3 million people, have hypertension. In this way, hypertension is emerging as a public health problem, and research on various approaches is needed. Therefore, in this study, we aimed to investigate the effect of blood pressure medication on the autonomic nervous system of hypertensive patients by comparing responses using an autonomic nerve test using acetylcholine (ACh). The study was conducted on a total of 30 middle-aged people, and they were divided into three groups: a group of hypertensive patients not taking blood pressure medication, a group taking blood pressure medication, and a group with normal blood pressure. The experimental method adopted was the quantitative sudomotor axon reflex test (QSART), and the activated sweat gland density (ASGD) on the subject's frequently used forearm was measured and converted into compare by surface area (1cm2; FSA, forearm surface area; BSA, body surface area). As a result, the ASGD of the hypertensive group not taking blood pressure medication was the highest compared to the other two groups. In addition, the higher the systolic blood pressure, diastolic blood pressure, and mean arterial pressure, the higher the ASGD tended to be. In conclusion, this study confirmed that taking blood pressure medication can lead to normalization of reflex action, that is, the autonomic nervous system. It is also significant in that it contributed to proving the efficacy of blood pressure medication.

Keywords: Hypertension, Blood pressure, QSART (quantitative sudomotor axon reflex test), ACh (acetylcholine), Blood pressure medication

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L02-02

Exploring the efficacy of music therapy in ameliorating depression and sleep disturbances in adolescents with ADHD during the COVID-19 pandemic

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In the wake of the World Health Organization's (WHO) declaration of the COVID-19 pandemic, a marked deterioration in mental health and sleep disturbances among adolescents has been globally observed, thereby amplifying the imperative for efficacious therapeutic interventions. This phenomenon is particularly pronounced in adolescents diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), who exhibit heightened vulnerability to depressive states and sleep dysregulation, exacerbated by the pandemic's psychosocial impacts. The present study endeavors to explore the efficacy of music therapy as a remedial strategy to ameliorate depressive symptoms and sleep perturbations in this demographic, contextualized within the COVID-19 milieu. A randomized assignment allocated participants to either a Music Therapy intervention group or a control group receiving no musical therapy. The intervention comprised a structured program of music therapy, entailing 21 sessions of 50 minutes each, administered three times per week, specifically designed to enhance mood regulation and sleep quality. Evaluative measures included assessments of physiological markers indicative of depression, notably Blood Pressure (BP) and Heart Rate (HR), alongside standardized scales for depression severity and sleep quality assessment. The findings revealed that participants in the Music Therapy group demonstrated a statistically significant reduction in BP and HR, indicative of ameliorated physiological responses to depression, coupled with an improvement in emotional responses towards depressive states, as compared to their counterparts in the control group. This amelioration was concomitantly associated with enhancements in sleep quality. These outcomes posit that systematic and targeted music therapy interventions can beneficially influence both physiological and emotional parameters in adolescents with ADHD, suggesting a viable therapeutic avenue for the enhancement of sleep quality amidst the challenges posed by the COVID-19 context.

Keywords: Music Therapy, Adolescents with ADHD, Sleep quality, Depression, Blood pressure

M02-01

Metabolite Profiling Using UPLC-QTOF-MS for the Evaluation of Laser Acupuncture in Arthritis

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This study aimed to investigate the metabolomic changes in arthritis patients following 830 nm laser acupuncture treatment using untargeted metabolite profiling by UPLC-QTOF-MS. A total of 40 participants were recruited, with 20 individuals in the placebo group and 20 receiving laser acupuncture. Serum samples were collected from all participants on the first and last days of the study, and metabolite profiling was performed across a mass range of 100-1500 m/z using UPLC-QTOF-MS. In the placebo group, no significant differences were observed between the first and last day in both PCA and PLS-DA analyses. However, in the treatment group, clear distinctions were identified in the serum metabolite profiles between the first and last day, as evidenced by PCA. These differences were further confirmed by PLS-DA analysis, and the absence of overfitting was validated through permutation testing. These findings suggest that 830 nm laser acupuncture induces significant changes in the serum metabolome of arthritis patients, highlighting potential biochemical pathways involved in the therapeutic effects of laser acupuncture. This study provides valuable insights into the mechanistic understanding of laser acupuncture in arthritis treatment, laying the groundwork for future research and clinical applications.

