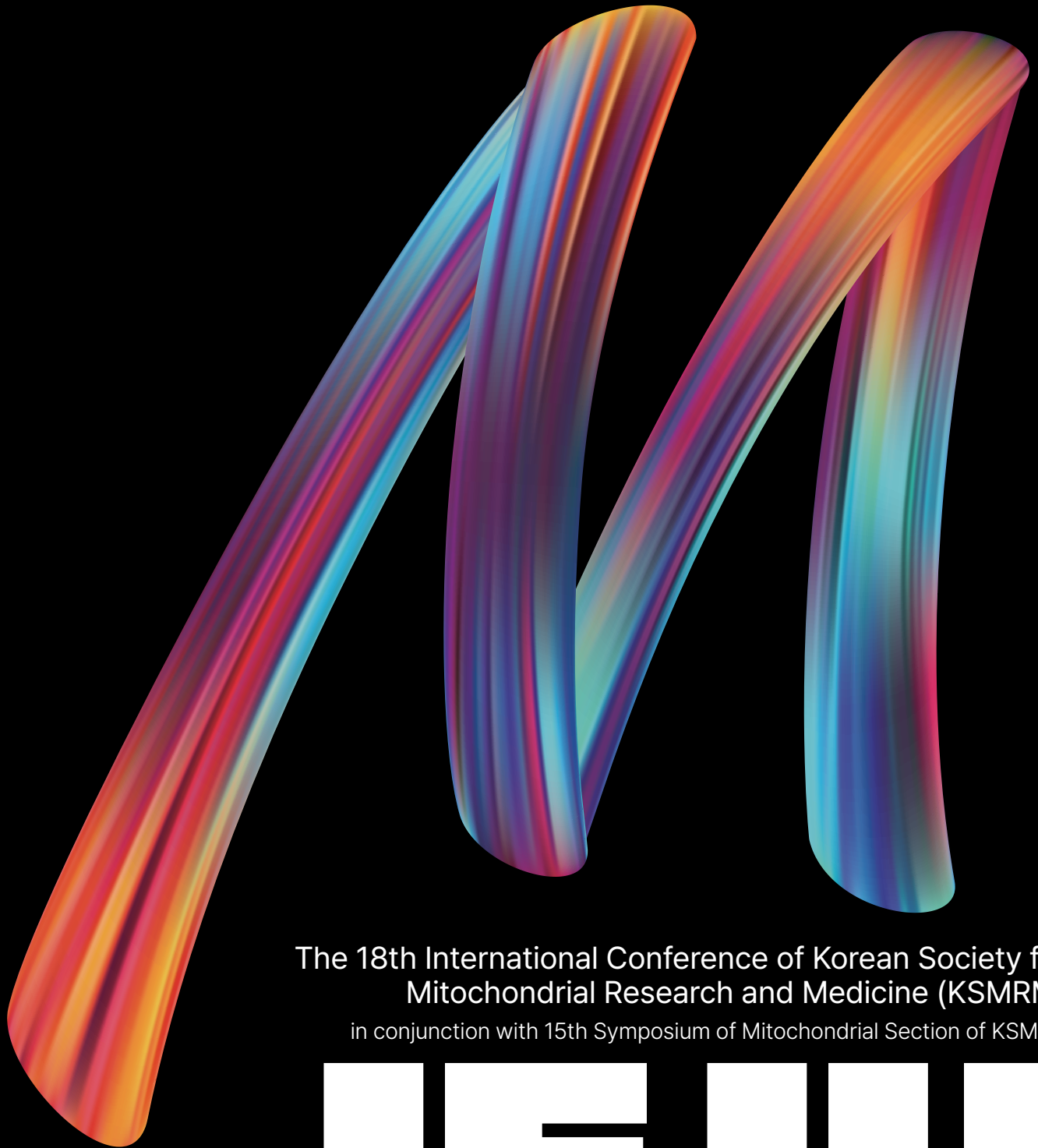


2024. 08. 28 – 08. 30

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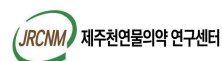
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Reference 1. 일본화학요법학회지, 2001;49(8) 500 2. 堀田 久範 他: 新薬と臨床 2004;53(8): 939 [CFN 00711] 3. 옵니세프 식품의약품안전처 의약품안전나라 <http://nedrug.mfds.go.kr> 4. Kazuhiro T et al., Investigation of the susceptibility trends in Japan to fluoroquinolones and other antimicrobial agents in a nationwide collection of clinical isolates: A longitudinal analysis from 1994 to 2016, Journal of infection and chemotherapy, 2018.

옵니세프 제형요약정보 [원료약품 및 분량] [캡슐] 1캡슐 중 세프디니르 100mg [세팅] 1g 중 cefdinir(세프디니르) 100mg [효능·효과][캡슐] 인프라[캡슐] 인프라[캡슐] 인프라, 만성농피증, 유선염, 항문주위농염, 외상 및 수술창의 표재성 2차 감염, 인후두염, 급성기관지염, 편도염, 폐렴, 신우신염, 방광염, 전구성요도염, 자궁부속기염, 자궁내막염, 비르틀원신염, 백일종, 경관신염, 외이염, 중이염, 부비동염, 치주조직염, 치관주위염, 악성 [세팅] 인프라[캡슐] 인프라, 급성기관지염, 편도염, 폐렴, 신우신염, 방광염, 성홍열, 중이염, 부비동염 [용법·용량][캡슐] 성인: 세프디니르로서 1회 100mg(약가), 1일 3회, 탈락투사환자: 1회 100mg(약가), 1일 1회 경구투여, 증상에 따라 적절히 증감한다. [세팅] 소아: 세프디니르로서 체중 kg당 1일 9-18mg(약가)를 3회 나누어 경구투여 [시용상의 주의사항] 신 중투여 1) 폐니실민계 항생물질에 과민반응의 병력이 있는 환자 2) 분인 또는 부모, 형제가 기관지 천식, 발진, 두드러기 등의 알레르기 증상을 일으키기 쉬운 체질인 환자 3) 중증의 신장에 환자 4) 경구섭취가 부적당한 환자 또는 비강구멍을 두어 환자, 전신상태가 나쁜 환자 5) 고령자 6) 대장염 병력을 가진 환자 금기 1) 이 약에 의한 쇼크의 병력이 있는 환자 2) 이 약 및 이약의 구성성분 또는 제형제 항생물질에 과민반응의 병력이 있는 환자 [제조원] 아우약품(주) 경기도 평택시 신단로 121번길 23 [판매원] 제일약품(주) 경기도 용인시 처인구 백암면 청강리길로 7

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[References] 1. 식품의약품안전처 의약품통합정보시스템 (<https://nedrug.mfds.go.kr>). 2. Data on file, Clinical Phase III trial in Korea (Pivotal Study), LG-DPL019 (2022), LG Chem. 3. Lee BW et al., (2022). Efficacy of Gemigliptin Add-on to Dapagliflozin and Metformin in Type 2 Diabetes Patients: A Randomized, Double-blind, Placebo-controlled Study (SOLUTION I) [Unpublished manuscript]. 4. Data on file, Clinical Phase III trial in Korea (Pivotal Study), LG-GLCL001 (2023), LG Chem.

[illegible]

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신장에 환자에게
용법·용량 조절없이 처방³

† Secondary endpoint 해당.

[Study design] We assessed the 24-week efficacy and safety of teneligliptin, a novel dipeptidyl peptidase-4 inhibitor, in Korean patients with type 2 diabetes mellitus (T2DM) that was inadequately controlled with diet and exercise. The present study was designed as a multicentre, randomized, double-blind, placebo-controlled, parallel-group, phase III study. Patients (n = 142) were randomized 2 : 1 into two different treatment groups as follows: 99 received teneligliptin (20 mg) and 43 received placebo.

[Primary endpoint result] Teneligliptin significantly reduced the HbA1c level from baseline compared with placebo after 24 weeks.

[References] 1. Hong S et al. Diabetes Obes Metab. 2016 May;18(5):528-32. 2. Eto T et al. Diabetes Obes Metab. 2012 Nov;14(11):1040-6. 3. Atef H. et al. Clinical Pharmacology in Drug Development 2013;3(4):246-254.

Selected Prescribing Information

[전문약물]

[제형명 테넬리아®정 20mg 조제] 테넬리글립틴(부활소산염수화물 31mg) **[효능 효과]** 이 약은 제 2형 당뇨병 환자의 혈당조절을 향상시키기 위해 식사요법 및 운동요법의 보조제로 투여한다. - 단독요법 - 병용요법 **[용법·용량]** 단독요법 또는 병용요법 시 이 약의 권장 용량은 1일 1회 20mg이다. 식사와 관계없이 복용할 수 있다. 설포닐우레이아 병용투여 시에는 저혈당발생의 위험을 감소시키기 위해 설포닐우레이아의 용량을 고려할 수 있다. 신장에 환자에게서 용법·용량 조절이 필요하지 않다. 경증에서 중증의 간장애 환자에서 용법·용량 조절이 필요하지 않다. **[사용상의 주의사항]** 1. **다음 환자에는 투여하지 말 것** 1) 이 약의 주성분 또는 다른 성분에 과민증이 있는 환자 2) 당뇨병성 케톤산증, 당뇨병성 혼수 또는 전후수, 제1형 당뇨병 환자(수액, 인슐린으로 신속히 혈당을 조절할 필요가 있는 환자)이므로 이 약의 투여는 적절하지 않다. 3) 중증간염증, 수술전후, 중증의 외상이 있는 환자(인슐린 주사에 의해 혈당관리가 필요하므로 이 약의 투여는 적절하지 않다.) 2. **다음 환자에는 신중히 투여할 것** 1) 중증의 간기능 장애가 있는 환자: 중증 간장애 환자에서의 임상경험이 없다. 2) 심부전: New York Heart Association(NYHA) functional class III-IV 환자에서의 임상경험이 없기 때문에 이 약의 사용이 권장되지 않는다. 3) 설포닐우레이아제 또는 인슐린을 투여중인 환자 4) 다음의 환자 또는 상태 (저혈당을 일으킬 우려가 있다.) (1) 뇌하수체기능부전 또는 부신 기능부전 (2) 영양불량상태, 기아상태, 불규칙한 식사섭취, 식사섭취량의 부족 또는 식약상태 (3) 격렬한 근육운동을 한 환자 (4) 과도한 일로 섭취자 5) 복부 수술 또는 장폐색의 과거 병력이 있는 환자 6) QT 간격 연장을 일으키기 쉬운 환자(심한 사맥 등의 부정맥 또는 과거 병력이 있는 환자, 율혈성 심부전 등의 심장질환이 있는 환자, 저칼륨혈증 환자 등). QT 간격 연장 등의 부작용을 발현할 우려가 있으므로, QT 간격 연장 또는 과거 병력이 있는 환자(신장성 QT 간격 연장증후군 등), 토르세이드 드 포인트의 과거 병력이 있는 환자는 투여를 피하는 것이 바람직하다. 7) 췌장염: 일본 및 국내 임상시험에서는 급성췌장염이 보고되지 않았으나, 유럽 임상시험에서 급성췌장염 1건 및 일본에서 시판 후에 급성 췌장염이 보고된 바 있다. 따라서 지속적인 중증 복통 및 구토와 같은 급성 췌장염의 특징적인 증상이 나타날 경우 의사의 전문적인 진단을 받을 것을 환자에게 알려주어야 한다. 만약 투여 시작 후 췌장염이 의심될 경우 테넬리글립틴과 다른 의심 가능성이 있는 약물의 투여를 중단해야 한다. * 중대한 약물이상반응* 참조 3. **이상반응**(발생률 1% 이상) (1) 외국(일본) 임상시험결과 및 시판 후 안전성 정보: 저혈당 (2) 국내 임상시험결과 1) 단독요법: 비인두염, 발 고통 2) 메트포르민 병용요법: 대장포진, 사지통증, 상복부통증, 위염, 어지러움, 상기도 감염 3) 메트포르민 및 글리메피리드 병용요법: 저혈당, 두통, 설사, 소화불량, 만성위염, 변비, 과민성대장증후군, 바이러스 상기도감염, 피로 4) 국내 임상시험결과와 확인된 저혈당 **[조제]** 100mg, 200mg, 400mg **[한독]** (주)한독 **[최종개정일]** 2021-06-12

*보다 자세한 정보는 제품설명서를 참조하시기 바랍니다.

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Reference) 1,UBIST D1 처방자료, 2012~2022, 2, 센지로이드 식약처 허가사항.

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 **한림제약**

References 1. Clin Endocrinol (Oxf). 2011;74:699-704. (리세넥스플라스팅 임상 3상 논문, ROAD study). 2. Clin Interv Aging. 2013;8:597-603. (리세넥스임정 임상 3상 논문, MROAD study). 3. J Bone Miner Metab. 2012;30:493-503. 4. Osteoporos Int. 2008;19:365-372. 5. J Clin Endocrinol Metab. 2008;93:3785-3793. 6. J Bone Miner Res. 2016;31:336-340. 7. Acta Orthop. 2015;86:100-107. 8. Osteoporos Int. 2008;19:681-686. 9. 해당 성분 주요 제품별 허가사항 및 골다공증치료제 일반원칙 고시 제2018-253호. 10. Arch Osteoporos. 2017;12:43. (National Osteoporosis Guideline Group Clinical guideline for the prevention and treatment of osteoporosis)

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Nitrogen Balance 개선

References. 1. Clinical study report of (IN,OPM,301). 2. Clinical study report of (IN,OPM,301). 3. 오미크론 바이러스, 오미크론 바이러스에 이주 허가4월. 미학을 반영한다.

Product Information 2018년 12월 10일 현재 (주) 3기비 소기업 지원사업은 중소기업의 성장과 발전을 위한 다양한 지원 프로그램을 제공하고 있습니다. 본 사업의 주요 내용은 다음과 같습니다. 1. 지원 대상: 중소기업의 창업자, 임직원, 경영진 등. 2. 지원 내용: 경영 컨설팅, 마케팅 지원, 기술 개발 지원, 인력 개발 지원, 자금 지원 등. 3. 지원 방법: 신청서 제출, 심사, 선정, 지원금 지급 등. 4. 지원 금액: 중소기업의 규모와 사업 내용에 따라 다르며, 최대 100만 원까지 지원합니다. 5. 지원 기간: 2018년 12월 10일부터 2019년 12월 31일까지입니다. 6. 문의처: (주) 3기비 소기업 지원사업 담당자 (전화: 02-1234-5678, 이메일: support@3gib.com) 7. 기타: 본 사업의 세부 내용은 (주) 3기비 소기업 지원사업 홈페이지에서 확인하실 수 있습니다.

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237014 DMAP-BNNDI-03-01

■ 근골격계

구분	제품명	성분·함량	효능·효과	상병코드	용법·용량	약가	보험코드	포장단위
관절염 치료제 (주사제)	하야론주사	Sodium Hyaluronate 25mg	변형성 슬관절증, 건관절주위염	[M17.0~] 양쪽 일차성 무릎관절증 [M19.0~] 기타 관절의 일차성 관절증, 어깨부분	주 1회, 1시린지를 5주간 투여	10,033원	653401281	10Syr./Box
	하야루주사			-		10,000원	비보험	5Syr./Box
	하야론 퍼스트	Sodium Hyaluronate 20mg	슬관절의 골관절염, 건관절주위염 치료	[M17.0~] 양쪽 일차성 무릎관절증 [M19.0~] 기타 관절의 일차성 관절증, 어깨부분	주 1회, 1시린지를 3주간 투여	14,138원	653401271	9Syr./Box
관절염 치료제	디레인캡슐	Diacerein 50mg	골(고관절, 슬관절)관절염(관절증, 퇴행성 관절질환)	[M170] 양쪽 원발성 무릎관절증 [M171] 기타 원발성 무릎관절증	1일 50~100mg 1~2회 분할하여 식후 경구투여	180원	653402870	30C, 500C
근이완제	에페날정	Eperisone HCl 50mg	근골격계질환에 수반하는 동통성 근육연축 : 경관완중후군, 건관절주위염, 요통	[M4800] 척추 협착, 척추의 여러부위 [M545] 아래허리통증 / [M791] 근통 [M6260~M6269] 근육긴장(선택부위) : 한 부위 코드로 3~4회 처방 후 다른 부위로 전환하여 처방 허리 및 부위(무릎, 발목, 발부위)의 처방은 삭감	1회 1정, 1일 3회 식후 경구투여	98원	653402620	30T, 500T
	에페날 서방정	Eperisone HCl 75mg			1회 1정, 1일 2회 식후 경구투여	162원	653404460	30T, 500T

■ 해열·진통·소염제

구분	제품명	성분·함량	효능·효과	상병코드	용법·용량	약가	보험코드	포장단위
소염 진통제	메피솔론	Methylprednisolone 4mg	내분비 장애, 류마티스성 장애, 교원성 질환, 피부 질환, 알레르기성 질환, 안과 질환, 위장관계 질환, 호흡기계 질환, 혈액 질환, 악성 종양성 질환, 부종성 질환, 신경계 질환, 기타	[L239] 상세불명 원인의 알레르기성 접촉피부염 [J804] 상세불명의 알레르기비염 [L500] 알레르기성 두드러기 * 기타 적응증에 따른 상병코드 입력	초기 복용량 1일 4mg ~ 48mg까지 다양하게 조절 (자세한 사항은 첨부 문서 참조)	83원	653404250	30T, 500T
	아세탈정	Aceclofenac 100mg	류마티스 관절염, 강직성 척추염, 골관절염	[M170] 양쪽 원발성 무릎관절증 [M171] 기타 원발성 무릎관절증 [M06900] 경도 상세불명의 류마티스관절염, 여러부위 [M06901] 중증도 상세불명의 류마티스관절염, 여러부위	1회 1정, 1일 2회	188원	653401660	30T, 100T, 500T
	멜시비캡슐	Meloxicam 7.5mg	골관절염의 급성악화, 류마티스 관절염 및 강직성 척추염의 증상치료	[M170] 양쪽 원발성 무릎관절증 [M1990~M1999] 상세불명의 관절증(선택부위) [M4890~M4899] 상세불명의 척추병증(선택부위) [M450~M459] 강직척추염(선택부위)	골관절염의 급성 악화 시 7.5mg 1회 1캡슐, 1일 1회 (최대 1일 15mg까지 증량)	230원	653402650	30C, 100C
		Meloxicam 15mg			류마티스 관절염 및 강직성 척추염 15mg 1회 1캡슐, 1일 1회	350원	653402660	30C, 100C
	엘리펜정	Acetaminophen 325mg, Tramadol HCl 37.5mg	중등도~중증의 급 만성 통증	[M5450, M5455~M5459] 요통(선택부위) [M5440, M5445~M5449] 좌골신경통을 동반한 요통 (선택부위) [M2550~M2559] 관절통(선택부위) [M7960, M7962~M7969] 사지의 통증(선택부위) * 그 외 기타 통증 코드 사용 가능 (NSAIDs 병용처방 : 급성통증은 14일 인정, 만성통증은 90일 인정)	초회 2정 투여 후 6시간 간격 투여 (1일 최대 8정 초과 금지)	162원	653401490	30T, 100T
	엘리펜 세미정	Acetaminophen 162.5mg, Tramadol HCl 18.75mg			초회 4정 투여 후 6시간 간격 투여 (1일 최대 16정 초과 금지)	107원	653401480	30T, 100T
	엘리펜 서방정	Acetaminophen 650mg, Tramadol HCl 75mg			초회 1정 투여 후 12시간 간격 투여 (1일 최대 4정 초과 금지)	355원	653404290	30T, 100T
	엘리펜세미 서방정	Acetaminophen 325mg, Tramadol HCl 37.5mg			초회 2정 투여 후 12시간 간격 투여 (1일 최대 8정 초과 금지)	237원	653404300	30T, 100T
	디뉴펜정	Dexibuprofen 300mg			1일 2~4회 경구투여 (1일 최대 1,200mg 초과 금지)	115원	653404310	30T, 300T
	록페린정	Loxoprofen sodium 68.1mg (Loxoprofen 60mg)	1. 류마티스관절염, 골관절염, 요통, 건관절주위염, 경관완중후군의 소염 진통 2. 수술후, 외상후 및 발치후의 소염 진통 3. 급성 상기도염의 해열 진통	[M5450, M5455~M5459] 요통(선택부위) [M06900] 경도 상세불명의 류마티스관절염, 여러부위	효능효과 1, 2의 경우 1회 1정, 1일 3회 투여 효능효과 3의 경우 1회 1정, 1일 2회 투여 (1일 최대 180mg까지 투여가능)	125원	653402930	30T, 300T
	셀브렉캡슐 100mg	Celecoxib 100mg	1. 골관절염(퇴행관절염)의 증상이나 징후 완화 2. 류마티스관절염의 증상이나 징후 완화 3. 강직척추염의 증상 및 징후 완화 4. 성인의 급성 통증 완화(수술 후, 발치 후 진통) 5. 원발월경통	[M170] 양쪽 원발성 무릎관절증 [M2550~M2559] 관절통(선택부위) [M450~M459] 강직척추염(선택부위) [M4780~M4789] 기타 척추증(선택부위)	(최소 권장량은 환자에 따라 조절, 식사와 관계없이 투여) 골관절염 (퇴행관절염) / 강직척추염: 200mg 1일 1회, 또는 1회 100mg씩 1일 2회 류마티스관절염: 200mg 1일 1회 또는 100mg 1일 2회 급성 통증 및 원발월경통: 초기 200mg 2캡슐 필요시 200mg 1캡슐 추가 투여, 둘째 날부터는 1회 200mg 1캡슐, 1일 2회	295원	653403880	30T, 100T
	셀브렉캡슐 200mg	Celecoxib 200mg			급성 통증 및 원발월경통: 초기 200mg 2캡슐 필요시 200mg 1캡슐 추가 투여, 둘째 날부터는 1회 200mg 1캡슐, 1일 2회	476원	653402450	30T, 100T
	셀레브론정	Celecoxib 100mg, 당귀, 목과 등	골관절염 퇴행관절염의 증상이나 징후의 완화	[M170] 양쪽 원발성 무릎관절증 [M171] 기타 원발성 무릎관절증 [M4780~M4789] 기타 척추증(선택부위)	성인 1회 2회, 1회 1정	567원	653405420	30T, 300T
	케토라신정	Ketorolac Tromethamine 10mg	1. 중등도 및 중증의 통증에 대한 단기요법 2. 다음의 수술 후 통증: 일반외과, 정형외과, 부인과, 치과수술 등	[N940] 배란통 [M5450, M5455~M5459] 요통(선택부위) [R073] 기타통통	성인 1회 10mg을 4~6시간마다 경구투여 (1일 40mg을 초과하지 않도록 하며, 약물 투여기간 은 7일을 초과하지 않는다) 주사제를 투여받은 환자가 정제 투여로 전환한 경우, 1일 혼용량은 90mg (고령자, 신장질환자, 및 체중 50kg 이하 환자는 60mg)을 초과해서는안 되며 정제 용량은 40mg을 초과하지 않는다.	162원	653400910	30T, 300T
	레이론정	당귀, 목과, 방풍, 속단, 오기피, 우슬, 위령선, 육계, 진교, 천궁, 천마, 홍화(25%에 탄올연조엑스	골관절증의 증상 완화	[M59] 상세불명의 다발관절증 [M60] 일차성 고관절증, 양쪽 [M300~M309] 기타 관절의 일차성 관절증(선택부위) [M390~M399] 기타 관절의 상세불명 관절증(선택부위) [M320~M329] 기타 이차성 관절증(선택부위) [M360~M369] 기타 명시된 관절증(선택부위) [M380~M389] 상세불명의 관절증(선택부위)	성인 1일 2회, 1회 1정 복용	187원	653404030	30T, 300T
소염 효소제	로메라제 장용정	Bromelain 100mg	부종(부기)을 동반한 염증 증상의 완화, 외상(상처) 또는 수술 후의 부종(부기)	[M860] 윤활막염 및 힘줄염 [S93] 발목 및 발부위의 관절 및 인대의 탈구, 염좌 및 긴장 [S93] 손목 및 손부위의 관절 및 인대의 탈구, 염좌 및 긴장 [L20] 급성 기관지염 [J03] 급성 편도염 [R600] 국소부종 [R609] 상세불명의 부종	성인 및 12세 이상의 소아 : 브로멜라인 으로서 1회 100mg, 1일 2회 복용한다. 식사 30분 전에 물과 함께 복용한다.	67원	653405150	100T, 500T