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Keywords: Laser acupuncture, Arthritis, Metabolomics, UPLC-QTOF-MS

M02-02

GC-MS-Based Metabolomic Profiling to Assess the Therapeutic Effects of Moxibustion on Obesity

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This study aimed to evaluate the therapeutic effects of moxibustion on obesity in mice through GC-MS-based metabolite profiling. The primary objective was to analyze the metabolic changes induced by moxibustion treatment in obese mice and assess its effectiveness. Obesity was induced in mice over a period of four weeks, with moxibustion administered once a week during this time. Metabolite profiling was performed using GC-MS, with samples collected from feces. Correlation analyses were conducted on the identified metabolites. Multivariate statistical analyses, including PCA and PLS-DA, were used to compare the metabolic profiles between normal and obese groups. These analyses revealed significant differences between the normal and obese groups, with 11 metabolites contributing to these distinctions. Furthermore, metabolic changes due to moxibustion treatment were identified, with a total of 7 metabolites contributing to these alterations. This study demonstrates that moxibustion treatment leads to significant metabolic changes in obese mice, as shown by GC-MS-based metabolite profiling. The findings highlight the potential of moxibustion as a therapeutic intervention for obesity, with specific metabolites serving as indicators of its effectiveness.

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Keywords: Obesitiy, Moxibustion, Metabolomics, GC-MS

M02-03

Applications of aptamers in medical diagnostics: focusing on POCT feasibility

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In recent years, the aging population has contributed to a rise in both chronic and acute diseases, and the global pandemic has increased attention to public health. These factors, along with others, have led to the growing importance of early diagnosis. Early diagnosis plays a crucial role in preventing the progression of diseases and contributes to reducing healthcare costs for both individuals and society through preemptive treatment. Traditionally, antibodies have been widely used as diagnostic tools; however, they have limitations such as nonspecific binding, vulnerability to changes in temperature and pH, high production costs, potential immune reactions, and large molecular size. By comparison, aptamers present a promising alternative due to their high specificity, relatively superior chemical stability, lower production and modification costs through the SELEX technique, lack of immunogenicity, and small molecular size. This review analyzes the precise mechanisms by which aptamer-based biosensors (aptasensors) detect disease-related biomarkers. In particular, studies were selected based on their

potential feasibility in point-of-care testing (POCT). The review focuses on both non-communicable diseases (e.g., cancer, ischemic heart disease) and communicable diseases (e.g., COVID-19, pneumonia), referencing the latest mortality data from the WHO and Statistics Korea. This review will assist in evaluating the potential for implementing aptasensors in clinical settings for medical diagnostics and contribute to promoting academic interest in the development of innovative biosensors for early diagnosis.

Keywords: Aptamer, Aptasensor, Point-of-care testing (POCT), Early diagnosis, Medical diagnostics

M02-04

TRPML1/3 regulates noncanonical autophagy in a PI4P-dependent manner

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Conjugation of ATG8 to single membranes (CASM) is a specific mechanism within noncanonical autophagy, where ATG8 is attached to single membranes in response to membrane damage or immune activation. Although phosphatidylinositol-4-phosphate (PI4P) has been implicated in CASM, the exact molecular mechanism remains unclear. Since the TRPML1/3 heteromer functions downstream of PI4P in canonical autophagy, we hypothesized that the PI4P-TRPML1/3 axis also plays a role in noncanonical autophagy. CASM was successfully induced using a lysosomotropic reagent, independently of canonical autophagy. In this condition, wild-type TRPML1/3 increased, whereas dominant-negative TRPML1/3 decreased CASM. Moreover, PI4P-insensitive TRPML1/3 reduced CASM, while specific activation of TRPML1/3 rescued this inhibition. Importantly, PI4P generated by PI4KIIIβ, rather than PI4KIIα, significantly enhanced CASM in TRPML1/3-expressing cells. Given that TRPML1/3 is a downstream effector of PI4P generated by PI4KIIα in canonical autophagy, these findings suggest that TRPML1/3 can regulate both canonical and noncanonical autophagy through PI4P, produced by distinct PI4K isoforms.