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MEDICOAPEX

메디코아펙스

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 토탈 서비스를 지향하는 업체로서 앞으로도 고객을 위한
 종합유통 서비스 업체로서 거듭나기 위해 최선을 다하겠습니다.

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밀리포어



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싸이티바

의약전문가용



**딜라트렌SR은 DILAF STUDY를 통해
 심방세동 환자에서의 심박수 조절 적응증을
 승인 받았습니다.**



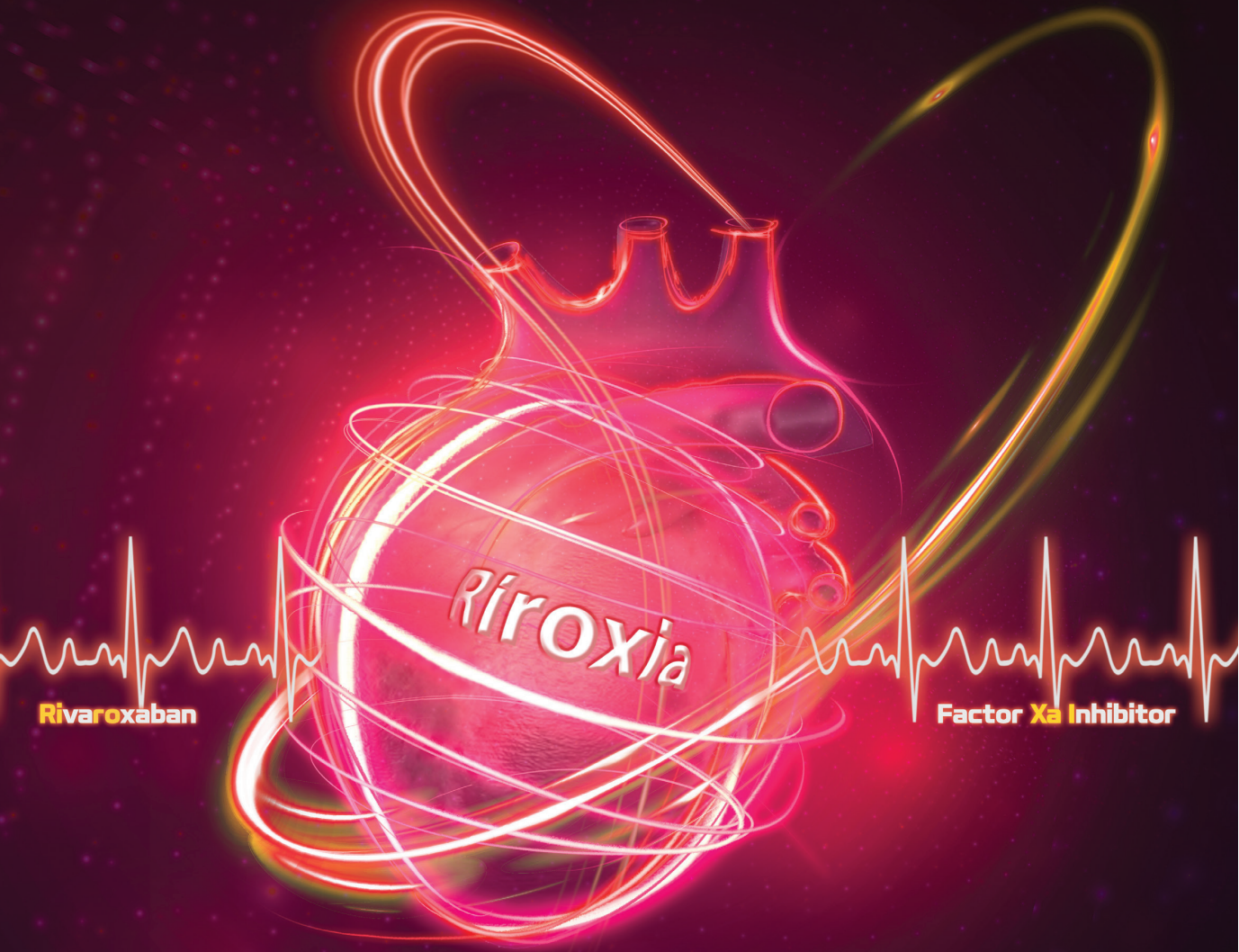
SR, sustained-release; EHRA, European Heart Rhythm Association; bpm, beats per minute
 References. 1. Choi JI, et al. Heart Rhythm. 2024 Apr. 2. Data on File.

종근당 1st QD NOAC

리록시아[®]

Rivaroxaban Tab. (micronized)

· 평생 **항응고제**를 복용하는 환자를 위한 Once daily NOAC ·



제품 요약정보

제품명: 리록시아[®]정(RiROXia[®] Tab.)

유효성분: 리바록사반(Rivaroxaban)

보험정보: 10 mg [643308410], 15 mg [643308460], 20 mg [643308420]

주성분 코드: 10 mg [511401ATB], 15 mg [511402ATB], 20 mg [511403ATB]

포장규격: 30정/병

식약처 분류: 혈액응고저지제 [333]



종근당

RRXA_CKD_202103_268(Expire 202601)



M1416R HIGH-SPEED BENCHTOP REFRIGERATED CENTRIFUGE

Swing-out Rotor

- Maximum Capacity: M-S4-400-P, 4*400mL
- Maximum Speed: M-S4-200-P, 5500rpm

Fixed-angle Rotor

- Maximum Capacity: M-F6-100CF, 6*100mL
- Maximum Speed: M-F24-2QG, 18,000rpm

Details

- Temperature range: -10°C to +40°C
- Dimension: 627*409*688mm



M1324R HIGH-SPEED REFRIGERATED MICROCENTRIFUGE

- Maximum Capacity: 5mL×10
- Maximum Speed: 15800rpm
- Display: Touch screen
- Temperature Control: -10°C to 40°C
- Dimension: 304mm*304mm*517mm



M1324 HIGH-SPEED MICROCENTRIFUGE (VENTILATED MODEL)

- Maximum Capacity: 5mL×10
- Maximum Speed: 15800rpm
- Display: Touch screen
- Temperature Control: -10°C to 40°C
- Dimension: 262mm*282mm*385mm

유한회사 바이오드림

BIO DREAM



BIO DREAM

정밀 기기 및 과학 기기 도매업

대표 이미지

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The 18th International Conference of Korean Society for
Mitochondrial Research and Medicine (KSMRM)
in conjunction with 15th Symposium of Mitochondrial Section of KSMCB

JEJU

Just Energize the Journey
to Understand Mitochondria



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GREETING

Dear colleagues and friends,

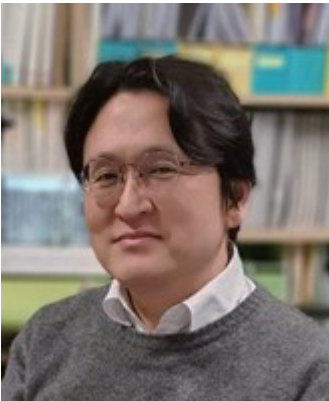
On behalf of the organizing committee,
I would like to express my sincere gratitude for your active participation and contribution to the Korean Society for Mitochondrial Research and Medicine (KSMRM).

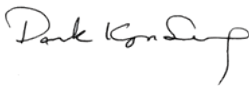
It is a great pleasure to announce that the 18th International Conference of the KSMRM will be held on August 28st ~ 30th, 2024, at the Ara Convention Hall, Jeju National University, Jeju, Korea.

This KSMRM conference invites two plenary lecturers and 19 session speakers to introduce cutting-edge knowledge of mitochondrial research and to provide a platform for young scientists to interact with other researchers. Your participation through exchanging ideas and in-depth discussions will be a great contribution to the success of the KSMRM 2024.

The organizing committee will try to make it a memorable, scientific, and social experience. I look forward to seeing you at the KSMRM 2024 in Jeju island.

Yours sincerely,





Park Kyu Sang
- President, Korean Society for Mitochondrial Research and Medicine
- Director, Mitohormesis Research Center, Ministry of Science, ICT & Future Planning, Korea

General Information

Overview

Title	The 18th International Conference of Korean Society for Mitochondrial Research and Medicine (KSMRM) in conjunction with 15th Symposium of Mitochondrial Section of KSMCB
Date	2024. 08. 28. (Wed.) - 2024. 08. 30. (Fri.)
Organized by	Korean Society for Mitochondrial Research and Medicine (KSMRM)

Venue



Floor Plan




Day 1 (제주대학교 의과대학 2층)

Day 2-3 (제주대학교 아라컨벤션홀 1층)

Programs

Oral Presentation	Oral Presentation
Session 1	Mitochondria in Translational Medicine
Session 2	Mitochondria in Metabolism
Session 3	Plenary Lecture
Session 4	Mitochondria in Translational Research (B-IRC 조인트 세션)
Session 5	Mitochondrial Genetic Disease and Therapeutics
Session 6	Plenary Lecture 2
Session 7	Mitochondria in Systems Biology

Secretariat

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Program

Wednesday, August 28 , 2024	
제주대학교 의과대학 1호관 2F 강당 / Auditorium 2F, Building #1, Medical School, Jeju University	
Time	Subject
13:00 ~ 14:00	Registration
Oral Presentation	Oral Presentation Chair: Byoung Heon Kang (UNIST), Hyoung Kyu Kim (Inje Univ.)
14:00 ~ 14:15	Transcriptome analysis in colon carcinogenesis by using Tlr13-deficient mouse model Rafique Asma (Jeju Nat'l Univ.)
14:15 ~ 14:30	Preventive ability of fucoxanthin against PM2.5-induced inflammation and aging in keratinocyte cells Pincha Devage Sameera Madushan Fernando (Jeju Nat'l Univ.)
14:30 ~ 14:45	Transplanting External Mitochondria Enhances Blood-Brain Barrier Integrity Soyoung Kim (UNIST)
14:45 ~ 15:00	Mitochondrial chaperone, TRAP1 regulates mitochondrial functions for thermogenesis in adipocytes. Sun A Yeom (UNIST)
15:00 ~ 15:15	Mitochondria-derived peptides humanin and formylated humanin promote STAT3-dependent skin repair Kyu-Hee Hwang (Yonsei Univ.)
15:15 ~ 15:30	PPARβ-induced changes in energy metabolism influence the proteome related to protein synthesis and quality control. Sol-YI Park (Yonsei Univ.)
15:30 ~ 15:45	Development of MitoRAISE, a real-time assessment of mitochondrial ATP synthesis response against inhibiting and stimulating substrates Eun Sol Chang (SAIHST)
15:45 ~ 15:50	Break
15:50 ~ 16:00	Opening & Welcome Remarks
Session 1	Mitochondria in Translational Medicine (Joint Session of JRCNM) Chair: Sang-Pil Yoon(Jeju Nat'l Univ.) Panel: Eui Tae Kim(Jeju Nat'l Univ.), Young-Sang Koh(Jeju Nat'l Univ.)
16:00 ~ 16:30	NLRP3 exacerbates EAE severity through ROS-dependent NET formation in the mouse brain Young-Min Hyun (Yonsei Univ.)
16:30 ~ 17:00	The involvement of CLU (clusterin) and PPARGC1A/PGC1α in mitophagy Han Jung Chae (Jeonbuk Univ.)
17:00 ~ 17:30	Establishment of a humanized mouse model reflecting human immune responses from atopic dermatitis patients Chang Ook Park (Yonsei Univ.)
17:30 ~ 18:00	Designing text mining services to support the curation efforts of the Swiss Institute of Bioinformatics: from CelloSaurus triage to Variomes variant sequence search Patrick Ruch (Swiss Institute of Bioinformatics)

Thursday, August 29 , 2024	
제주대학교 아라컨벤션홀 / Ara Convention Hall, Jeju National University	
Time	Subject
Session 2	Mitochondria in Metabolism (Joint Session of KDA) Chair: Hyon-Seung Yi(Chungnam Nat'l Univ.), Dongryeol Ryu(GIST) Panel: Jin Ho Koh (Yonsei Univ.), Dong Wook Choi (Korea Univ.)
09:00 ~ 09:25	Implication of T cell senescence in the progression of diabetes and metabolic liver disease Hyon-Seung Yi(Chungnam Nat'l Univ.)
09:25 ~ 09:50	The preservation of mitochondrial cristae protects from cardiomyopathy Jae-Han Jeon(Kyungpook Nat'l Univ.)
09:50 ~ 10:15	Locking and unlocking mechanisms of Atg32-mediated mitophagy Koji Okamoto (Osaka University)
10:15 ~ 10:40	Spatiotemporal dynamics of intracellular metabolites using genetically encoded biosensors. Hiromi Imamura (Kyoto University)
10:40 ~ 11:00	Coffee Break
Session 3	Plenary Lecture Chair: Minho Shong (KAIST), Jae Myoung Suh (KAIST)
11:00 ~ 12:00	Metabolism, Cellular Decisions and the Language That Unites Them Jared Rutter (University of Utah)
12:00 ~ 12:30	Luncheon Seminar
12:30 ~ 13:30	Poster Viewing
Session 4	Mitochondria in Translational Research(Joint Session of B-IRC) Chari: Sang Ki Park(POSTECH), Yoon Tae Lee(POSTECH) Panel: Min Sik Lee (POSTECH), Bo Am Seo (Yonsei Univ.)
13:30 ~ 14:00	Mitochondrial disorder as a risk factor for neurodegenerative diseases Hojae Han(Seoul Nat'l Univ.)
14:00 ~ 14:30	Remodeling of endoplasmic reticulum via lipid metabolism Wonyul Jang(Seoul Nat'l Univ.)
14:30 ~ 15:00	In vivo mapping of subcellular proteomes in aging and disease Jae Myoung Suh (KAIST)
15:00 ~ 15:30	Exploring regulatory pathways for calcium communication between ER and mitochondria Sang Ki Park(POSTECH)
15:30 ~ 15:50	Coffee Break
Session 5	Mitochondrial Genetic Disease and Therapeutics Chair: Hong Kyu Lee (Seoul Nat'l Univ.), Young-Mock Lee (Yonsei Univ.) Panel: Hyejin Park(KAIST), Su Myung Jung (Sungkyunkwan Univ.)
15:50 ~ 16:20	Induced Pluripotent Stem Cells and their Derived Neurons as Cell Models for Studies of the MERRF Syndrome Yau-Huei Wei (Changhua Christian Hospital, Taiwan)
16:20 ~ 16:50	Mitochondrial Transfer as a Novel Therapeutic Approach in Mitochondrial Disease Treatment Tsu-Kung Lin (Kaohsiung Chang Gung Memorial Hospital, Taiwan)
16:50 ~ 17:20	Mitochondrial DNA mosaicism in normal human somatic cells Young Seok Ju(KAIST)
17:20 ~ 17:50	Mitochondrial genome editing Hyunji Lee(Korea Univ.)
17:50 ~ 18:00	Break
18:00 ~ 19:00	Poster Session
19:00 ~	Banquet

Organization

President	Kyu-Sang Park (Yonsei University)
Vice President	Young-Mock Lee (Yonsei University)
KSMCB Mitochondria Div. Cochair	Jin Han (Inje University) Byoung Heon Kang (UNIST)
Secretary General	Hyon-Seung Yi (Chungnam Nat'l University)
Scientific Committee Chair	Hyun-Woo Rhee (Seoul Nat'l University) Jun Namkung (Yonsei University Wonju College of Medicine)
Public Relation, Cochair	Hyoung Kyu Kim (Inje University)
Treasurer, Chair	Koon Soon Kim (Daejeon Endo Internal Medicine) SungWoo Cho (Inje University College of Medicine) Hyeongseok Kim (Chungnam Nat'l University)
Clinical Research Committee Chair	Ji-Hoon Na (Yonsei University)
Auditors	Minho Shong (Chungnam Nat'l University) In-Kyu Lee (Kyungpook Nat'l University)
Director	Hong Kyu Lee (Advisor at PAEAN Biotechnology Inc.) Myunghee Jung (Seoul Nat'l University) In-Kyu Lee (Kyungpook Nat'l University) Eun Bo Shim (Kangwon University) Ki-Up Lee (University of Ulsan) Hun Taeg Chung (University of Ulsan) Minho Shong (Chungnam Nat'l University) Hongdeok Yun (Seoul Nat'l University) Kyong Soo Park (Seoul Nat'l University) Young Jun Seo (Seoul Nat'l University) Gyesoon Yoon (Ajou University) Young Kyu Ko (Korea Universtiy) Youngmi Kim Pak (Kyung Hee University) Young Hyun Yoo (Dong-A University) Soon Ha Kim (LG chem.) Myung-Shik Lee (Sungkyunkwan University) Jin Han (Inje University) Jung Jun Min (Jeonnam University) Sung Soo Kim (Kyung Hee University) ongkyeong Chung (Seoul Nat'l University) YongKyung Choe (KRIBB) Young-Myeong Kim (Kangwon Nat'l University)

Friday, August 30 , 2024	
제주대학교 아라컨벤션홀 / Ara Convention Hall, Jeju National University	
Time	Subject
Session 6	Plenary Lecture 2 Chair: Joo Yeon Yoo(POSTECH), Kyu-Sang Park (Yonsei Univ.)
09:00 ~ 10:00	Exercise-induced cardiac adaptation Jin Han(Inje Univ.)
Session 7	Mitochondria in Systems Biology Chair: Young Seok Ju(KAIST), Sun Jae Lee(GIST) Panel: Kwang-eun Kim(Yonsei Univ.), Yunju Jo(GIST)
10:00 ~ 10:30	Cross-tissue single-cell and spatial cell atlas to understand human diseases Jong-Eun Park(KAIST)
10:30 ~ 11:00	Quasi-spatial single-cell transcriptome based on physical properties defines early aging associated niche in liver tissue Chuna Kim(KRIBB)
11:00 ~ 11:30	Single-cell long-read sequencing technologies and applications Jihwan Park(GIST)
11:30 ~ 12:10	General Assembly & Closing Ceremony

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to **U**nderstand Mitochondria



Session 1

Mitochondria in Translational Medicine (Joint Session of JRCNM)

Chair: Sang-Pil Yoon(Jeju Nat'l Univ.)

Panel: Eui Tae Kim(Jeju Nat'l Univ.)

Young-Sang Koh(Jeju Nat'l Univ.)

Young-Min Hyun, Ph.D.

Position: Professor
Department: Anatomy
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Education

1991.03-1997.02	B.A.	Yonsei University, Seoul, Korea
1997.03-1999.02	M.S.	Yonsei University, Seoul, Korea
2002.02-2006.05	Ph.D.	Australian National University, Canberra, Australia

Professional Experience

2005.11-2006.06	Postdoc	Brown University School of Medicine
2006.07-2011.06	Postdoc	University of Rochester Medical Center
2011.07-2016.01	Res. Assist. Professor	University of Rochester Medical Center
2016.03-	Professor	Yonsei University College of Medicine

Publications

1. Choi C#, Jeong YL#, Park K-M#, Kim M, KIM S, Jo H, Lee S, Kim H, Choi G, Choi YH, Seong JK, Namgoong S, Chung Y, Jung Y-S*, Grannenman JG*, Hyun Y-M*, Kim JK*, Lee Y-H* (2024) TM4SF19-mediated control of lysosomal activity in macrophages contributes to obesity-induced inflammation and metabolic dysfunction. Nat. Commun. Mar;15(1):2779 doi: 10.1038/s41467-024-47108-8 * Co-corresponding authors.

2. Byun DJ, Lee L, Ko K, Hyun Y-M (2024) NLRP3 exacerbates EAE severity through ROS-dependent NET formation in the mouse brain. Cell Commun. Signal. Feb;22(1):96 doi: 10.1186/s12964-023- 01447-z

3. Bae SH, Yoo JE, Choe YH, Kwak SH, Choi JY, Jung J, Hyun Y-M (2021) Neutrophils infiltrate into the spiral ligament but not the stria vascularis in the cochlea during lipopolysaccharide-induced inflammation. Theranostics Jan.;11(6):2522-2533.

4. Hyun Y-M, Seo S-U, Choi WS, Kwon H-J, Kim D-Y, Jeong S, Kang G-Y, Yi E, Kim M, Ryu HJ, Looney MR, Choi EY, Kim HS (2020) Endogenous DEL-1 restrains melanoma lung metastasis by limiting myeloid cell-associated lung inflammation. Sci. Adv. Nov.;6(45):eabe4882

5. Hyun Y-M, Choe YH, Park SA, Kim M (2019) LFA-1 (CD11a/CD18) and Mac-1 (CD11b/CD18) distinctly regulate neutrophil extravasation through hotspots I and II. Exp. Mol. Med. Apr.;51(4):39. Corresponding author.

6. Jung JS, Yoo EJ, Choe YH, Park SC, Lee HJ, Lee HJ, Noh BH, Kim SH, Kang GY, Lee KM, Yoon SS, Jang DS, Yoon JH, Hyun Y-M*, Cho JY* (2019) Cleaved Cochlin Sequesters Pseudomonas Aeruginosa and Activates Innate Immunity in the Inner Ear. Cell Host Microbe Apr.;25(4):1-13 * Co-corresponding authors.

NLRP3 exacerbates EAE severity through ROS-dependent NET formation in the mouse brain

Da Jeong Byun, Jaeho Lee, Kyungryung Ko, Young-Min Hyun

Department of Anatomy and Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Republic of Korea

Neutrophil extracellular trap (NET) has been implicated in the pathology of multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE). However, the specific contributions of NLRP3, a NET-associated molecule, to EAE pathogenesis and its regulatory role in NET formation remain unknown. To investigate the detrimental effect of NETs supported by NLRP3 in MS pathogenesis, we induced EAE in WT and NLRP3 KO mice and monitored the disease severity. At the peak of the disease, NET formation was assessed by flow cytometry, immunoblotting, and immunofluorescence staining. To further identify the propensity of infiltrated neutrophils, NET-related chemokine receptors, degranulation, ROS production, and PAD4 expression levels were evaluated by flow cytometry. In some experiments, mice were injected with DNase-1 to eliminate the formed NETs. Our data revealed that neutrophils significantly infiltrate the brain and spinal cord and form NETs during EAE pathogenesis. NLRP3 significantly elevates NET formation, primarily in the brain. NLRP3 also modulated the phenotypes of brain-infiltrated and circulating neutrophils, augmenting CXCR2 and CXCR4 expression, thereby potentially enhancing NET formation. NLRP3 facilitates NET formation in a ROS-dependent and PAD4-independent manner in brain-infiltrated neutrophils. Finally, NLRP3-supported NET formation exacerbates disease severity, triggering Th1 and Th17 cells recruitment. Collectively, our findings suggest that NLRP3-supported NETs may be an etiological factor in EAE pathogenesis, primarily in the brain. This study provides evidence that targeting NLRP3 could be a potential therapeutic strategy for MS, specifically by attenuating NET formation.



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Education

1985~1989	Bachelor's Degree	Duksung Women's University
1997~2001	Ph.D	Chonbuk National University
2004~2008	PharmD	University of Florida

Professional Experience

2020~present	Professor	Chonbuk National University
2002~2020	Professor	Chonbuk National University
2013~present	Joint Faculty Member	Chonbuk National University
2020~2022	Founding Dean	Chonbuk National University
2017~present	Director	Chonbuk National University Hospital

AcademicExperience

2002~present	Regular Member, Council Member, Treasurer, Academic Director, General Affairs Director, and Vice President, The Korean Society of Pharmacology
2002~present	Regular Member, Membership Committee Chair, Academic Committee Chair, Korean Pharmaceutical Association
2010~present	Regular Member, Academic Committee Chair, External Cooperation Committee Chair, Korean Society of Cancer Prevention
2010~present	Editor-in-Chief, Membership Committee Chair, External Cooperation Committee Chair, Korean Society of Clinical Pharmacy

Publications

1. Triple threat: neutrophil ER stress, NETosis, airway inflammation escalation. Trends Cell Biol. 2024 Jun 3:S0962-8924(24)00074-6.
2. CLU (clusterin) and PPARGC1A/PGC1α coordinately control mitophagy and mitochondrial biogenesis for oral cancer cell survival. Autophagy. 2024 Jun;20(6):1359-1382
3. Aging phenotype in AD brain organoids: Track to success and challenges. Ageing Res Rev. 2024 Apr;96:102256.
4. Chalcone suppresses tumor growth through NOX4-IRE1α sulfonation-RIDD-miR-23b axis. Redox Biol. 2021 Apr;40:101853
5. TMBIM6 (transmembrane BAX inhibitor motif containing 6) enhances autophagy through regulation of lysosomal calcium. Autophagy. 2021 Mar;17(3):761-778

The involvement of CLU (clusterin) and PPARGC1A/PGC1α in mitophagy

Han-Jung Chae

School of Pharmacy, Jeonbuk National University, Korea

Mitophagy, the selective elimination of defective mitochondria, is crucial for maintaining mitochondrial homeostasis and sustaining cancer growth during chemotherapeutic stress. This study demonstrates that CLU (clusterin) localizes to mitochondria to induce mitophagy, thereby controlling mitochondrial damage in oral cancer cells. Overexpression and knockdown experiments confirm CLU's role as an adaptor protein that interacts with BAX and LC3, recruiting autophagic machinery around damaged mitochondria in response to cisplatin treatment. CLU also activates class III phosphatidylinositol 3-kinase (PtdIns3K) around damaged mitochondria. Inhibition of mitophagic flux leads to the accumulation of mitophagosomes, resulting in reactive oxygen species (ROS)-dependent apoptosis during cisplatin treatment. Additionally, PPARGC1A/PGC1α (PPARG coactivator 1 alpha) is shown to activate mitochondrial biogenesis during CLU-induced mitophagy, maintaining the mitochondrial pool. Inhibiting PPARGC1A using small interfering RNA (siPPARGC1A) and the pharmacological inhibitor SR-18292 counteracts CLU-dependent cytoprotection, leading to mitophagy-associated cell death. Co-treatment with SR-18292 and cisplatin synergistically suppresses tumor growth in oral cancer xenograft models. In conclusion, CLU and PPARGC1A are essential for sustaining cancer cell growth by activating mitophagy and mitochondrial biogenesis, respectively



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Education

1996.03-2002.02	MD	Yonsei University College of Medicine
2004.09-2006.08	MS	Yonsei University College of Medicine
2010.03-2015.08	PhD	Yonsei University College of Medicine

Professional Experience

2016.03-2019.02	Assistant Professor	Yonsei University College of Medicine
2019.03-2024.02	Associate Professor	Yonsei University College of Medicine
2024.03-present	Professor	Yonsei University College of Medicine

Academic Society

2024	Councilor of International Eczema Council
2019	Member of the American Association of Immunologists
2018	Board Member of the Korean Society for Investigative Dermatology
2017	Associate of International Eczema Council
2017	Member of the Korean Association of Immunologists
2017	Board Member of the Korean Society for Immunodermatology
2016	Board Member of the Korean Society of Atopic Dermatitis
2014	Member of the Society for Investigative Dermatology

Publications

1. Park CO*#, Kim SM#, Lee KH, Bieber T. Biomarkers for phenotype-endotype relationship in atopic dermatitis: a critical review. EBioMedicine. 2024 Apr 12;103:105121. *Corresponding author
2. Qiao Z, Zhang K, Liu H, Roh Y, Kim MG, Lee HJ, Koo B, Lee EY, Lee M, Park CO*, Shin Y*. CSMP: A Self-Assembled Plant Polysaccharide-Based Hydrofilm for Enhanced Wound Healing. Adv Healthc Mater. 2024 Mar;13(6):e2303244. *Co-corresponding author
3. Jeong H, Lee N, Uhm C, Cho K, Oh H, Oh Y, Zhang K, Kim HL, Goldenring JR, Lim KM*, Park CO*, Nam KT*. RAB25 coordinates filaggrin-containing keratohyalin granule maturation and affects atopic dermatitis severity. Allergy. 2023 Apr;78(4):1007-1019. *Co-corresponding author
4. Chu H, Kim SM, Zhang K, Wu Z, Lee H, Kim JH, Kim HL, Kim YR, Kim SH, Kim WJ, Lee YW, Lee KH, Liu KH*, Park CO*. Head and neck dermatitis is exacerbated by Malassezia furfur colonization, skin barrier disruption, and immune dysregulation. Front Immunol. 2023 Feb 22;14:1114321. *Co-corresponding author

Establishment of a humanized mouse model reflecting human immune responses from atopic dermatitis patients

Chang Ook Park, MD,PhD

Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University
College of Medicine, Seoul, Korea

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by complex pathogenesis. Despite the development of Th2-targeted therapies, the management of AD continues to rely on a 'one-size-fits-all' strategy. Thus, while diverse AD mouse models are used to investigate effective treatments targeting the causes of AD, these models face limitations due to the translational gap between mice and humans. To address this issue, we have developed a humanized mouse model (AVATAR mouse) that accurately replicates human AD patients. In AVATAR mouse, CD3+ T cells from AD patients sensitized with house dust mites (HDM) were administered intravenously as pathogenic cells, while CD3-depleted peripheral blood mononuclear cells (PBMCs) from AD patients were injected intradermally as antigen-presenting cells (APCs) into immunodeficient NSG mice. This approach allowed the AVATAR mouse to develop AD-like inflammatory responses upon exposure to HDM. Single-cell RNA sequencing analysis of the AVATAR mouse has confirmed an increase in IRF4+ type 2 conventional dendritic cells (cDC2s) and Th2-related genes, corresponding to those observed in human AD skin. Furthermore, TCRβ deep sequencing revealed that HDM-sensitized AVATAR mice share T cell clones with HDM-sensitized patients who exhibit T cell expansion during atopy patch tests. This finding indicates that the AVATAR mouse model accurately reflects the HDM-specific T cell responses of AD patients. Our results demonstrate a correlation between clinical and laboratory parameters indicating AD severity in individual AD patients and their corresponding matched AVATAR mice. This suggests that the model accurately reflects the individual immune responses of human AD patients, providing a valuable platform for the development of precision medicine for atopic dermatitis.



Patrick Ruch, Ph.D.

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Education

2002	Doctorat ès Sciences	Computer sciences, University of Geneva
1997	Master of Sciences	INSTN/CNAM/Marne-la-Vallée, France.
1996	Master of Philosophy (Logics)	Panthéon-Sorbonne University, Paris.

Professional Experience

2019-present	Head of Research	HES-SO HEG Genève
2014-2019	Chairman	Information sciences department, HES-SO Genève
2012-present	Group leaders	SIB Swiss Institute of Bioinformatic
2009-present	Professor (full since 2017),	HES-SO Genève, Department of Information Science
2008-2009	Staff scientist	IBM Zürich Research Labs, Rueschlikon
2006-2008	Research	Associate, radiology departments, University Hospitals of Geneva
2005-2006:	Research scientist,	National Institute of Health, NCBI-NLM, Bethesda, MD.

Publications

Mottin L, Goldman JP, Jäggi C, Achermann R, Gobeill J, Knafo J, Ehram J, Wicky A, Gérard CL, Schwenk T, Charrier M, Tsantoulis P, Lovis C, Leichtle A, Kiessling MK, Michielin O, Pradervand S, Foufi V, Ruch P. Multilingual RECIST classification of radiology reports using supervised learning. Front Digit Health. 2023 Jun 14;5:1195017. doi: 10.3389/fdgt h.2023.1195017. eCollection 2023.

Pasche E, Mottaz A, Gobeill J, Michel PA, Caucheteur D, Naderi N, Ruch P. Assessing the use of supplementary materials to improve genomic variant discovery. Database (Oxford). 2023 Mar 31;2023:baad017. doi: 10.1093/database/baad017.

Caucheteur D, May Pendlington Z, Roncaglia P, Gobeill J, Mottin L, Matentzoglou N, Agosti D, Osumi-Sutherland D, Parkinson H, Ruch P. COVoc and COVTriage: novel resources to support literature triage. Bioinformatics. 2023 Jan 1;39(1):btac800. doi: 10.1093/bioinformatics/btac800.

Naderi N, Mottaz A, Teodoro D, Ruch P. Analyzing the Information Content of Text-Based Files in Supplementary Materials of Biomedical Literature. Stud Health Technol Inform. 2022 May 25;294:876-877. doi: 10.3233/SHTI220614.

Goldman JP, Mottin L, Zaghir J, Keszthelyi D, Lokaj B, Turbé H, Gobeill J, Ruch P, Ehram J, Lovis C. Classification of Oncology Treatment Responses from French Radiology Reports with Supervised Machine Learning. Stud Health Technol Inform. 2022 May 25;294:849-853. doi: 10.3233/SHTI220605. Pasche E, Mottaz A, Caucheteur D, Gobeill J, Michel PA, Ruch P. Variomes: a high recall search engine to support the curation of genomic variants. Bioinformatics. 2022 Mar 11;38(9):2595-601. doi: 10.1093/bioinformatics/btac146.

Designing text mining services to support the curation efforts of the Swiss Institute of Bioinformatics: from CelloSaurus triage to Variomes variant sequence search.

Patrick Ruch

SIB Swiss Institute of Bioinformatics

Motivation: The SIB Swiss Institute of Bioinformatics maintains premier molecular biology databases such as UniProt. To keep up with the novelty of science, SIB curation effort relies on text mining solutions. After a brief introduction of the SIB (e.g., ELIXIR backbone, SIBiLS, CelloSaurus triage services), we focus on Variomes, a recently launched SIB Text Mining services to support respectively UniProt's annotation of germline and somatic variant curation tool. Variomes is used to identify and interpret clinically actionable variants. Searching for evidence in the literature is mandatory according to ASCO/AMP/CAP practice guidelines; however, it is both labor-intensive and error-prone. We developed a system to perform triage of publications relevant to support an evidence-based decision. The system is also able to prioritize variants. Our system searches within pre-annotated collections such as MEDLINE and PubMed Central.

Methods: We assess the search effectiveness of the system using three different experimental settings: literature triage; variant prioritization and comparison of Variomes with LitVar.

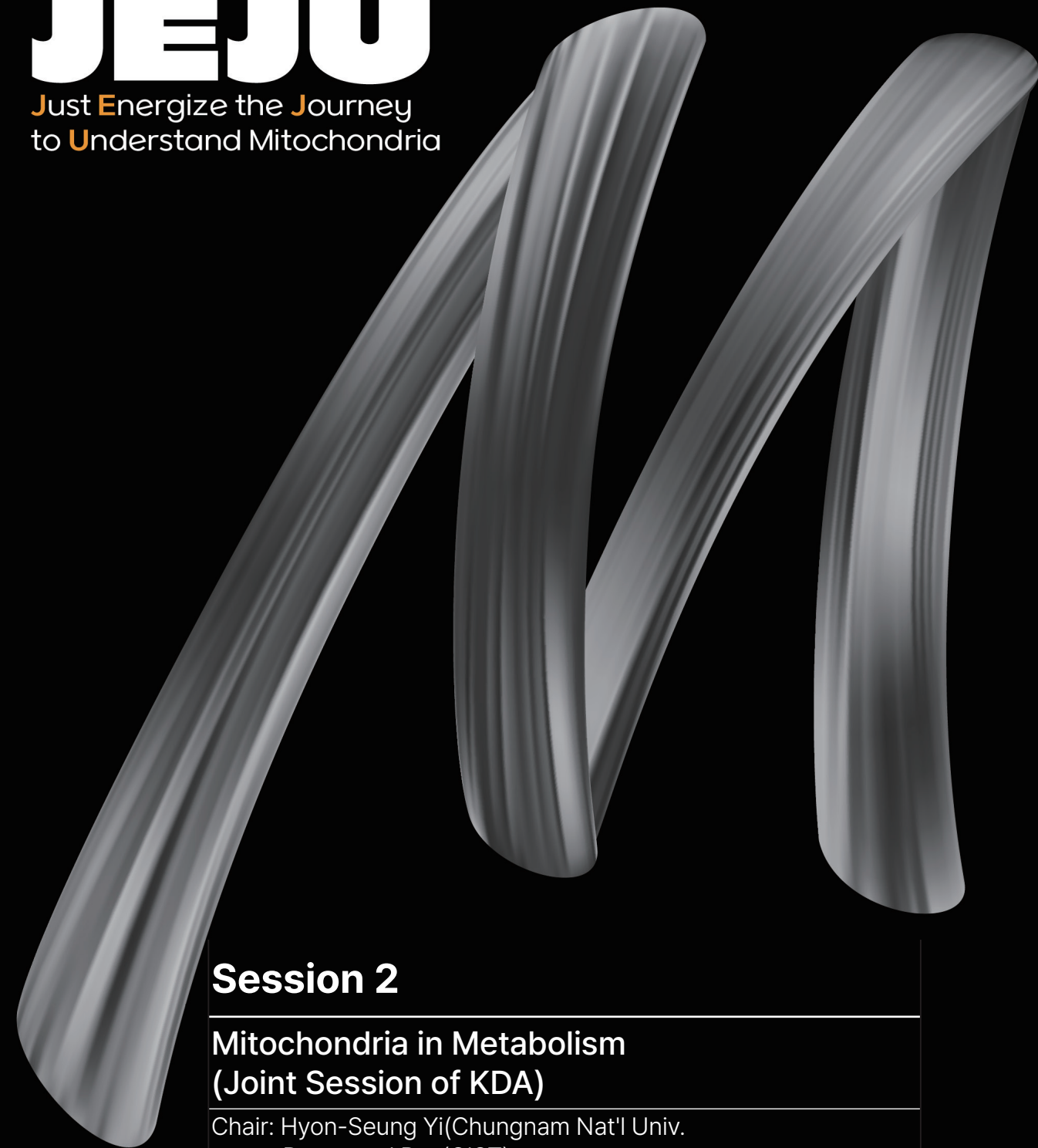
Results: Almost two-thirds of the publications returned in the top-5 are relevant for clinical decision-support. Our approach enabled identifying 81.8% of clinically actionable variants in the top-3. Variomes retrieves on average +21.3% more articles than LitVar and returns the same number of results or more results than LitVar for 90% of the queries when tested on a set of 803 queries; thus, establishing a new baseline for searching the literature about variants. Further, we evaluate how information derived from the literature can statistically correlate with SIFT/Polyphen methods, thus suggesting that variant search in literature can improve the large-scale characterization of variants of unknown significance and complement existing methods.