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Keywords: TRPML1/3, Noncanonical autophagy, PI4P, Conjugation of ATG8 to single membranes

M02-05

PFN1 mediates TRPML3-regulated membrane dynamics

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TRPML3 is a calcium-permeable channel present in various subcellular compartments, including the plasma membrane, endocytic, and autophagic pathways. Our previous study demonstrated that TRPML3 provides Ca2+ for autophagosome formation and functions as a downstream effector of PI3P. While TRPML3 is known to participate in membrane remodeling processes such as autophagy, its role in other types of membrane remodeling remains unclear. In this study, we report that TRPML3 also regulates cell migration through interaction with the actin/phosphoinositide-binding protein profilin 1 (PFN1). The TRPML3-PFN1 interaction affected both cell migration and autophagy, highlighting its importance in membrane dynamics. PFN1 localized in early autophagic structures, and its binding to the monophosphate form of phosphoinositides was crucial for the interaction with TRPML3 and autophagy. These findings suggest that the intracellular Ca2+ channel TRPML3 controls various membrane remodeling processes via actin/phosphoinositide-binding protein PFN1, providing new insights into the molecular mechanisms regulating membrane dynamics.

Acknowledgement: RS-2024-00355756

Keywords: TRPML3, Membrane remodeling, Profilin 1, Autophagy, Cell migration

M02-06

Role of MTFMT in macrophage polarization and its association with chronic inflammatory disease

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Mitochondrial methionyl-tRNA formyltransferase (MTFMT) plays an essential role in mitochondrial translation by adding a formyl group to methionyl-tRNA to produce tRNAfMet, initiating mitochondrial protein synthesis. Research has shown that depletion of MTFMT leads to mitochondrial dysfunction by impairing translational efficiency and reducing inflammatory response. This study explores the impact of MTFMT depletion on macrophage polarization by genetically ablating MTFMT in monocytes. Macrophages are key regulators of chronic inflammation, responsible for eliminating pathogens and recruiting T lymphocytes during the early inflammatory phase. Following this, macrophages phagocytose cellular debris and secrete cytokines, such as TGFβ, to promote tissue repair. Proper macrophage polarization into classically activated (M1) and alternatively activated (M2) phenotypes is critical for balancing the inflammatory response and initiating tissue healing. M1 macrophages are pro-inflammatory and microbicidal, while M2 macrophages are anti-inflammatory, promoting the resolution of inflammation and tissue repair. These two phenotypes exhibit distinct metabolic profiles: M1 macrophages primarily depend on glycolysis, whereas M2 macrophages rely more on mitochondrial oxidative metabolism. In our experiments, we generated MTFMT knockout THP-1 cells to assess the enzyme's role in macrophage polarization. We observed a significant reduction in the polarization capacity of MTFMT-deficient cells toward both M1 and M2 phenotypes compared to wild-type cells. Furthermore, these cells showed impaired macrophage functions, including proinflammatory cytokine induction and phagocytosis. Our results suggest that MTFMT is integral to the proper reprogramming required for macrophage polarization and that its depletion affects macrophage behavior, potentially influencing chronic inflammation and tumor-associated macrophage activity.

Keyword : MTFMT, Macrophage, Polarization, Inflammation, Repair

M02-07

Involvement of endocan in vascular dysfunction in angiotensin II-induced hypertensive mice

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Background: Hypertension is a major risk factor for cardiovascular disease and a leading cause of death worldwide. Vascular endothelial dysfunction plays an important role in the initiation and maintenance of hypertension. Endocan (endothelial cell-specific molecule-1), a soluble proteoglycan primarily expressed in endothelial cells, has recently been found to have elvated in serum of hypertensive patients. Clinical studies suggest that this elevation may be associated with endothelial dysfunction in hypertension. However, there is insufficient research data on the involvement of endocan in vascular dysfunction in hypertension. The aim of this study is to investigate the involvement of endocan in vascular endothelial dysfunction associated with hypertension and to explore its underlying mechanisms.
Methods: Eight-week-old male C57BL/6 mice were administered with normal saline or endocan (0.6mg/kg by intraperitoneal injection every two days) or angiotensin II (1000 ng/kg/min) by osmotic minipumps for 4 weeks. Angiotensin II-induced hypertensive mice were treated with either control IgG antibody (9 ug/ml) or neutralizing endocan antibody (9 ug/ml) twice

a week. Systolic blood pressure was determined using the tail-cuff system. After the mice were sacrificed, the serum endocan levels were assessed in all groups using a mouse endocan enzyme-linked immunosorbent assay (ELISA) kit. Vascular function was investigated in mesenteric resistance arteries using a multi-wire myograph system. Human umbilical vein endothelial cells (HUVECs) was treated with angiotensin II at different concentrations (0, 0.01, 0.1, 1, 10 uM) for 24 hours.