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Mitochondrial Research and Medicine (KSMRM)
in conjunction with 15th Symposium of Mitochondrial Section of KSMCB

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Session 2

Mitochondria in Metabolism (Joint Session of KDA)

Chair: Hyon-Seung Yi (Chungnam Nat'l Univ.)
Dongryeol Ryu (GIST)

Panel: Jin Ho Koh (Yonsei Univ.)
Dong Wook Choi (Korea Univ.)

Hyon-Seung Yi

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Education		
2000.03-2006.02	B.S.	Gachon Medical School
2009.03-2011.02	M.S.	Gachon University
2011.02-2015.02	Ph.D.	KAIST
Professional Experience		
2018.09-2022.8	Assistant Professor	Chungnam National University
2022.09-	Associate Professor	Chungnam National University
Publications		
<div>1. Hepatic T-cell senescence and exhaustion are implicated in the progression of fatty liver disease in patients with type 2 diabetes and mouse model with nonalcoholic steatohepatitis. <i>Cell Death Dis.</i> 2023 Sep 21;14(9):618.</div> <div>2. Mitochondrial defects aggravate liver cancer via aberrant glycolytic flux and T cell exhaustion. <i>J Immunother Cancer.</i> 2022 May;10(5):e004337.</div> <div>3. Skeletal muscle mitochondrial defects are linked to low bone mass caused by bone marrow inflammation in male mice. <i>J Cachexia Sarcopenia Muscle.</i> 2022 Jun;13(3):1785-1799.</div> <div>4. Immunometabolic signatures predict recovery from thyrotoxic myopathy in patients with Graves' disease. <i>J Cachexia Sarcopenia Muscle.</i> 2022 Feb;13(1):355-367.</div> <div>5. An adipocyte-specific defect in oxidative phosphorylation increases systemic energy expenditure and protects against diet-induced obesity. <i>Diabetologia.</i> 2020 Apr;63(4):837-852.</div>		

Implication of T cell senescence in the progression of diabetes and metabolic liver disease

Hyon-Seung Yi

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Immunosenescence and exhaustion are involved in the development and progression of type 2 diabetes (T2D) and metabolic liver diseases, including fatty liver, fibrosis, and cirrhosis in humans. However, the comprehensive observation of relationship between the senescence and exhaustion of T cells and insulin resistance-associated liver diseases remain incompletely understood. Patients with T2D were enrolled. To evaluate systemic immunophenotypes, peripheral blood mononuclear cells were obtained from all participants. Magnetic resonance imaging (MRI)-based proton density fat fraction and MRI-based elastography were used in an open-bore, vertical field 3.0T scanner to measure liver fat and fibrosis, respectively. Serum scores (non-alcoholic fatty liver disease (NAFLD) liver fat score, hepatic steatosis index, NAFLD Fibrosis Score, and Fibrosis-4) were also calculated. To identify immunosenescence and exhaustion of hepatic T cells in advanced liver diseases, gene-cell matrix of single cell transcriptomics was download from the public database. Body mass index does not affect T cell senescence and the populations of inflammatory cytokine-producing CD4+ and CD8+ T cells in the patients with T2D. However, the patients with higher level of HOMA-IR show significantly increased population of the CD28-CD57+ senescent T cells among CD4+ and CD8+ T cells compared to the patients with lower level of HOMA-IR. Moreover, T cell senescence is significantly associated with several serum predictive scores for liver steatosis and fibrosis. Frequency of senescent CD4+ and CD8+ T cells and the level of HOMA-IR are also positively correlated with liver fibrosis severity by measuring MRI-based elastography in patients with T2D. High expressions of genes-related to senescence and exhaustion were observed in CD4+ and CD8+ T cells of the patients with non-alcoholic steatohepatitis (NASH) or liver cirrhosis. The present study demonstrates that the T cell senescence is associated with insulin resistance, hepatic steatosis, and liver fibrosis in patients with T2D. Single cell transcriptome data suggest that inflammatory response induced by senescent and exhausted T cells is implicated in the development of NASH and liver cirrhosis in humans.



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The preservation of mitochondrial cristae protects from cardiomyopathy

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Cardiomyopathy, resulting from various etiologies such as diabetes, drugs (e.g., anthracyclines), and viral infections, is a devastating medical condition without specific treatments. Here, we demonstrate that a doxorubicin challenge provokes mitochondrial dysfunction and disorganized mitochondrial cristae structure in the heart, which in turn leads to aberrant mtDNA release into the cytosol.

Pyruvate dehydrogenase kinase (PDK), a mitochondrial matrix enzyme, was induced in this pathological situation. Inhibition of PDK protected the mitochondrial contact site and cristae organizing system (MICOS) proteins, thereby reducing mtDNA release into the cytosol. This was sufficient to mitigate doxorubicin-induced cardiomyopathy and related PANoptosome formation. Our findings reveal a novel role of PDK in the preservation of mitochondrial cristae under pathological conditions, which could be further applied in the treatment of other diseases.

Education		
1999.03-2005.02	MD	Kyungpook National University
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Professional Experience		
2013.05-2017.02	Clinical fellow/ clinical professor	Kyungpook National University Hospital
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Professional Experience		
Full member	Korean Diabetes Association	
Full member	Korean Society for Lipid and Atherosclerosis	
Full member	Korean Endocrine Society	
Publications		

1. Shrestha S, Lee YB, LChanda D, Thoudam T, Sinam IS, Lim CW, Kim M, Wang J, Lee KM, Ma J, Saxena R, Choi J, Oh CJ, Lee H, Jeon YH, Cho SJ, Jung HY, Park KG, Choi HS, Suh JM, Auwerx J, Ji B, Liangpunsakul S, Jeon JH, Lee IK. Upregulation of the ERRγ-VDAC1 axis underlies the molecular pathogenesis of pancreatitis. Proc Natl Acad Sci U S A. 2023 May 16;120(20):e2219644120ee H, Choi YK, Park BY, Kim MJ, Youn YJ, Kim SH, Jung SJ, Song DK, Jin HK, Bae JS, Lee IK, Jeon JH*, Hong CW*. Diabetes Primes Neutrophils for Neutrophil Extracellular Trap Formation through Trained Immunity. Research (Wash D C). 2024 Apr 23;7:0365

2. Kim MJ, Oh CJ, Hong CW, Jeon JH*. Comprehensive overview of the role of mitochondrial dysfunction in the pathogenesis of acute kidney ischemia-reperfusion injury: a narrative review. J Yeungnam Med Sci. 2024 Apr;41(2):61-73

3. Lee H, Jeon JH*, Kim ES*. Mitochondrial dysfunctions in T cells: focus on inflammatory bowel disease. Front Immunol. 2023 Sep 22;14:1219422.

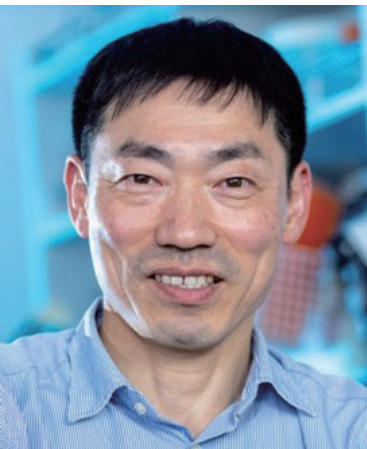
4. Oh CJ, Kim MJ, Lee JM, Kim DH, Kim IY, Park S, Kim Y, Lee KB, Lee SH, Lim CW, Kim M, Lee JY, Pagire HS, Pagire SH, Bae MA, Chanda D, Thoudam T, Khang AR, Harris RA, Ahn JH*, Jeon JH*, Lee IK*. Inhibition of pyruvate dehydrogenase kinase 4 ameliorates kidney ischemia-reperfusion injury by reducing succinate accumulation during ischemia and preserving mitochondrial function during reperfusion. Kidney Int. 2023 Oct;104(4):724-739

5. Chanda D, Thoudam T, Sinam IS, Lim CW, Kim M, Wang J, Lee KM, Ma J, Saxena R, Choi J, Oh CJ, Lee H, Jeon YH, Cho SJ, Jung HY, Park KG, Choi HS, Suh JM, Auwerx J, Ji B, Liangpunsakul S, Jeon JH*, Lee IK*. Upregulation of the ERRγ-VDAC1 axis underlies the molecular pathogenesis of pancreatitis. Proc Natl Acad Sci U S A. 2023 May 16;120(20):e2219644120



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Education		
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Professional Experience		
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1995.05-1996.06	Postdoctoral Fellow	Institute of Genetic Ecology, Tohoku University, Sendai, Japan (Tamotsu Otaki lab)
1996.07-1999.06	Postdoctoral Fellow	Department of Molecular Biology and Oncology, UT Southwestern Medical Center, Dallas, TX, USA (Ronald Butow lab)
1999.09-2002.01	HFSP Long-Term Fellow	Institute for Physiological Chemistry, University of Munich, Munich, Germany (Walter Neupert lab)
2002.01-2005.02	Research Assistant Professor	Department of Biology, University of Utah, Salt Lake City, UT, USA (Janet Shaw lab)
2005.02-2006.11	Research Assistant Professor	Department of Biochemistry, University of Utah School of Medicine, Salt Lake City, UT, USA (Janet Shaw lab)
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2010.04-present	Associate Professor (Principal Investigator)	Graduate School of Frontier Biosciences, Osaka University, Suita, Japan
Professional Experience		
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1992.07-present	Academic Member	Molecular Biology Society of Japan
2018.09-present	Delegate Member	Japan Society for Cell Biology
2009.04-present	Academic Member	Japan Biochemical Society

Publications

1. Tian Y, Okamoto K. The nascent polypeptide-associated complex subunit Egd1 is required for efficient selective mitochondrial degradation in budding yeast. *Sci Rep*, 14:546. doi: 10.1038/s41598-023-50245-7

2. Onishi M, Kubota M, Duan L, Tian Y, Okamoto K. The GET pathway serves to activate Atg32-mediated mitophagy by ER targeting of the Ppg1-Far complex. *Life Sci Alliance*, (2023), 6:e202201640. doi: 10.26508/lsa.202201640

Locking and unlocking mechanisms of Atg32-mediated mitophagy

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Autophagy-dependent selective clearance of dysfunctional or excess mitochondria, termed mitophagy, is an evolutionarily conserved process that contributes to mitochondrial quality and quantity control. Accumulating evidence suggests that both aberrantly accelerated and suppressed mitophagy may compromise cellular homeostasis, ultimately leading to a myriad of disorders. Thus, cells must utilize regulatory mechanisms to properly control mitophagic activities. In the budding yeast *Saccharomyces cerevisiae*, mitophagy is induced in a manner dependent on Atg32, a single-pass membrane protein that directly interacts with Atg11, a selective autophagy scaffold protein necessary for core Atg protein assembly, thereby efficiently recruiting the autophagy machinery to mitochondria. Upon mitophagy induction, Atg32 is accumulated on the mitochondrial surface and phosphorylated by casein kinase 2 (CK2). This posttranslational modification is crucial for mitophagy, as it stabilizes Atg32-Atg11 interactions. Currently, how CK2-mediated Atg32 phosphorylation acts in Atg32-Atg11 interactions remains obscure. In this study, we demonstrate that Atg11 contains two distinct C-terminal domains for Atg32 binding, Atg11Finger commonly critical for selective autophagy pathways and Atg11Claw specifically crucial for mitophagy, and that Atg32 is a self-inhibitory protein preventing Atg11 binding via its intramolecular interactions. CK2-dependent Atg32 phosphorylation stabilizes Atg32-Atg11Finger interactions to relieve Atg32 self-inhibition, subsequently promoting Atg32-Atg11Claw interactions to achieve mitophagy initiation. We also found that Atg1, a master kinase essential for autophagy priming, phosphorylates Atg11 to further stabilize Atg32-Atg11Claw interactions. These findings imply that CK2 and Atg1 regulate Atg32-Atg11 interactions at the early and late stages, respectively, of mitophagy initiation.



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Education

1993.04-1997.03	Bachelor	The University of Tokyo
1997.04-1999.03	Master	The University of Tokyo
1999.04-2002.03	Ph.D.	The University of Tokyo

Professional Experience

2002.04-2006.03	Postdoc	Japan Science and Technology Agency
2006.04-2007.09	JSPS Research fellowship for Young Scientists (PD)	Osaka University,10-
2007.10-2011.03	Researcher	Japan Science and Technology Agency
2011.04-present	Associate Professor	Kyoto University

Professional Experience

2002.10-present	Member	The Biophysical Society of Japan
2001.04-present	Member	Protein Science Society of Japan
2011.05-present	Member	The Japanese Biochemical Society

Publications

1. Choi J, Matoba N, Setoyama D, Watanabe D, Ohnishi Y, Yasui R, Kitai Y, Oomachi A, Kotobuki Y, Nishiya Y, Pieper MP, Imamura H, Yanagita M, Yamamoto M. The SGLT2 Inhibitor Empagliflozin Improves Cardiac Energy Status via Mitochondrial ATP Production in Diabetic Mice, Communications Biology. 2023 Mar; 6(1): 278.

2. Imamura H, Sakamoto S, Yoshida T, Matsui Y, Penuela S, Laird DW, Mizukami S, Kikuchi K, Kakizuka A. Single-cell Dynamics of Pannexin-1-facilitated Programmed ATP Loss during Apoptosis, eLife. 2020 Oct; 9: e61960.

3. Imamura H, Nhat KP, Togawa H, Saito K, Iino R, Kato-Yamada Y, Nagai T, Noji H. Visualization of ATP Levels inside Single Living Cells with Fluorescence Resonance Energy Transfer-based Genetically Encoded Indicators, Proceedings of the National Academy of Sciences. 2009 Sep; 106(37); 15651-15656.

Spatiotemporal dynamics of intracellular metabolites using genetically encoded biosensors

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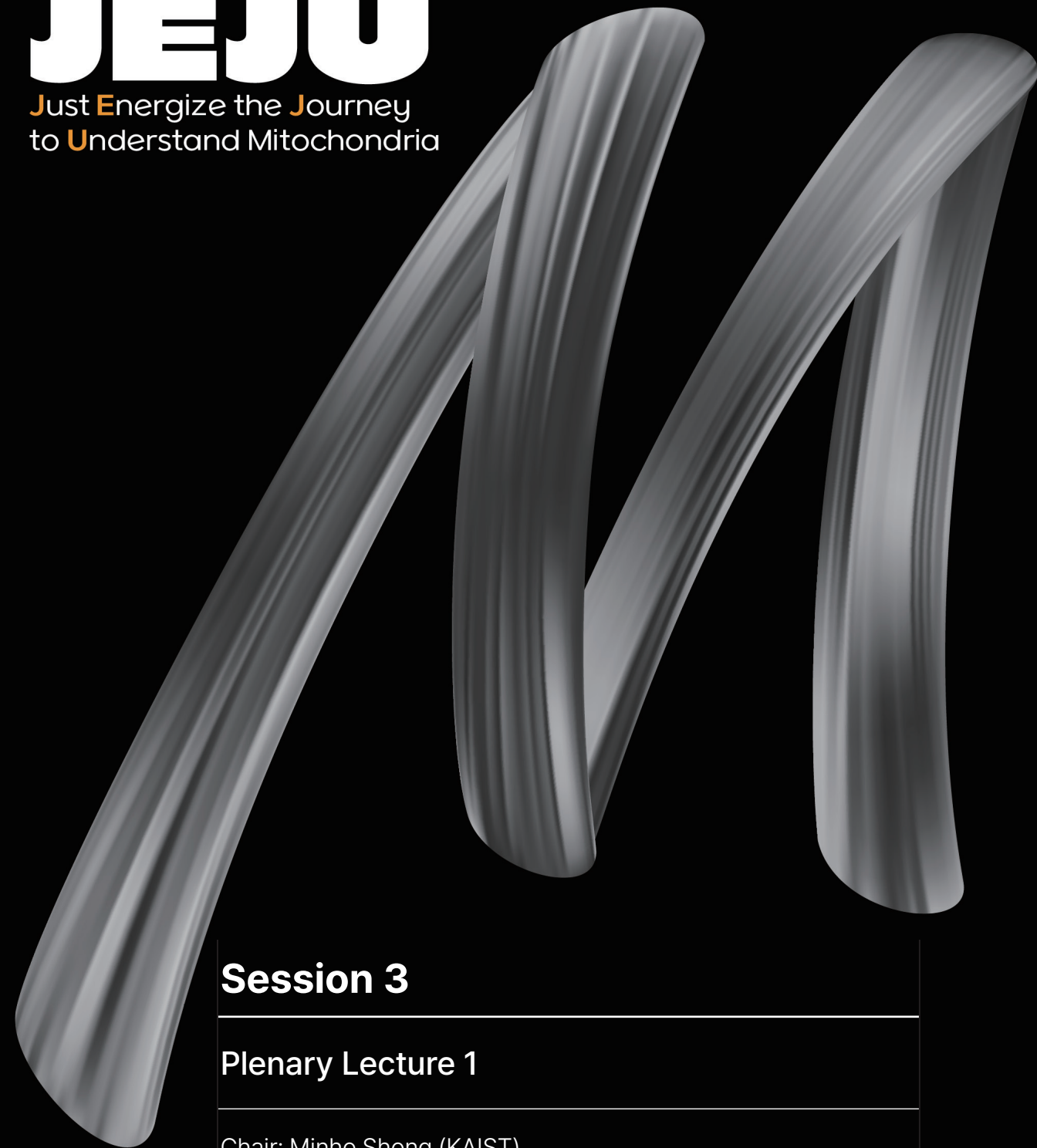
One major function of mitochondria is to produce ATP, a primary cellular energy currency that plays a crucial role in various cellular processes. Metabolites of multiple nutrients, such as sugars, fatty acids, and amino acids, enter into mitochondria, providing the free energy necessary for synthesizing ATP. However, how intracellular metabolites, including ATP, change in space and time in association with biological events and in response to environmental stresses is yet well studied. For over a decade, we have developed genetically encoded biosensors for metabolites, including ATeam and OLIVE, Förster resonance energy transfer (FRET)-based biosensors for ATP and branched-chain amino acids, respectively. By imaging the cells expressing these biosensors, concentrations of the metabolites inside single living cells have been successfully visualized. In addition, the metabolite concentrations of a specific intracellular location, such as the mitochondrial matrix, have been also monitored by attaching an appropriate signal sequence to the biosensors. Thus, these biosensors have enabled us to understand the dynamics of the metabolites inside single living cells at high spatial and temporal resolutions. These biosensors have been applied across a wide range of cell types, from cardiomyocytes to cancer cells, and even to model organisms like the fruit fly and mouse. This broad application has allowed us to understand the dynamics, distribution, and dynamics of the metabolites in various biological processes, including insulin secretion, cell division, and apoptosis.



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Session 3

Plenary Lecture 1

Chair: Minho Shong (KAIST)
Jae Myoung Suh (KAIST)

Jared Rutter, Ph.D.

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Education		
1991.09 - 1996.05	BS	Brigham Young University, Provo, UT
1996.08 - 2001.04	PhD	University of Texas – Southwestern Medical CTR, Dallas, TX
2001.09 - 2003.08	Postdoctoral Fellow	University of Texas – Southwestern Medical CTR, Dallas, TX

Professional Experience		
2020 -	Distinguished Professor of Biochemistry	University of Utah School of Medicine, Salt Lake City, UT
2015 -	Investigator	Howard Hughes Medical Institute, Salt Lake City, UT
	Dee Glen and Ida Smith Endowed Chair for Cancer Research	University of Utah, Salt Lake City, UT
2013 -	Co-Leader	Nuclear Control of Cell Growth and Proliferation Program, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT
2013 -	Co-Director	Diabetes and Metabolism Research Center, University of Utah, Salt Lake City, UT
2013 - 2020	Professor of Biochemistry	University of Utah School of Medicine, Salt Lake City, UT
2009 - 2013	Associate Professor with Tenure	University of Utah School of Medicine, Salt Lake City, UT
2003 - 2009	Assistant Professor of Biochemistry	University of Utah School of Medicine, Salt Lake City, UT
2001 - 2003	Sara and Frank McKnight Independent Fellow of Biochemistry	University of Texas-Southwestern Medical Center, Dallas, TX
1996 - 2001	Graduate Research Assistant	University of Texas-Southwestern Medical Center, Dallas, TX

Publications

1. Visker JR, Cluntun AA, Velasco-Silva JN, Eberhardt DR, Shankar TS, Hamouche R, Ling J, Kwak H, Hillas Y, Aist I, Tseliou E, Navankasattusas S, Chaudhuri D, Ducker GS, Drakos SG, Rutter J. Enhancing mitochondrial pyruvate metabolism ameliorates myocardial ischemic reperfusion injury. *bioRxiv*. 2024. <https://www.biorxiv.org/content/10.1101/2024.02.01.577463v1>

2. Berg JA, Zhou Y, Ouyang Y, Cluntun AA, Waller TC, Conway ME, Nowinski SM, Van Ry T, George I, Cox JE, Wang B, Rutter J. MetaboVerse: Automated discovery and visualization of diverse metabolic regulatory patterns. *Nat. Cell Bio.* 2023. In press. Available on *bioRxiv*.

3. Hicks KG, Cluntun AA, Schubert HL, Hackett SR, Berg JA, Leonard PG, Ajalla Aleixo MA, Zhou Y, Bott AJ, Salvatore SR, Chang F, Blevins A, Barta P, Tilley S, Leifer A, Guzman A, Arok A, Fogarty S, Winter JM, Ahn H-C, Allen KN, Block S, Cardoso IA, Ding J, Dreveny I, Gasper C, Ho Q, Matsuura A, Palladino MJ, Prajapati S, Sun P, Tittmann K, Tolan DR, Unterlass J, VanDemark AP, Vander Heiden MG, Webb BA, Yun C-H, Zhap P, Wang B, Schopfer FJ, Hill CP, Nonato MC, Muller FL, Cox JE, and Rutter J. Protein-Metabolite Interactomics of Carbohydrate Metabolism Reveals Regulation of Lactate Dehydrogenase. *Science*. 2023. Mar 10;379(6636):996-1003. PMID: 36893255

4. Winter JM, Fresenius HL, Cunningham CN, Wei P, Keys HR, Berg J, Bott A, Yadav T, Ryan J, Sirohi D, Tripp SR, Barta P, Agarwal N, Letai A, Sabatini DM, Wohlever ML, Rutter J. Collateral deletion of the mitochondrial AAA+ ATPase ATAD1 sensitizes cancer cells to proteasome dysfunction. *Elife*. 2022 Nov 21;11:e82860. PMID: PMC9815822.

Metabolism, Cellular Decisions and the Language That Unites Them

Jared Rutter

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Mitochondria are dynamic and complex organelles that play a central role in all aspects of biology, including energy production, intermediary metabolism, and apoptosis. These broad cellular functions also place mitochondria as a central player in human health and disease. We have focused recently on deciphering the biochemical and cellular functions of conserved uncharacterized mitochondrial proteins. This has revealed new mechanisms for several critical aspects of mitochondrial function, including the Mitochondrial Pyruvate Carrier (MPC), which is required for efficient mitochondrial pyruvate uptake. By perturbing the metabolic program of cells, MPC manipulation profoundly affects cellular decisions related to stem cell homeostasis and proliferation. This observation suggests that metabolism is not a passive enabler of cell behaviors, but instead plays a decisive role. One of our current areas of focus, which will be discussed, is to determine the mechanisms whereby metabolism and metabolites affect behaviors via direct modulation of proteins involved in signaling, transcription and other regulatory mechanisms. As we discover these mechanisms, which we hypothesize to be extensive within biology, we will be enabled to impinge on such phenomena for therapeutic benefit in disease states.



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Session 4

Mitochondria in Translational Research (Joint Session of B-IRC)

Chari: Sang Ki Park(POSTECH)

oon Tae Lee(POSTECH)

Panel: Min Sik Lee (POSTECH)

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Education		
1983.03-1987.02	DVM, BS	College of Veterinary Medicine, Seoul National University
1987.03-1989.02	MS	College of Veterinary Medicine, Seoul National University
1989.03-1993.02	PhD	College of Veterinary Medicine, Seoul National University (Veterinary Physiology)
1993.03-1993.07	Researcher	Medical School, State University of New York at Buffalo, USA

Professional Experience		
1993.08-2011.08	Professor	College of Veterinary Medicine, Chonnam National University
2006.04-2011.08	Director	Biotherapy Human Resources Center (BK21)
2007.09-2009.08	Dean	College of Veterinary Medicine, Chonnam National University
2011.09-Present	Professor	College of Veterinary Medicine, Seoul National University
2013.09-2020.08	Director	BK21PLUS Program for Creative Veterinary Science Research Center
2020.03-Present	Adjunct Professor	University of Connecticut, USA
2020.09-2023.02	Director	BK21 FOUR Future Veterinary Medicine Leading Education & Research Center
2021.03-2023.02	Dean	College of Veterinary Medicine, Seoul National University

Professional Experience		
2000.04-Present	Associate Editor	Journal of Veterinary Science
2006.10-Present	Director	Korean Physiological Society
2014.01-2023.12	Associate Editor	International Journal of Stem Cells
2017.01-2023.11	Associate Editor	Molecular and Cells
2020.11-Present	Director	Korean Veterinary Medical Association

Publications

1. Cho JH, Chae CW, Lim JR, Jung YH, Han SJ, Yoon JH, Park JY, **Han HJ**. Sodium butyrate ameliorates high glucose-suppressed neuronal mitophagy by restoring PRKN expression via inhibiting the RELA-HDAC8 complex. Autophagy. 2024 Jul;20(7):1505-1522

2. Lee HJ, Chae CW, **Han HJ**. Enhancing the therapeutic efficacy of mesenchymal stem cell transplantation in diabetes:Amelioration of mitochondrial dysfunction-induced senescence. Biomed Pharmacother. 2023 Dec;168:115759.

Mitochondrial disorder as a risk factor for neurodegenerative diseases

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Neurons are long-lived cells with the same lifespan as the organism, and mitochondria protect neuronal survival and energy production against a variety of stresses as a safeguard and powerhouse in neuron. Therefore, it is not surprising that disturbances of mitochondrial function are closely related with the mechanisms underlying nervous system abnormalities, including neurodegenerative diseases (NDs). In recent years, metabolic stress has been recognized as risk factor for NDs, with mitochondrial dysfunction reported to be the major pathogenesis. However, in most cases, it is unclear where mitochondria sit in relation to the overall disease cascades that ultimately causes neuronal dysfunction and death, and there is still controversy regarding the x`question of whether mitochondrial dysfunction is a necessary step in ND. Therefore, we focused on the loss of mitochondrial integrity in NDs, such as Alzheimer's diseases (AD), and studied the mechanisms underlying mitochondrial dysfunction (including mitochondrial biogenesis, dynamics, transport, ER-mitochondrial interaction and mitophagy etc.). In our recent studies, i) High glucose induced neuronal mitochondria dysfunction by TGM2-mediated MAM formation and by loss of PINK1/Parkin mediated mitophagy, ii) Glucocorticoid induced neuronal mitochondrial dysfunction by loss of NIX-mediated mitophagy and dysregulated MAM formation, iii) Prenatal stress-mediated Miro1 downregulation also induced mitochondrial perinuclear clamping and reduced mitochondrial distribution at synapse, and iv) Alcohol induced neuronal mitochondria dysfunction by CAMKII/Drp1 mediated excessive mitochondrial fission and MCI-1S mediated MAM formation. Our results suggest that the understanding of mechanisms underlying mitochondrial dysfunction that occurs in AD induced by various risk factors may offer novel targets for future therapeutic development.



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Education

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2004.03 -2010.02	B.A.	Seoul National University, Seoul, Korea

Professional Experience

2018.06-2024.01	Postdoc	Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP), Berlin, Germany
2017.03-2018.05	Postdoc	Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea

Publications

8 Jeongsik Kim, Dahyun Kim, Dong-Kyun Kim, Sang-Hee Lee, Wonyul Jang*, Dae-Sik Lim* (2024) "Formation of a giant unilocular vacuole via macropinocytosis-like process confers anoikis resistance" *Co-corresponding authors eLife, doi.org/10.7554/eLife.96178.1

7. Wonyul Jang, Volker Haucke (2024) "ER remodeling via lipid metabolism" Trends in Cell Biology, doi.org/10.1016/j.tcb.2024.01.011

6. Michael Ebner, Dmytro Puchkov, Orestes López-Ortega, Pathma Muthukottiappan, Yanwei Su, Christopher Schmied, Silke Zillmann, Iryna Nikonenko, Jochen Koddebusch, Gillian L. Dornan, Max T. Lucht, Vonda Koka, Wonyul Jang, Philipp Alexander Koch, Alexander Wallroth, Martin Lehmann, Britta Brügger, Mario Pende, Dominic Winter, Volker Haucke (2023) "Nutrient-regulated control of lysosome function by signaling lipid conversion" Cell, DOI:10.1016/j.cell.2023.09.027

5. Wonyul Jang, Dmytro Puchkov, Paula Samsó, YongTian Liang, Michal Nadler-Holly, Stephan J. Sigrist, Ulrich Kintscher, Fan Liu, Kamel Mamchaoui, Vincent Mouly, Volker Haucke (2022) "Endosomal lipid signaling reshapes the endoplasmic reticulum to control mitochondrial function" Science, 378, 6625

• Highlighted in: M. Zanellati and S. Cohen. (2022) "The endosome as engineer" Science, 378, 6625 (1173-1174).

4. York Posor*, Wonyul Jang*, Volker Haucke (2022) "Phosphoinositides as membrane organizers" Nat Rev Mol Cell Biol, DOI: 10.1038/s41580-022-00490-x (*co-first author)

3. Mouhannad Malek, Anna M. Wawrzyniak, Peter Koch, Christian Luchtenborg, Manuel Hessenberger, Timo Sachsenheimer, Wonyul Jang, Britta Brügger, Volker Haucke (2021) " Inositol triphosphate-triggered calcium release blocks lipid exchange at endoplasmic reticulum-Golgi contact sites" Nat Commun, 12, 2673

2. Wonyul Jang, Tackhoon Kim, Ja Seung Koo, Sang-kyum Kim and Dae-Sik Lim (2017) "Mechanical cue-induced YAP instructs Skp2-dependent cell cycle exit and oncogenic signaling" EMBO Journal, 36(17):2510-2528.

• Highlighted in: R. T. Bottcher, Z. Sun, R. Fassler (2017) "A forceful connection: mechanoregulation of oncogenic YAP" EMBO Journal (News and Views), 36(17): 2467-2469.

1. Mi Young Seo*, Wonyul Jang*, and Kunsoo Rhee (2015) "Integrity of the Pericentriolar Material Is Essential for Maintaining Centriole Association during M Phase" PLOS ONE, 10(9), e0138905. (*co-first author)

Remodeling of endoplasmic reticulum via lipid metabolism

Wonyul Jang¹

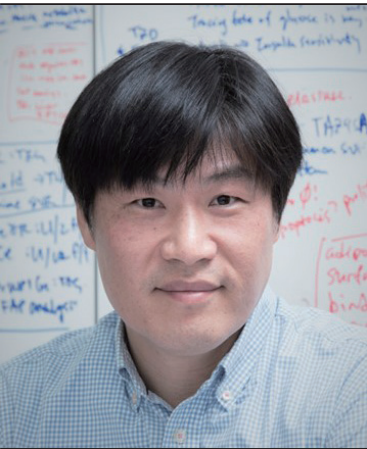
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Eukaryotic cells contain a variety of intracellular lipid membrane-bound compartments called organelles that mediate the important biochemical functions necessary for life. The field of studying organelle biology has recently grown fast owing to the advent of new microscopy that allowed the high-resolution imaging of organelles and organelle specific probes. Consequently, unlike our classic textbook image of organelles usually depicted as static and isolated, emerging pictures show organelles undergo dynamic fusion, and fission, and actively communicate with each other by establishing close apposition between the membranes of two organelles, the so-called membrane contact sites. Rewiring such organelle dynamics is essential for cells to appropriately adapt to altering environments such as nutrient deprivation. Unlike other organelles that have multiple copies in cells, each cell contains only one ER. This ER extends throughout the cell and occupies a large fraction of the cytoplasmic volume via its elaborate, giant membrane architecture consisting of different morphological domains, namely tubule, sheets, and nuclear envelope. However, the underlying mechanism of ER morphological dynamics and the relationship between its form and function still remain elusive. In this talk, I will present how cells reshape ER during nutrient starvation and rewire their metabolic states by communicating with neighboring organelles.



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Publications		
1. Choi S, Kang JG, ..., Lim DS*, Suh JM*. Hippo-YAP/TAZ signalling coordinates adipose plasticity and energy balance by uncoupling leptin expression from fat mass. Nature Metabolism. 2024 May; 6(5):847-860		
2. Park I, Kim KE, Kim J, ..., Lee KS*, Kim JS*, Suh JM*, Rhee HW*. Mitochondrial matrix RTN4IP1/OPA10 is an oxidoreductase for coenzyme Q synthesis. Nature Chemical Biology. 2024 Feb; 20(2):221-233.		
3. Park A, Kim KE, ..., Kim WK*, Bae KH*, Suh JM*. Mitochondrial matrix protein LETMD1 maintains thermogenic capacity of brown adipose tissue in male mice. Nature Communications. 2023 Jun; 14(1):3746		
4. Choi J, Oh TG, ..., Yoshihara E*, Evans RM*, Suh JM*. Estrogen-Related Receptor γ Maintains Pancreatic Acinar Cell Function and Identity by Regulating Cellular Metabolism. Gastroenterology. 2022 Jul; 163(1):239-256.		
5. Kim KE, Park I, Kim J, ..., Kim JS*, Rhee HW*, Suh JM*. Dynamic tracking and identification of tissue-specific secretory proteins in the circulation of live mice. Nature Communications. 2021 Sep; 12(1):5204.		

In vivo mapping of subcellular proteomes in aging and disease

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To facilitate the understanding of metabolic changes associated with aging and disease processes 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 mitoAPEX, a peroxidase-based proximity labeling enzyme containing a mitochondrial matrix targeting sequence. Upon label activating conditions, mitoAPEX rapidly (<1 min) catalyzes production of biotin radicals which biotinylate proteins within a ~20 nm radius. Mass analysis of biotinylated proteomes from proximity labeled mitoAPEX mouse tissues confirmed specific and efficient labeling of the mitochondrial proteome and revealed tissue-specific patterns of the matrix proteome. The labeled muscle proteomes from young and old mitoAPEX mice revealed significant changes in the quantity and composition of protein species. Of these, RTN4IP1, was shown to be downregulated in muscle tissue of old mice. However, in contrast to previous reports, our analysis of RTN4IP1 shows RTN4IP1 is localized to the mitochondrial matrix and not the outer membrane. In addition to the mitoAPEX mice, we developed another in vivo proximity labeling tool, iSLET (in situ Secretory protein Labeling via ER-anchored TurboID), 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 mitoAPEX and iSLET mice will contribute to the in vivo characterization of mitochondrial and secreted proteomes, respectively, providing new insights into mitochondrial function and interorgan communication networks in aging and associated disease processes.



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Publications		
1. Nhung TTM#, Long NP#, Nghi TD, Suh Y, Anh NH, Jung CW, Triet HM, Jung MK, Woo Y, Yoo JY, Noh SJ, Kim SJ, Lee SB, Park S, Thomas G, Simmen T, Mun JY, Rhee HW, Kwon SW, Park SK. Genome-wide kinase-MAM interactome screening reveals the role of CK2A1 in MAM Ca2+ dynamics linked to DEE-66. Proc Natl Acad Sci USA 120 (32)		
2. Cho E#, Woo Y*#, Suh Y, Suh BK, Kim SJ, Nhung TTM, Yoo JY, Nghi TD, Lee SB, Mun DJ, Park SK*. Ratiometric measurement of MAM Ca2+dynamics using a modified CalfluxVTN. (2023) Nat Communications. 14, 3586		
3. Mun DJ, Goo BS, Suh BK, Hong JH, Woo Y, Kim SJ, Kim S, Lee SB, Won Y, Yoo JY, Cho E, Jang EJ, Nhung TTM, Triet HM, An H, Lee H, Nguyen MD, Park SY, Baek ST, and Park SK* Gcap14 is a novel microtubule plus-end-tracking protein coordinating microtubule-actin crosstalk during neurodevelopment. (2023) Proc Natl Acad Sci USA 120 (8) e2214507120		
4. Goo BS, Mun DJ, Kim S, Nhung TTM, Lee SB, Woo Y, Kim SJ, Suh BK, Park SJ, Lee HE, Park K, Jang H, Rah JC, Yoon KJ, Baek ST, Park SY *, and Park SK * Schizophrenia-associated Mitotic Arrest Deficient-1 (MAD1) regulates the polarity of migrating neurons in the developing neocortex. (2022) Molecular Psychiatry. 28, 856–870		
5. Kwak C, Shin S, Park JS, Jung M, Nhung TTM, Kang MK, Lee C, Kwon TH, Park SK*, Mun JY*, Kim JS*, Rhee HW*. Contact-ID, a new tool for profiling organelle contact site, reveals regulatory proteins of mitochondria-associated membrane formation. (2020) Proc Natl Acad Sci USA. 117 (22) 12109-12120		

Exploring regulatory pathways for calcium communication between ER and mitochondria

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Endoplasmic reticulum (ER) and mitochondria form a unique subcellular compartment called mitochondria-associated ER membranes (MAMs). Disruption of MAMs impairs Ca2+ homeostasis, triggering pleiotropic effects in the neuronal system. Genome-wide kinase-MAM interactome screening identifies casein kinase 2 alpha 1 (CK2A1) as a regulator of composition and Ca2+ transport of MAMs. CK2A1-mediated phosphorylation of PACS2 at S207/208/213 facilitates MAM localization of PACS2-PKD2-CK2A1 complex, regulating PKD2-dependent mitochondrial Ca2+ influx. We further reveal that mutations of PACS2 (E209K and E211K) associated with developmental and epileptic encephalopathy 66 (DEE66) impair MAM integrity through the disturbance of PACS2 phosphorylation at S207/208/213. This, in turn, causes the reduction of mitochondrial Ca2+ uptake and the dramatic increase of cytosolic Ca2+ level, thereby, inducing neurotransmitter release at the axon boutons of glutamatergic neurons. In conclusion, our findings suggest a molecular mechanism that MAM alterations induced by pathological PACS2 mutations modulate Ca2+-dependent neurotransmitter release.

As exemplified by this study, accurately measuring Ca2+ concentrations within MAM has been a persistent challenge. We recently proposed MAM-Calflux as an MAM-specific BRET-based Ca2+ indicator. This approach not only enables precise ratiometric Ca2+ measurement but also serves as a quantitative marker for MAM. MAM-Calflux, functioning as a ratiometric indicator, accurately estimates steady-state MAM Ca2+ levels and reveals uneven intracellular MAM Ca2+ distribution. Significantly, it discerns abnormal MAM Ca2+ accumulation in neurons from a Parkinson's disease mouse model.