Results: Administration of endocan significantly increased systolic blood pressure. Endothelium-dependent relaxation (EDR) was significantly reduced in the mesenteric resistance arteries from endocan-treated mice compared to vehicle-treated mice. However, there was no difference in vascular relaxation induced by sodium nitroprusside administration between the two groups. Furthermore, endothelium-dependent relaxation was significantly reduced in angiotensin II-induced hypertensive mice which was associated with increase in serum endocan level. Treatment of angiotensin II to HUVECs induced concentration-dependent elevation of endocan levels in cell culture medium and cell lysate. Administration of neutralizing endocan antibodies to angiotensin II-induced hypertensive mice decreases blood pressure. Endothelium-dependent relaxation was significantly improved in the mesenteric resistance arteries of neutralizing endocan antibody-treated hypertensive mice compared to the control IgG antibody-treated hypertensive mice.

Conclusion: In this study, we suggest that increase in circulating endocan level causes vascular dysfunction by impairing vascular relaxation, which may lead to elevated blood pressure.

Keywords: Endocan, ESM-1, Hypertension, Vascular endothelial dysfunction

M02-08

Starch-based cryopreservation of polymer-coated dog red blood cells

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Blood transfusion is a highly effective method for saving lives in emergencies in human and companion animals. Similar to humans, animals have different blood types, and receiving incompatible blood can cause transfusion reactions or even death. To prevent hemolytic reactions, polymer-based coatings can be applied to incompatible donor or xenogeneic red blood cells (RBCs), masking antigens on the red blood cell membrane and reducing their antigenicity. This study focuses on identifying the best cryoprotectant for long-term storage of canine stealth blood. Of the cryoprotectants tested, a concentration of 25% (w/v) hydroxyethyl starch (HES; 12.5% final concentration) achieved the highest recovery rates—about 70% for normal canine RBCs and 53% for stealth RBCs. Under high magnification scanning electron microscopy, the stealth RBCs treated with 12.5% HES showed a shape and size similar to normal canine RBCs both before and after freezing. Additionally, the thawed stealth RBCs retained their immune camouflage properties, as confirmed by agglutination tests. These findings suggest that HES is an effective non-permeable cryoprotectant for the long-term preservation of polymer-coated canine RBCs.

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Key words: Cryopreservation, Universal blood, Hydroxyethyl starch

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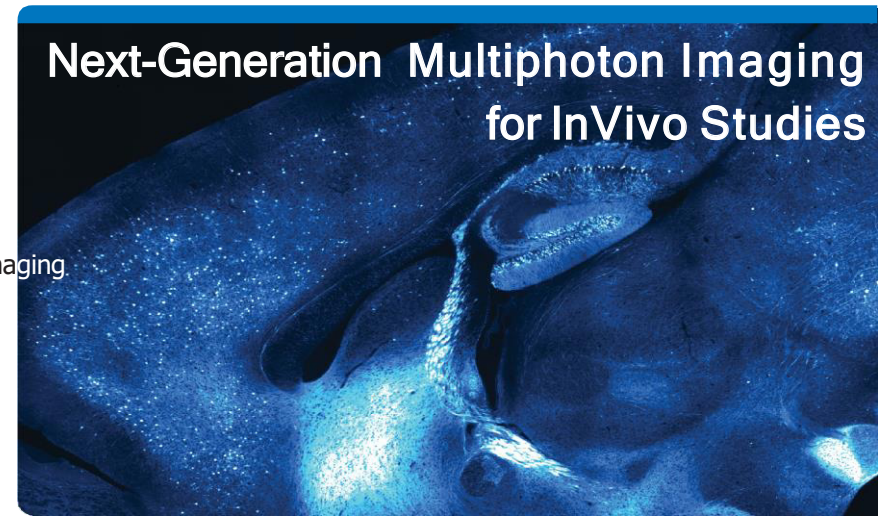

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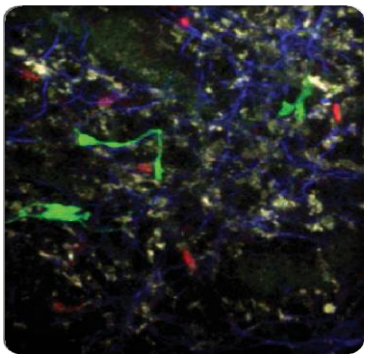

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