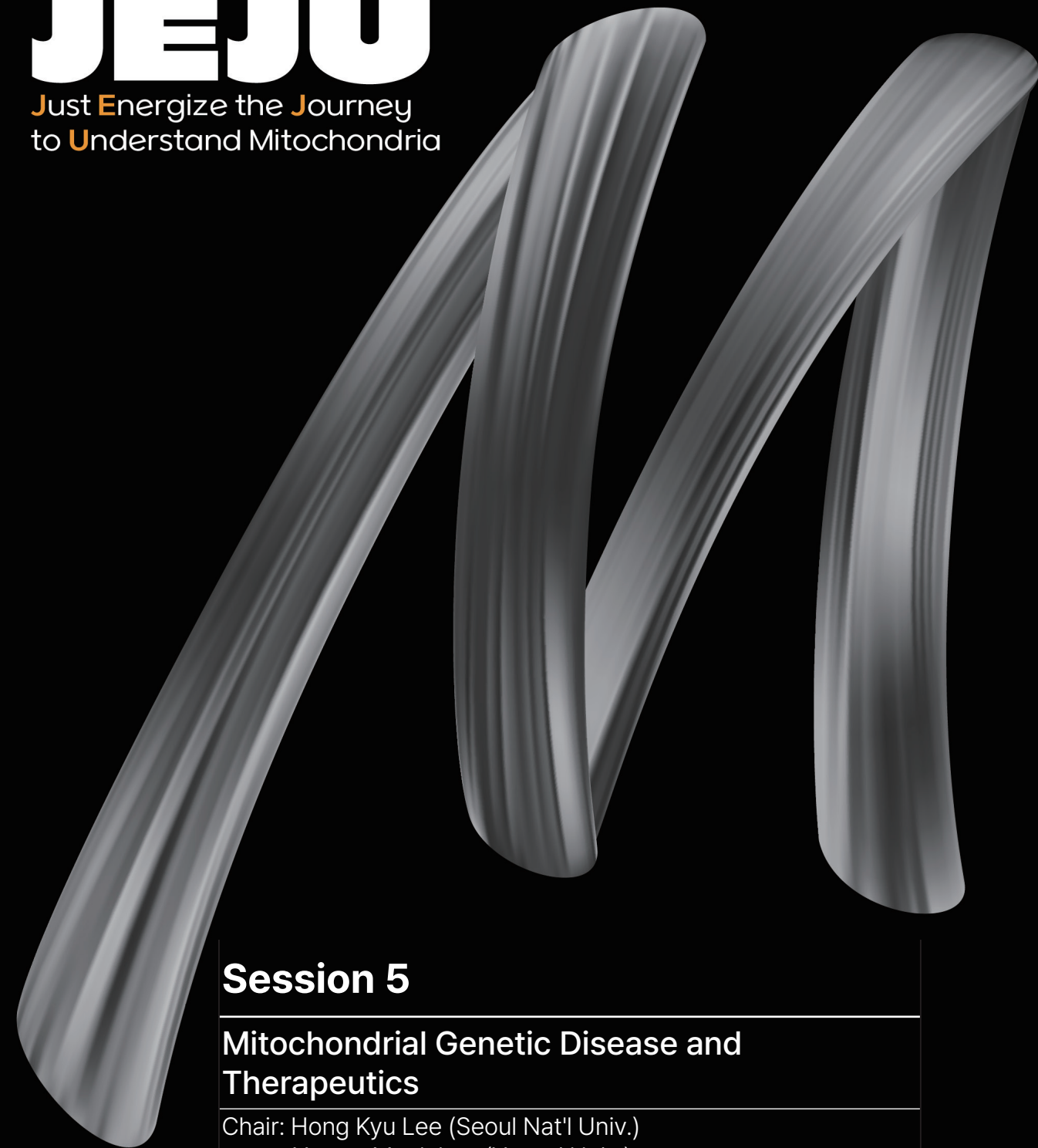
Together, understanding calcium communication between ER and mitochondria in these studies provide promising routes to organelle networks in health and disease



The 18th International Conference of Korean Society for
Mitochondrial Research and Medicine (KSMRM)
in conjunction with 15th Symposium of Mitochondrial Section of KSMCB

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Session 5

Mitochondrial Genetic Disease and Therapeutics

Chair: Hong Kyu Lee (Seoul Nat'l Univ.)
Young-Mock Lee (Yonsei Univ.)

Panel: Hyejin Park(KAIST)
Su Myung Jung (Sungkyunkwan Univ.)

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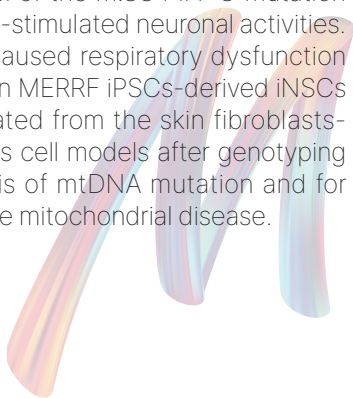
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Publications		
1. Wu SB, Ma YS, Wu YT, Chen YC, Wei YH. Mitochondrial DNA mutation-elicited oxidative stress, oxidative damage and altered gene expression in cultured cells of patients with MERRF syndrome. Mol. Neurobiol. 2010; 41:256-266.		
2. Wu SB, Wei YH. AMPK-mediated increase of glycolysis as an adaptive response to oxidative stress in human cells: Implication of the cell survival in mitochondrial diseases. Biochim. Biophys. Acta – Molecular Basis of Disease 2012; 1822:233-247.		
3. Wu YT, Lee HC, Liao CC, Wei YH. Regulation of mitochondrial FoF1ATPase activity by Sirt3-catalyzed deacetylation and its deficiency in human cells harboring 4977 bp deletion of mitochondrial DNA. Biochim. Biophys. Acta – Molecular Basis of Disease 2013; 1832:216-227.		
4. Hsu SH, Chen CT, Wei YH. Inhibitory effects of hypoxia on metabolic switch and osteogenic differentiation of human mesenchymal stem cells. Stem Cells 2013; 31:2779-2788.		
5. Wu YT, Wu SB, Wei YH. Metabolic reprogramming of human cells in response to oxidative stress: Implications in the pathophysiology and therapy of mitochondrial diseases. Curr. Pharm. Des. 2014; 20:5510-5526.		
6. Wang CH, Chen YF, Wu CY, Wu PC, Huang YL, Kao CH, Lin CH, Kao LS, Tsai TF, Wei YH. Cisd2 modulates the differentiation and functioning of adipocytes by regulating intracellular Ca2+ homeostasis. Hum. Mol. Genet. 2014; 23:4770-4785.		
7. Chen YC, Wu YT, Wei YH. Depletion of mitoferrins leads to mitochondrial dysfunction and impairment of adipogenic differentiation in 3T3-L1 preadipocytes. Free Radic. Res. 2015; 49:1285-1295.		

Induced Pluripotent Stem Cells and their Derived Neurons as
Cell Models for Studies of the MERRF Syndrome

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Mitochondrial DNA (mtDNA) mutation may cause a wide spectrum of mitochondrial diseases that are frequently manifested in muscle, brain, and heart. We first demonstrated that mtDNA mutation-elicited mitochondrial dysfunction and overproduction of reactive oxygen species (ROS) and metabolic reprogramming in affected cells play an important role in the pathogenesis of mitochondrial diseases. We have generated a series of induced pluripotent stem cells (iPSCs) from skin fibroblasts of several patients with MERRF syndrome associated with the m.8344A>G mutation and demonstrated that they could be differentiated into neurons, cardiomyocytes, and other cell types. The MERRF patient iPSCs and differentiated progeny recapitulated the mtDNA mutation, mitochondrial dysfunction, ROS overproduction and altered expression of antioxidant enzymes. The m.8344A>G mutation was segregated randomly in the reprogramming process, which resulted in a wide range of the mutation load in different iPSC clones. Interestingly, we found that the m.8344A>G mutation load in iPSCs may change during subculture. Besides, we identified several novel mtDNA mutations in the iPSCs. Recently, we induced MERRF iPSCs to differentiate into the induced neural stem cells (iNSCs) and cortical neurons under defined conditions. After 4 weeks of differentiation, immunofluorescence staining was performed to characterize the neurons differentiated from MERRF iPSCs and normal iPSCs. All the neurons derived from the iPSCs expressed Tuji and other neuron-specific markers and exhibited neuronal morphology after differentiation. The oxygen consumption rates were decreased in the basal, ATP-coupled, and the maximal respiration in MERRF iPSCs-derived cortical neurons after 3 weeks of differentiation. The intracellular ROS levels were increased in the MERRF iPSCs-derived iNSCs and cortical neurons containing high levels of m.8344A>G mutation compared with the neurons derived from iPSCs with low levels of m.8344A>G mutation. Some of the antioxidant enzymes were increased in MERRF iPSC-derived neurons. We found that the protein levels of synaptophysin and vesicular glutamate transporter 2 (vGLUT2) were decreased in mutant MERRF neurons. These findings indicate that neural immaturity and synaptic protein loss could result in the impairment of neuronal activity and plasticity in MERRF neurons harboring m.8344A>G mutation. By electrophysiological recordings, we monitored the in vivo neuronal behaviors of MERRF neurons and found that neurons harboring a highlevel of the m.8344A>G mutation exhibited impairment of the spontaneous and evoked potential-stimulated neuronal activities. The above findings suggest that the m.8344A>G mutation caused respiratory dysfunction and metabolic reprogramming in response to oxidative stress in MERRF iPSCs-derived iNSCs and neurons. In summary, the iNSCs and neurons differentiated from the skin fibroblasts-derived iPSCs of patients with MERRF syndrome may serve as cell models after genotyping for studies of the molecular mechanism of the pathogenesis of mtDNA mutation and for screening for novel therapeutic agents to treat patients with the mitochondrial disease.



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Academic Society		
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Publications		
<p>1. Yang YL, Lin TK, Huang YH. MiR-29a efficiently suppresses the generation of reactive oxygen species and α-synuclein in a cellular model of Parkinson's disease by potentially targeting GSK-3β. Eur J Pharmacol. 2024 Jul 5;974:176615.</p> <p>2. Lin YH, Lin KL, Wang XW, Lee JJ, Wang FS, Wang PW, Lan MY, Liou CW, Lin TK. Miro1 improves the exogenous engraftment efficiency and therapeutic potential of mitochondria transfer using Wharton's jelly mesenchymal stem cells. Mitochondrion. 2024 May;76:101856. (Correspondent author)</p> <p>3. Cha CH, Lin TK, Wu CN, Yang CH, Huang YW, Hwang CF. Relationship of Hearing Loss to Parkinson's Disease, Dementia, and APOE Genotype in Adults. Medicina (Kaunas). 2024 Apr</p> <p>4. Chou PC, Lee Y, Chang YY, Hung CF, Chen YF, Lin TK, Shih FY, Chen WF, Lin PY, Chong MY, Wang LJ. The Interrelationship of Benefit Finding, Demoralization, and Stigma among Patients with Parkinson's Disease and Their Caregivers. Healthcare (Basel). 2024 Apr</p> <p>5. Lan MY, Lin TK, Lace B, Utkus A, Burnyte B, Grigalioniene K, Lin YH, Inashkina I, Liou CW. Unraveling the Pathogenetic Mechanisms Underlying the Association between Specific Mitochondrial DNA Haplogroups and Parkinson's Disease. Cells. 2024 Apr 17;13(8):694.</p>		

Mitochondrial Transfer as a Novel Therapeutic Approach in Mitochondrial Disease Treatment

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The cellular power plants mitochondria possess their own genome. Alterations in mitochondrial DNA (mtDNA) causes mitochondrial bioenergetic dysfunction, decrease ATP supply which lead to many human diseases. A large scale (usually 4,977-base pairs) deletion in mtDNA is the common cause of several sporadic diseases including Pearson's syndrome, Kearns-Sayre syndrome (KSS) and chronic progressive external ophthalmoplegia (CPEO). Point mutation in mt-tRNALys (mt.3243A>G) and mt-tRNALeu (mt.8344A>G) lead to mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) and myoclonic epilepsy with ragged-red fibers (MERRF), respectively. For now, there is still no curable treatment for mitochondrial diseases. There are a number of approaches aiming to modulate mitochondrial function in mitochondrial diseases, including antioxidants supplement, exposure to hypoxia, stem cell therapies, replacing defective mtDNA in an oocyte and supplementation of a tissue with exogenous mitochondria through mitochondrial transplantation. Furthermore, there are potential therapeutic strategies trying to correct mutated point mutations utilizing gene editing therapies. Recently our serial studies focusing on mitochondrial transplantation therapy (MTT) may pave a new way to developing effective therapy. We have demonstrated that human Wharton's jelly mesenchymal stem cells (WJMSCs) can transfer healthy mitochondria to disease cells harboring mtDNA deletion or mutation and effectively reduce mtDNA mutation burden as well as improve mitochondrial bioenergetics. Our preliminary results present that WJMSCs-conducted MTT also reduce large-scale deletion of mtDNA in KSS patient's fibroblasts. In this talk, we will share our data of WJMSCs-based MTT and discuss the potential therapeutic strategy of MTT for the enhancement of mitochondrial function in diseases relevant to mitochondrial disorder



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KSBMB, ASHG, AACR, ASCO		
Publications		
1. An J*, Nam CH, Kim R, Lee Yunah, Won H, ..., Ju YS#. Mitochondrial DNA mosaicism in normal human somatic cells. <i>Nature Genetics</i> In press		
2. Nam CH*, Youk J*, Kim JY, Lim J, ..., Kwon HW#, Kim MJ#, Ju YS#. Widespread somatic L1 in normal colorectal epithelium. <i>Nature</i> . 2023.		
3. Park S*, Mali NM*, Kim R*, Choi J-W, ..., Oh JW#, Ju YS#. Clonal dynamics in early human embryogenesis inferred from somatic mutation. <i>Nature</i> . 2021.		
4. Yuan Y*, Ju YS*, Kim Y*, Li J, Wang J, ... , & Liang H. Comprehensive molecular characterization of mitochondrial genomes in human cancers. <i>Nat Genet</i> . 2020.		
5. Lee JJ-K*, Park S*, Park H, Kim S, ... , Ju YS# (Lead Contact) & Kim YT#. Tracing oncogene rearrangements in the mutational history of lung adenocarcinoma. <i>Cell</i> . 2019.		
6. Ju YS*, Alexandrov LB, Gerstung M, Martincorena I, ... , Campbell PJ. Origins and functional consequences of somatic mitochondrial DNA mutations in human cancer. <i>eLife</i> . 2014.		

Mitochondrial DNA mosaicism in normal human somatic cells

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KAIST

Somatic cells accumulate genomic alterations with age; however, our understanding of mitochondrial DNA (mtDNA) mosaicism remains limited. Here we investigated the genomes of 2,096 clones derived from three cell types across 31 donors, identifying 6,451 mtDNA variants with heteroplasmy levels of 0.3%. While the majority of these variants were unique to individual clones, suggesting stochastic acquisition with age, 409 variants (6%) were shared across multiple embryonic lineages, indicating their origin from heteroplasmy in fertilized eggs. The mutational spectrum exhibited replication-strand bias, implicating mtDNA replication as a major mutational process. We evaluated the mtDNA mutation rate (5.0×10^{-8} per base pair) and a turnover frequency of 10–20 per year, which are fundamental components shaping the landscape of mtDNA mosaicism over a lifetime. The expansion of mtDNA-truncating mutations toward homoplasmy was substantially suppressed. Our findings provide comprehensive insights into the origins, dynamics and functional consequences of mtDNA mosaicism in human somatic cells.



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Publications

1. Sung-Ik Cho*, Kayeong Lim*, Seongho Hong*, Jaesuk Lee, Annie Kim, Chae Jin Lim, Seungmin Ryou, Ji Min Lee, Young Geun Mok, Eugene Chung, Sanghun Kim, Seunghun Han, Sang-Mi Cho, Jieun Kim, Eun-Kyoung Kim, Ki-Hoan Nam, Yeji Oh, Minkyung Choi, Tae Hyeon An, Kyoung-Jin Oh, Seonghyun Lee† and Hyunji Lee† and Jin-Soo Kim†. Engineering TALE-linked deaminases to facilitate precision adenine base editing in mitochondrial DNA. Cell. 2024 Jan; 187, 95-109.

2. Da Eun Yoon, Na-Rae Kim, Soo-Ji Park, Tae Yeong Jeong, Bokkee Eun, Yongcheol Cho, Soo-Yeon Lim, Hyunji Lee, Je Kyoung Seong and Kyoungmi Kim†. Precise Base Editing Without Unintended Indels in Human Cells and Mouse Primary Myoblasts. Experimental and Molecular Medicine. 2023 Sep; 55, 2586-2595.

3. Hong Thi Lam Phan, Hyunji Lee† and Kyoungmi Kim†. Trends and prospects in mitochondrial genome editing. Experimental and Molecular Medicine. 2023 May; 55, 871-878.

4. Seonghyun Lee*, Hyunji Lee*, Gayoung Baek, Eunji Namgung, Joo Min Park, Sanghun Kim, Seongho Hong and Jin-Soo Kim. Enhanced mitochondrial DNA editing in mice using nuclear exported TALE-linked deaminases and nucleases. Genome Biology. 2022 Oct; 23:211.

5. Seonghyun Lee, Hyunji Lee, Gayoung Baek and Jin-Soo Kim. Precision mitochondrial DNA editing with high-fidelity DddA-derived base editors. Nature Biotechnology. 2022 Oct; 41:378-386.

Mitochondrial genome editing

Hyunji Lee

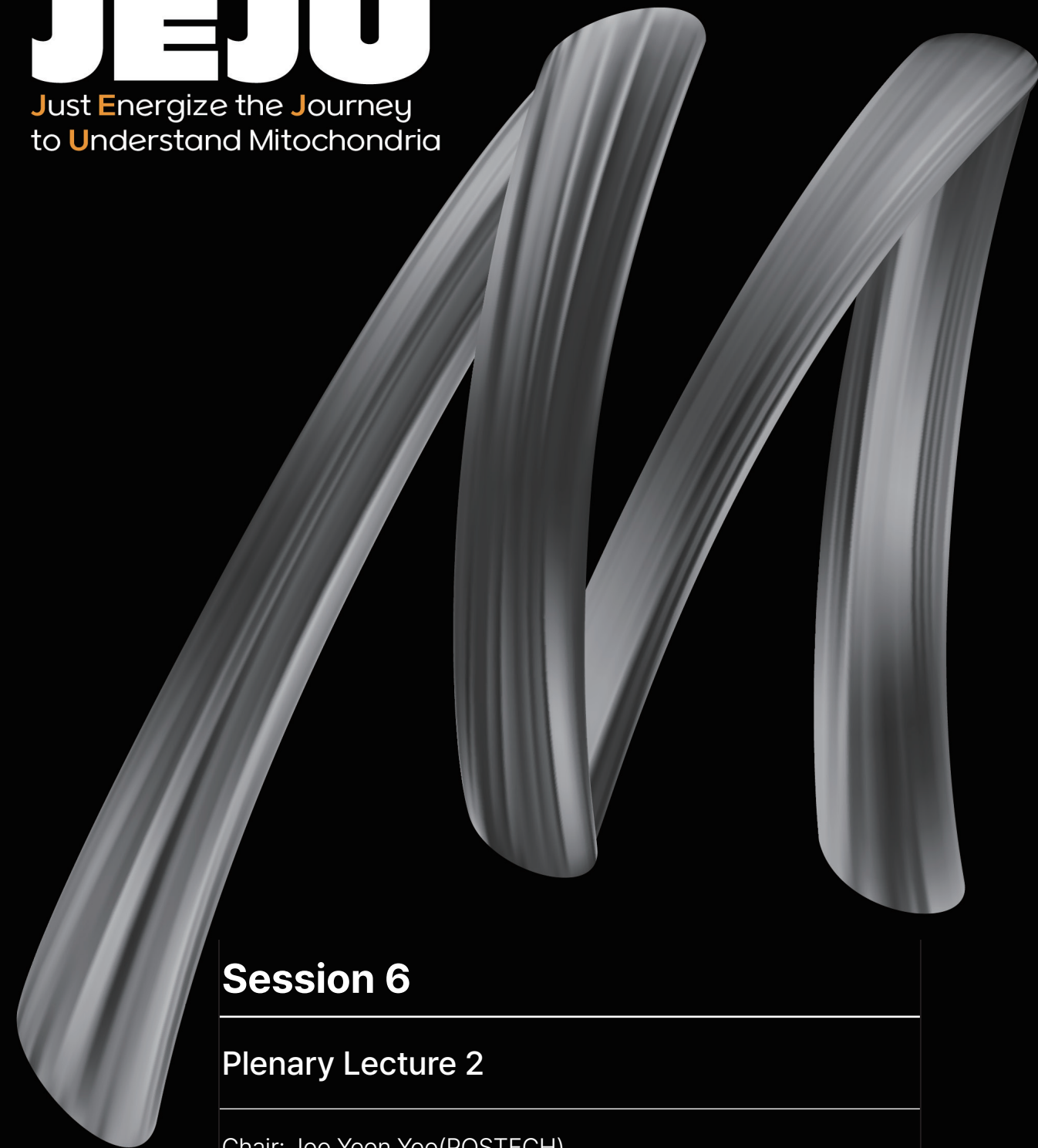
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Mitochondria is of fundamental importance in programmed cell death, cellular metabolism, and intracellular calcium concentration modulation. Within the mitochondria there is DNA with genetic information important for mitochondrial function called mitochondrial DNA (mtDNA). Inherited mitochondrial disorders via mtDNA mutation cause several diseases in various organs and systems. Nevertheless, mtDNA editing, which plays an essential role in the treatment of mitochondrial disorders, still faces several challenges. Therefore, the development of animal models or treatments for mitochondrial genetic diseases has been quite limited. Recently, programmable editing tools such as cytosine base editors derived from DddA (DdCBE), transcription activator-like effector (TALE)-linked deaminases (TALED) for mtDNA base editing have emerged with considerable potential for correcting pathogenic mtDNA variants. I describe recent advances in this field, including structural biology and repair mechanisms, and introduce the advanced strategies required to apply mtDNA base editors to mice and various mitochondrial DNA editing mouse model created using them. Ultimately, the potential medical applications and disease modeling of mtDNA editing for the treatment of mitochondrial diseases are discussed.



The 18th International Conference of Korean Society for
Mitochondrial Research and Medicine (KSMRM)
in conjunction with 15th Symposium of Mitochondrial Section of KSMCB

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Session 6

Plenary Lecture 2

Chair: Joo Yeon Yoo(POSTECH)
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Professional Experience

2023	Director	Cardiovascular & Metabolic Disease Core-Facility Center, Ministry of Education
2021	Director	Smart Marine Therapeutic Center, Inje University
2019	Director	INNOPOLIS Gimhae, Ministry of Science and ICT, Korea
2006	Director	Cardiovascular and Metabolic Disease Center, Inje University
1994	Professor	College of Medicine, Inje University

Academic Society

2006.11-2009.12	Vice president	Korean Society for Mitochondrial Research and Medicine (KSMRM)
2010.01-2014.12	Secretary General	KSMRM
2015.01-2019.12	Vice President	KSMRM
2020.01-2022.12	President	KSMRM

Publications

1. Cereblon contributes to cardiac dysfunction by degrading Cav1.2α. European Heart Journal, 2022
2. Tetrahydrobiopterin in energy metabolism and metabolic diseases. Pharmacological Research, 2020
3. C1q/TNF-α-Related Protein 1 (CTRP1) maintains blood pressure under dehydration conditions. Circulation Research, 2018
4. Current and upcoming mitochondrial targets for cancer therapy. Seminars in Cancer Biology, 2017
5. FOXM1-induced PRX3 regulates stemness and survival of colon cancer cells via maintenance of mitochondrial function. Gastroenterology, 2015.

Exercise-induced cardiac adaptation

Jin Han

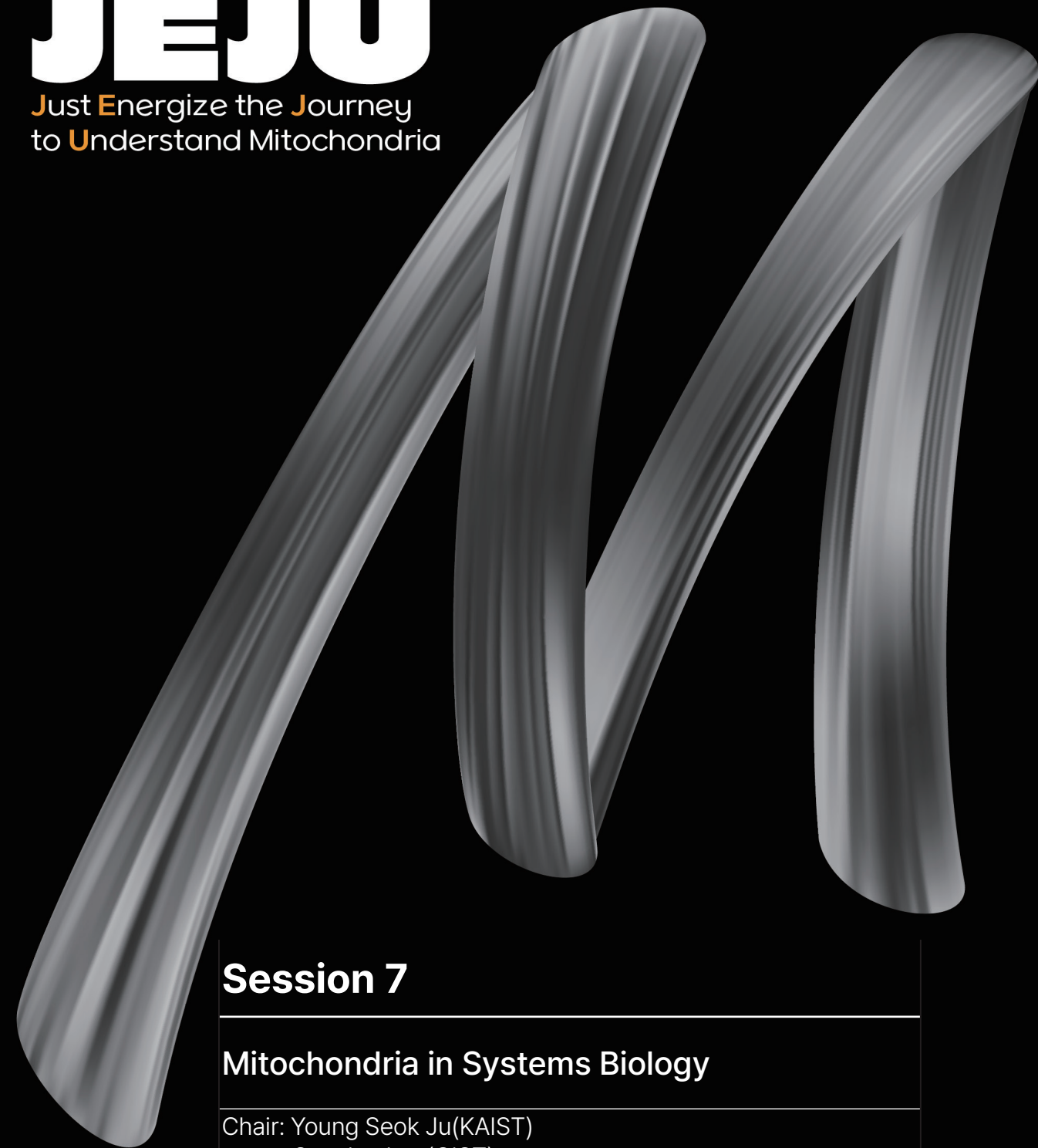
Cardiovascular and Metabolic Disease Center, College of Medicine, Inje University

The heart is the primary pump that circulates blood through the entire cardiovascular system, serving many important functions in the body. Exercise training provides favorable anatomical and physiological changes that reduce the risk of heart disease and failure. Compared with pathological cardiac hypertrophy, exercise-induced physiological cardiac hypertrophy leads to an improvement in heart function. Exercise-induced cardiac remodeling is associated with gene regulatory mechanisms and cellular signaling pathways underlying cellular, molecular, and metabolic adaptations. We found that aerobic exercise training decreased cereblon (CRBN), a substrate recognition protein in the E3-ligase ubiquitin complex. The binding target of CRBN varies according to tissues and cells, and the protein regulates various biological functions by regulating tissue-specific targets. As new endogenous targets of CRBN have been identified over the past decade, the physiological and pathological functions of CRBN and its potential as a therapeutic target in various diseases have greatly expanded. Here, I will present a cellular and molecular signaling pathway of CRBN to understand the exercise-induced cardiac adaptation.



The 18th International Conference of Korean Society for
Mitochondrial Research and Medicine (KSMRM)
in conjunction with 15th Symposium of Mitochondrial Section of KSMCB

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Session 7

Mitochondria in Systems Biology

Chair: Young Seok Ju(KAIST)
Sun Jae Lee(GIST)

Panel: Kwang-eun Kim(Yonsei Univ.)
Yunju Jo(GIST)

Jong-Eun Park, PhD

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Cross-tissue single-cell and spatial cell atlas to understand human diseases

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The recent advent of single-cell RNA sequencing technology has enabled the detailed characterization of human cells in various organs from diverse disease states. As single-cell data continues to pour out, it has become crucial to integrate them effectively into a comprehensive atlas. However, the discrepancy in metadata terminology and bioinformatic analysis pipeline across publicly deposited datasets often hinders the integration at the cell count matrix level. In this study, using an automatic public data search process, we unbiasedly collected over 20 million single-cell transcriptomic profiles from more than 500 independent studies, which contain more than 2,000 single-cell transcriptome datasets from diverse human organs and disease states. We invented a single-cell data remapping pipeline for the efficient re-analysis of the whole dataset from the raw sequence files at its highest genome coverage while excluding the biases from computational data processing steps. Metadata information has been curated and classified to provide harmonized terminology for the entire dataset. The integration of remapped single-cell transcriptome dataset minimizes the batch effect, allowing for the robust identification of cell types and the organ-specific, disease-specific, and sex-specific gene signatures for each cell type. As our remapping pipeline utilizes a genomic binning approach, the splicing patterns and intergenic transcripts were also retrieved, maximizing the interpretability of the single-cell transcriptome. Using this reference atlas of human cell types, we provide a universal reference for the deconvolution and interpretation of multi-organ spatial transcriptomics data collection. Finally, we have applied large language model to replicate the manual curation process, which could reach up to ~90% accuracy. In conclusion, we represent a fully curated, annotated, and harmonized cell network that could provide a fundamental axis for future data integration.

Education

2005.03-2009.02	B.S.	Seoul National Univ., Biological Science
2009.03-2015.08	Ph.D.	Seoul National Univ., Biological Science

Professional Experience

2015.09-2017.02	Postdoc	IBS center for RNA biology, Seoul National University
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Publications

1. **Kang, J.***, Lee, J.-H.*; ..., Lee, S.-H.#, Choi, J. K.#, **Park J.-E# (2024)**. Systematic dissection of tumor-normal single-cell ecosystems across a thousand tumors of 30 cancer types. *Nature Communications*, **15**:4067

2. **Kim, S.***, Leem, G.*; ..., Kang C. M.#, Bang. S.#, **Park J.-E# (2024)**. Integrative analysis of spatial and single-cell transcriptome data from human pancreatic cancer reveals an intermediate cancer cell population associated with poor prognosis. *Genome Medicine*, 16:20.

3. Kwon, J.* **Kang, J.***, ..., An H. J.#, Lee H.-O.#, **Park J.-E#**, Choi, J. K.# (2023). Single-cell mapping of combinatorial target antigens for CAR switches using logic gates. *Nature Biotechnology*, 1-13.

4. **Kang, J.***, Kim, M.*; Yoon, D. Y.* **Kim, W. S., ...**, **Park, M.**, Lee, J. S., **Park J.-E.#**, & Kim, S. M.# (2023). AXL+ SIGLEC6+ dendritic cells in cerebrospinal fluid and brain tissues of patients with autoimmune inflammatory demyelinating disease of CNS. *Clinical Immunology*, 109686.

5. **Park, J.-E.***, ..., Taghon, T., Haniffa, M., Teichmann, S.A., (2020), A cell atlas of human thymic development defines T cell repertoire formation. *Science* 367, eaay3224



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Education

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Professional Experience

2016.03-2019.12	Postdoctoral Fellow	Seoul National University
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Publications

1. Sung, S. *, Kim, E. *, Niida, H., Kim, C#, and Lee, J#. (2023). Distinct characteristics of two types of alternative lengthening of telomeres in mouse embryonic stem cells. *Nucleic Acids Res* 51, 9122–9143 (#co-corresponding author)

2. Kang, J., Kim, M., Kwon, E., Lee, K., Kim, C#, Kwon, K., and Yang, Y. (2023). Identification of novel genes associated with exercise and calorie restriction effects in skeletal muscle. *Aging* 15. (#co-corresponding author)

3. Jeong, J., Han, J., Jung, Y., Lee, S., Park, S., Park, M., Shin, M., Kim, N., Kang, M., Kim, S., Lee, K., Kwon, K., Kim, C., Yang, Y., Hwang, G., & Kwon, E. (2023). A new AMPK isoform mediates glucose-restriction induced longevity non-cell autonomously by promoting membrane fluidity. *Nature communications*, 14(1), 288.

4. Kim, J., and Kim, C#. (2022). A beginner's guide to assembling a draft genome and analyzing structural variants with long-read sequencing technologies. *STAR Protocols* 3, 101506

5. Kim, S., and Kim, C#. (2021). Transcriptomic Analysis of Cellular Senescence: One Step Closer to Senescence Atlas. *Mol. Cells* 44, 136–145.

6. Kim, E., Kim, J., Kim, C., and Lee, J. (2021). Long-read sequencing and de novo genome assemblies reveal complex chromosome end structures caused by telomere dysfunction at the single nucleotide level. *Nucleic Acids Res.* 49, 3338–3353.

7. Kim, C. *, Sung, S. *, Kim, J.-S. *, Lee, H., Jung, Y., Shin, S., Kim, E., Seo, J.J., Kim, J., Kim, D., et al. (2021). Telomeres reformed with non-telomeric sequences in mouse embryonic stem cells. *Nature Communications* 12, 1097.

8. Kim, C*, Sung, S*, Kim, J*, Lee, J. (2020). Damages, repair and reconstruction of telomeres and subtelomeric regions: implications for genetic variability and karyotype evolution. *BioEssays* 42(6):1900177

9. Kim, C*, Kim, J*, Kim, S*, Cook, D.E., Evans, K.S., Andersen, E.C., and Lee, J. (2019). Long-read sequencing reveals intra-species tolerance of substantial structural variations and new subtelomere formation in *C. elegans*. *Genome Research* 29: 1023-35. (On the Cover)

10. Seo, B*, Kim, C*, Hills, M*, Sung, S., Kim, H., Kim, E., Lim, D.S., Oh, H.-S., Choi, R.M.J., Chun, J., et al. (2015). Telomere maintenance through recruitment of internal genomic regions. *Nature Communications* 6. (*co-first author, Top 5 Basic Science Achievement, BRIC)

Quasi-spatial single-cell transcriptome based on physical properties defines early aging associated niche in liver tissue

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



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Education

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Professional Experience

2019.03~	Associate Professor	School of Life Sciences, GIST
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2014.08~2015.06	Postdoctoral Fellow	Department of Life Sciences, POSTECH

Professional Experience

2019	Committee	Korean Society for Molecular and Cellular Biology
2019	Committee	Korean Society for Biochemistry & Molecular Biology
2019	Committee	Korea Genome Organization
2021	Committee	Korean Society for Bioinformatics

Publications

1. Kim GD*, Shin SI*, Jung SW, An H, Choi SY, Eun M, Jun CD, Lee S#, Park J# (2024) Cell Type- and Age-Specific Expression of lncRNAs across Kidney Cell Types. J Am Soc Nephrol. doi: 10.1681/ASN.0000000000000354

2. Yoon B, Kim H, Jung SW#, Park J# (2024) Single-cell lineage tracing approaches to track kidney cell development and maintenance. Kidney Int. S0085-2538(24)00244-8

3. Eun M*, Kim D*, Shin SI, Yang HO, Kim DK, Choi SY, Park S, Moon KC, Kim DK, Lee H*, Park J* (2024) Chromatin accessibility analysis and architectural profiling of human kidneys reveal key cell types and a regulator of diabetic kidney disease. Kidney Int. 105(1) 150-164

4. Luo H, Xia X, Huang LB, An H, Cao M,, Park J*, Xu H* (2022) Pan-cancer single-cell analysis reveals the key role of cancer-associated fibroblasts in the tumor microenvironment. Nat Comm. 13(1):6619.

5. An H, Eun M, Yi J, Park J (2022) CRESSP : A comprehensive pipeline for prediction of immunopathogenic SARS-CoV-2 epitopes using structural properties of proteins. Brief. Bioinform. 10;23(2):bbac056.

6. Luo H, Xia X, Kim GD, Liu Y,, Wei T*, Park J*, Xu H* (2021) Characterizing dedifferentiation of thyroid cancer by integrated analysis. Sci Adv. 7(31):eabf3657.

7. Dhillon P, Park J* et al. (2021) The Nuclear Receptor ESRRA Protects from Kidney Disease by Coupling Metabolism and Differentiation. Cell Metab. 2;33(2):379-394.e8. (co-corresponding author)

Mouse Single-Cell Long-Read Splicing Atlas by Ouro-Seq

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Almost exclusive to multicellular life forms, alternative splicing increases transcriptome and proteome diversity. Although single-cell multi-omics technologies have enabled groundbreaking research in the field of biomedical science, there have been limited studies on expression patterns of transcript isoforms, one of the critical layers of cellular information, due to technical limitations. Here, we introduce Ouro-Seq, a novel single-cell long-read sequencing framework that combines a versatile artifact removal mechanism without length bias and a robust DNA size selection method for the comprehensive characterization of intact full-length mRNA species of varying sizes (up to 6 kbp) at a single-cell resolution. Using Ouro-Seq, we constructed the Mouse Single-Cell Splicing Atlas by collecting full-length transcriptomes of 103,304 nuclei or cells from 12 major organs and tissues of adult mice (*Mus musculus*). We characterized transcript usage patterns for the majority of protein-coding genes across ~200 mouse cell types in full length. With the resolution of single cells and single mRNA species, our atlas captured previously unappreciated complexity of functional heterogeneity across individual cells. We also developed Ouro-Enrich which enables targeted sequencing for full-length transcriptome of mitochondrial genes in individual cells. Our long-read scRNA-seq technology and whole-organism single-cell splicing atlas will help advance the understanding of alternative splicing and enhance our comprehension of various healthy and diseased cells.



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Poster Session

P-01

Transcriptome analysis in colon carcinogenesis by using Tlr13-deficient mouse model (Oral Presentation - 1)

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Maintaining a balanced intestinal environment relies on proper interactions between the host and its microbiota. Disruptions in these interactions can lead to inflammatory bowel diseases. Toll-like receptors (TLRs) detect microbial components and are crucial for host-microbe interactions in both healthy and diseased states. TLR13 is known for enhancing the host's defense against pathogenic bacteria. However, its role in maintaining intestinal equilibrium and its impact on colitis-associated colon cancer (CAC) have not been fully explored. This study investigates how TLR13-mediated signaling influences intestinal health and tumor development by using in vivo mouse model of CAC. Transcriptome analysis showed that numerous Differentially Expressed Genes (DEGs) are upregulated in tumor regions compared to normal colon regions in both wild-type (WT) and Tlr13-deficient (KO) genotypes. A heat map of 4,806 DEGs revealed that the KO tumor group had a distinct gene expression profile compared to the other groups. Notably, the KO tumor vs. KO normal group had the highest number of DEGs (879 upregulated and 2,974 downregulated). The Kyoto Encyclopedia of Genes and Genomes pathway enrichment showed the lowest False Discovery Rate values in the KO tumor versus KO normal group, with pathways related to cancer, intestinal diseases, and cytokine signaling being upregulated. Overall, Tlr13-deficient mice displayed significant changes in the gene expression profile of colonic tumor tissue. In accordance, Tlr13-deficient mice were more susceptible to CAC, with increased production of IL-6, IL-12, and TNF- α cytokines and enhanced STAT3, NF- κ B, and MAPK signaling in colon tissues. These results indicate that TLR13 exhibits a protective function in maintaining intestinal homeostasis and inhibiting CAC. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (RS-2023-00270936).
Keywords: Toll-like receptor 13; Microbiota; Intestinal homeostasis; Colon cancer; STAT3 signaling

P-02

Protective effect of Jeramon pulp against ultraviolet B ray-induced human HaCaT keratinocyte aging

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The purpose of this study was to confirm that the pulp components of Jeramon, Korea's first lemon variety, prevent aging of human HaCaT keratinocytes induced by ultraviolet B (UVB) rays. Jeramon pulp (JP) was extracted with ethanol and used in the experiment at a concentration of 50 μ g/ml, and 30 mJ/cm2 UVB was irradiated to the cells to induce aging. As a result of measuring the superoxide anion and hydroxyl radical scavenging effect of JP using electron spin resonance technology, it was confirmed that the scavenging effect was significant. After staining with H2DCFDA, a reactive oxygen species (ROS) measurement reagent, the use of JP as a strong UVB-induced ROS scavenger was confirmed through flow cytometry and confocal microscopy. Intracellular calcium concentration measured with Fluo-4 AM fluorescent dye was found to be significantly increased by UVB light and effectively decreased by JP. Western blotting assay proved that the expression of MMPs protein caused by UVB light irradiation in cells was partially inhibited by the pretreatment of JP, but the opposite was true for tissue inhibitor of metalloproteinase-1. Moreover, it was shown that the activity of MMP was also suppressed. As a result of confirming the expression of signal-related proteins that caused this result, the expression of Phospho-JNK, phospho-SEK, phospho-c-Jun, and c-Fos induced by UVB was significantly suppressed by JP. Therefore, JP seems to be an excellent natural material for inhibiting photo-ageing and improving skin aging (RS-2023-00270936).

P-03

Protective Effects of 3,5,7-Trihydroxyflavone on Particulate Matter 2.5 and Ultraviolet B Radiation-induced Oxidative Stress and Apoptosis in HaCaT Keratinocytes

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Ultraviolet B radiation (UVB) and particulate matter 2.5 (PM2.5) exposure both induce oxidative stress in biological systems, leading to various harmful effects on human health. This study investigated whether 3,5,7-trihydroxyflavone (THF), a flavonoid, that has antioxidant, anti-apoptotic, and anti-inflammatory properties, prevents UVB and PM2.5-induced apoptosis in HaCaT human keratinocytes. The results demonstrated that THF strongly inhibited PM2.5 and/or UVB radiation-induced reactive oxygen species (ROS) production, lipid peroxidation, mitochondrial damage, protein carbonylation, and DNA damage. THF protected cells from apoptosis induced by PM2.5 and/or UVB radiation. Furthermore, THF efficiently regulates the pro-apoptotic and anti-apoptotic proteins in response to PM2.5 treatment via caspase signaling pathways. In addition, THF decreased PM2.5-induced apoptosis by inhibiting the MAPK signaling pathway, as shown by the use of MAPK inhibitors. The findings suggest that THF has antioxidant properties and may protect cells from oxidative damage and apoptosis caused by PM2.5 and UVB radiation (RS-2023-00270936).

P-04

Preventive ability of fucoxanthin against PM2.5-induced inflammation and aging in keratinocyte cells (Oral Presentation - 2)

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Fucoxanthin is a natural carotenoid, exists in marine brown algae, and is processed with a wide range of therapeutic abilities against cancer, diabetes, and obesity. Particulate matter 2.5 (PM2.5) is referred to as a small particle with a ≤ 2.5 μ m diameter, which is associated with inflammation, cardiovascular dysfunction, cancer, and aging. Therefore, the present study was focused on assessing the preventive ability of fucoxanthin against PM2.5-mediated human HaCaT keratinocyte dysfunctions. Initial assessments proved that fucoxanthin could restore the PM2.5-impaired cell viability and fucoxanthin reduced PM2.5-induced cellular reactive oxygen sepsis (ROS) generation which was assessed by H2DCFDA staining. Furthermore, fucoxanthin alleviates PM2.5- induced cellular lipid peroxidation, DNA damage, and mitochondria membrane depolarization. Western blot assessment revealed that fucoxanthin can mitigate the PM2.5-induced nuclear factor- κ B, proinflammatory cytokine expression, and inflammasome activation. Additionally, colony formation and cell cycle assessments revealed that fucoxanthin could alleviate PM2.5-impaired cell proliferation. Also, fucoxanthin alleviated the PM2.5-mediated senescence-associated β -galactosidase and matrix metalloproteinases expression. Collectively, fucoxanthin mitigated the PM2.5-induced skin cell inflammation, senescence, and aging, suggesting that fucoxanthin is a potential therapeutic agent to prevent PM2.5-mediate skin cell damage (RS-2023-00270936).

P-05

Investigating the Efficacy of 3,4-Dihydroxycinnamic Acid in Modulating PM2.5-induced Cellular Dysfunction and Apoptosis in HaCaT Keratinocytes

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3,4-Dihydroxycinnamic acid (DCA), a phenolic compound prevalent in plant tissues, exhibits significant antioxidant, anti-inflammatory, and immunomodulatory activities in vitro and in vivo. Particulate matter 2.5 (PM2.5) induces oxidative stress and cellular dysfunction in human HaCaT keratinocytes. This study aimed to investigate DCA's potential in mitigating PM2.5-induced cellular dysfunction and apoptosis in HaCaT keratinocytes. Cells were exposed to PM2.5 with or without DCA (40 μ M) treatment. Cell viability, oxidative stress markers, mitochondrial dysfunction, and apoptotic pathways were assessed via electron spin resonance, confocal, and western blot analysis. DCA treatment reduced PM2.5-induced oxidative stress, decreased reactive oxygen species production and lipid peroxidation, and attenuated mitochondrial dysfunction and DNA damage. DCA modulated apoptosis-related protein expression, decreasing pro-apoptotic factors caspase-3, and caspase- 9. These comprehensive results demonstrated DCA's effectiveness in modulating PM2.5-induced cellular dysfunction and apoptosis in HaCaT keratinocytes, suggesting its potential protective agent against PM2.5-induced cellular damage in skin cells. (RS-2023-00270936)



P-06

ATF5 modulates thermogenic responses and differentiation in Brown Adipose Tissue during cold exposure

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Obesity is a significant global health issue closely linked to diabetes. A key factor in the context of obesity is thermogenesis, which plays a pivotal role in regulating energy expenditure to maintain body temperature. Brown adipose tissue (BAT) is vital for non-shivering thermogenesis, energy balance, and metabolic health, with mitochondria playing a key role in energy and heat production. Cold exposure stimulates BAT thermogenesis, making it a critical period for studying the mechanisms involved. This study provides mechanistic insights into BAT thermogenesis and specifically examines the influence of ATF5 (activating transcription factor 5), a key regulator of the mitochondrial stress response (MSR), on the modulation of heat generation and differentiation during mitochondrial stress and cold exposure within the context of BAT. Male C57BL/6 mice at 6 weeks of age were exposed to 4°C, and BAT and inguinal white adipose tissue (iWAT) were collected for quantitative real-time PCR (qPCR) analysis. In vitro, brown adipocytes were cultured for 7 days, with gene expression evaluated via qPCR and protein levels by Western blotting. ATF5 expression was inhibited using siAtf5, and changes were analyzed. Oxygen consumption rates (OCR) and fatty acid oxidation (FAO) flux were measured in brown adipocytes. Heat maps represented gene and protein expression differences. In our study, we observed that cold exposure triggered a notable increase in ATF5 expression and thermogenic gene expression within BAT. Particularly, ATF5 expression in BAT exhibited a significant elevation during exposure to cold. Moreover, acute cold exposure induced ATF5 expression not only in BAT but also in iWAT. Furthermore, under brown adipocytes differentiation conditions, ATF5, lipolysis, and MSR-related protein expression showed notable increments. To further elucidate the role of ATF5 in BAT, Atf5 knockdown experiments were conducted in brown adipocytes, resulting in reduced MSR-related gene expression. Additionally, Atf5 knockdown led to diminished mitochondrial function in both undifferentiated and differentiated brown adipocytes, as confirmed by measuring OCR. Acute cold exposure induces ATF5 expression in BAT, with ATF5 playing a crucial role in brown fat preadipocyte differentiation in vitro. Importantly, our findings indicate that siAtf5 induces a reduction in citrate flux generated through FAO following palmitate treatment, underscoring ATF5’s critical involvement in fatty acid metabolism in brown adipocytes. Furthermore, inhibition of adipose triglyceride lipase (ATGL) decreased ATF5 expression in both brown adipocytes and BAT. Acute cold exposure induces ATF5 expression in BAT, emphasizing ATF5’s crucial role in the differentiation of brown fat precursor cells in vitro. Additionally, ATF5 inhibition resulted in impaired mitochondrial function in both undifferentiated and differentiated brown adipocytes, as evidenced by reduced OCR. These findings underscore ATF5’s potential as a key regulator of thermogenesis, offering significant implications for developing therapeutic strategies targeting obesity and diabetes-related complications.

P-07

Transplanting External Mitochondria Enhances Blood-Brain Barrier Integrity (Oral Presentation - 3)

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Angiogenesis is vital for supplying nutrients and oxygen to damaged brain areas. However, when angiogenesis is rapidly induced by events like strokes or tumor formation, the newly formed blood vessels often lack full maturation, unlike those developed under normal circumstances. This immaturity is primarily due to the incomplete development of brain microvascular endothelial cells (BMECs), leading to the formation of fragile and permeable blood vessels. BMECs are unique in their heavy dependence on mitochondria to maintain the blood-brain barrier (BBB). This is because they require more energy, have a high metabolic rate, and need to sustain tight cellular junctions, all of which increase their mitochondrial volume. The role of mitochondria in BMECs during angiogenesis was not fully understood. To promote the maturation of BMECs and explore the relationship between angiogenesis and mitochondrial function, a technique called mitochondrial transplantation was employed. Here, we explore if mitochondria from umbilical cord-derived mesenchymal stem cells (UC-MSCs) could restore both the integrity of the BBB and mitochondrial functionality in immature BMECs. We developed a microfluidic organ-on-a-chip platform to efficiently monitor and examine the angiogenesis of BMEC to enhance our investigation of endothelial cell sprouting. Human BMECs were induced to undergo acute angiogenesis with a cocktail of angiogenic factors. As a proof of concept, we utilized mitochondria isolated from UC-MSCs and co-incubated them with the angiogenesis-induced HBMECs. Our findings show that mitochondria derived from UC-MSCs, when transplanted, are effectively absorbed into the cells. Importantly, these mitochondria have a transformative impact on the damaged and disjointed blood vessels, restoring their functional properties. This research initiates a groundbreaking method for converting dysfunctional blood vessels into operational ones. Additionally, it broadens our knowledge about the potential uses of cellular organelles in developing new therapeutic strategies for BBB-related diseases.

P-08

Low-dose chitosan oligosaccharide suppresses spheroidogenesis of melanoma cells

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Melanoma, known to be a highly heterogenous tumor, shows metastatic properties among skin cancers. Chitosan oligosaccharide (COS) has a wide variety of biological potentials including anti-cancer activity, but the feasible anti-cancer effects of COS on melanoma have not been thoroughly determined. Therefore, we investigated the anti-cancer effects of COS on A2058 melanoma cells with cell viability assay, wound healing assay, spheroidogenic activity and morphometry under different environments, and Western blotting. COS showed little effects on cell viability and wound healing of A2058 melanoma cells, up to 500 µg/mL. COS inhibited spheroid formation below 50 µg/mL, with higher efficacy in fetal bovine serum-supplemented environment as compared to growth factor-supplemented environment. At the concentration of 50 µg/mL COS, the number of spheroids was increased, and the size decreased with significance. Spheroidogenesis, linked to the anoikis-resistant epithelial-mesenchymal transition, was closely related to the expression of fibronectin, N-cadherin, and CD44. COS increased the expression of N-cadherin, E-cadherin, and vimentin in 2D monolayer culture and decreased fibronectin in 3D spheroid culture in a dose-dependent manner. These results suggest that low-dose COS might be a potent anti-metastatic natural product without any toxic effects. (This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (RS-2023-00270936))

P-09

Myristoleic acid ameliorates the action of fine particulate matter on the rat dermal papilla cell by activating the Wnt/β-catenin pathway and reducing nuclear p62 accumulation

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Air pollution including particulate matter (PM) engenders health issues and increases disease-related mortality. In particular, fine particulate matter (PM 2.5, particles with an aerodynamic diameter of 2.5 µm or less) adversely affects health by being inhaled into the lungs, entering the circulatory system, and damaging several tissues. However, the action of PM 2.5 on the hair loss remains unclear. On the other hand, myristoleic acid, derived from seeds of plants in the Myristicaceae family, promotes the growth of rDPCs. Therefore, in this study, we explored the impact of PM 2.5 and whether myristoleic acid may protect the action of PM 2.5 in rat dermal papilla cells (rDPCs), which are key regulators of hair growth. PM 2.5 inhibited the growth of rDPCs, induced DNA damage, and reduced the expression of DP signature genes and growth factors. PM 2.5 disrupted the Wnt signaling pathway, which is crucial for hair follicle regeneration, by decreasing the mRNA levels of Wnt ligands and LRP6, and the phosphorylation of GSK3β and β-catenin. Additionally, PM 2.5 suppressed autophagy by increasing mTOR phosphorylation and p62 expression, while decreasing the expression of Beclin1, Atgs, and LC3A/B. However, myristoleic acid restored the reduced proliferation of rDPCs by PM 2.5 through activating the Wnt/β-catenin pathway and autophagy. Furthermore, myristoleic acid reduced PM 2.5-induced p62 accumulation in the nucleus of DNA-damaged cells. Our findings provide insights into the mechanisms underlying the adverse effects of PM 2.5 on hair follicles and suggest that myristoleic acid could potentially reverse PM 2.5-induced hair follicle damage. [Funding: This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (RS-2023-00270936)]

Keywords: Myristoleic acid, fine particulate matter, dermal papilla cells, autophagy, Wnt/β-catenin

P-10

Evogliptin, a DPP-4 inhibitor, prevents cardiac lipotoxicity and mitochondrial dysfunctions in type 2 diabetic mice model

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Dipeptidyl peptidase-4 (DPP-4) inhibitors are glucose-lowering drugs for type 2 diabetes mellitus (T2DM). We tested whether evogliptin® (EVO), a DPP-4 inhibitor, could protect against diabetic cardiomyopathy (DCM) and the underlying mechanisms. Eight-week-old db/db mice were administered EVO (100 mg/kg/day) daily by oral gavage for 12 weeks. db/db control mice and C57BLKS/J as wild-type (WT) mice received equal amounts of the vehicle. We examined the improvement in cardiac contraction/relaxation ability, cardiac fibrosis, and myocardial hypertrophy by EVO treatment. EVO lowered the blood glucose and HbA1c levels and improved insulin sensitivity, Cardiac systolic/diastolic function, hypertrophy, and fibrosis were improved in the EVO-treated group. EVO prevented cardiac lipotoxicity by reducing the accumulation of lipid droplets in the myocardium through suppression of CD36, ACSL1, FABP3, PPARgamma, and DGAT1 and enhancement of the phosphorylation of FOXO1. The EVO-mediated improvement in mitochondrial function and reduction in damage were achieved through activation of PGC1α/NRF1/TFAM, which activates mitochondrial biogenesis. Collectively, EVO improves cardiac function by reducing lipotoxicity and mitochondrial injury and provides a potential therapeutic option for DCM.

Keywords: Dipeptidyl peptidase-4, evogliptin, diabetic cardiomyopathy, cardiac fibrosis, lipotoxicity

P-11

Mitochondrial Chaperone, TRAP1 Interacts with MOTS-c to Modulate Cellular Metabolism. (Oral Presentation - 4)

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Mitochondria, the powerhouses of the cell, play a pivotal role in cellular metabolism. The mitochondrial chaperone TRAP1 (Tumor necrosis factor receptor-associated protein 1) is known for its protective functions against cellular stress, aiding in the folding and stabilization of mitochondrial proteins to maintain their functionality. Recent studies have identified MOTS-c (Mitochondrial open reading frame of the 12S rRNA-c), a mitochondrial-derived peptide, as a key regulator of metabolic homeostasis. MOTS-c has been shown to participate in various metabolic pathways, contributing to cellular homeostasis and metabolic disease prevention through its roles in promoting glucose uptake, improving insulin sensitivity, and anti-inflammatory effects. In this study, we investigate the interaction between TRAP1 and MOTS-c. We hypothesize that MOTS-c binding with TRAP1 through TRAP1 client binding site. Furthermore, we explore the possibility that inhibiting TRAP1, using an inhibitor such as MitoQ, liberates MOTS-c, allowing it to interact with other proteins and potentially revealing novel regulatory mechanisms in cellular metabolism. Elucidating the interaction between TRAP1 and MOTS-c could unveil novel therapeutic strategies for treating metabolic diseases such as inflammation, diabetes, and metabolic syndrome.

P-12

Implications of catecholamine levels on aging-related muscle loss

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Objective
The objective of this study is to investigate the association between catecholamine levels and age-related muscle loss. While catecholamines are known to play a crucial role in muscle biogenesis, persistent elevation of catecholamine levels, as seen in conditions such as pheochromocytoma or paraganglioma, has been linked to muscle wasting. However, the direct correlation between catecholamine levels and age-related muscle loss in humans remains unclear.

Methods
This retrospective study was conducted to evaluate the plasma levels of metanephrine and normetanephrine as well as clinical characteristics for 899 patients with adrenal incidentaloma on computed tomography undertaken for health examination or nonadrenal diseases from August 2014 to March 2024 in South Korea. The total abdominal muscle area (TAMA), low-attenuation abdominal muscle area (LAMA), normal-attenuation abdominal muscle area (NAMA), and extramyoecellular lipid area (EMCLA) were measured using cross-sectional CT data of the L3 lumbar vertebrae. Effect of beta-adrenergic agonists and beta blockers on protein kinase A and extracellular signal-regulated kinase pathway was determined in differentiated C2C12 myotubes.

Results
In this study, we compared the levels of catecholamines (metanephrine and normetanephrine) with age, sex, muscle mass, and fat mass in 899 patients diagnosed with adrenal incidentaloma over a 10-year period. The analysis revealed that the average metanephrine levels in men were 0.17 nmol/L, and normetanephrine levels were 0.63 nmol/L, significantly higher than those in women (p<0.05). Both metanephrine and normetanephrine levels showed a significant increase with advancing age (each with r=0.121, p=0.01 and r=0.249, p<.001). Normal-attenuation abdominal muscle area (NAMA) was positively correlated with metanephrine level, (r=0.163, p<.001) whereas fat mass showed a negative correlation. These findings indicate statistically significant differences in the impact of each factor on catecholamine levels. The beta-blockers atenolol and metoprolol increased ERK phosphorylation without significant effects on PKA signaling in differentiated C2C12 myotubes.

Conclusions
This study analyzed the effects of age, sex, muscle mass, and fat mass on catecholamine levels in patients with adrenal incidentaloma. The results indicate that catecholamine levels are higher in men, older individuals, and those with greater muscle mass and lower fat mass. Moreover, proper concentrations of catecholamine are important for maintaining muscle mass in humans. In vitro study also suggest that atenolol and metoprolol may be candidates for muscle preservation in the aged population.

P-13

Mitochondrial chaperone, TRAP1 regulates itochondrial functions for thermogenesis in adipocytes.

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Adipose tissue is pivotal for metabolism and energy homeostasis. Especially, brown and beige adipose tissues are important for regulating energy expenditure through adaptive thermogenesis. Both types of adipose tissue highly depend on mitochondrial functions for their role in thermogenesis. The mitochondrial molecular chaperone, tumor necrosis factor receptor-associated protein 1 (TRAP1), modulates cellular metabolism by altering the conformations, activity, and stability of various mitochondrial proteins. However, the role of TRAP1 in the thermogenic activity of adipose tissues has not been elucidated. In this study, it is identified that TRAP1 is a key modulator in regulating thermogenic activity of adipose tissue. Under cold exposure, adipose-specific TRAP1 knockout mice exhibit lower rectal temperatures compared to controls. In addition, they show enlarged lipid droplets, which indicate reduced lipid metabolism during cold exposure. Taken together, TRAP1 is necessary for thermogenesis under cold exposure in adipose tissues. These findings suggest that TRAP1 could be a promising target protein for therapeutic strategies in obesity and metabolic disorders.

P-14

Mitochondria-derived peptides humanin and formylated humanin promote STAT3-dependent skin repair (Oral Presentation - 5)

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Mitochondrial dysfunction is a hallmark of aging and other age-related diseases. Mitochondrial-derived peptides (MDPs), encoded by mitochondrial DNA, are implicated in age-related diseases. However, the role of MDPs in skin tissue remains unclear. This study investigates the effects of two MDPs, humanin (HN) and its formylated form (f-HN), on the wound healing process. HN and f-HN were administrated subcutaneously in vivo skin-hairless mice and applied to normal human epidermal keratinocytes in vitro. Both treatments significantly improved wound healing area recovery in skin tissue by day 8. Furthermore, HN and f-HN enhanced wound healing by promoting neovascularization and elevating collagen production, leading to improved re-epithelialization. In vitro assays showed that both MDPs increased phosphorylation of the STAT3 protein. F-HN also upregulated angiogenesis-related gene expression and promoted cell migration via the STAT3 signaling pathway, an effect inhibited by BP-1-102, a STAT3 inhibitor. These findings reveal a regulatory mechanism of MDPs in mouse skin wound healing through the STAT3 signaling pathway and suggest MDPs as a potential therapeutic agent for tissue repair. This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and BK21 FOUR program through the NRF under Ministry of Education.

Keywords: Mitochondrial-derived peptides, Humanin, Formylated Humanin, Skin wound healing, Angiogenesis, STAT3 signaling

P-15

PPARβ-induced changes in energy metabolism influence the proteome related to protein synthesis and quality control. (Oral Presentation - 6)

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Introduction: The expression of peroxisome proliferator-activated receptor beta (PPAR β), a nuclear receptor, impacts energy metabolism (EM), which may influence the synthesis of proteins and the regulation of protein quality control (PQC). In this study, we investigated the effects of PPAR β expression on metabolic and PQC proteomes using wild-type (Wt), skeletal muscle-specific PPAR β transgenic (mTG), and knockout (mKO) models.

Methods: Using Wt, mTG, and mKO mouse models, we conducted proteomics analysis on the Tibialis anterior (TA) muscle using LC-MS. After analyzing differentially expressed proteins, pathway enrichment analysis was performed to classify the altered proteins into specific metabolic pathways and functional groups.

Results: Pathway enrichment analysis revealed that in the mTG models, proteins associated with EM pathways such as OXPHOS, AMPK signaling, and glycolysis were significantly upregulated. Conversely, proteins related to protein synthesis and PQC pathways were downregulated in the mTG models. This suggests that PPAR β may promote energy metabolism while inhibiting protein synthesis and PQC processes. In the mKO models, there was no significant increase in the expression of proteins related to protein synthesis and PQC.

Conclusion: Our data suggest that PPAR β primarily regulates energy metabolism, which affects muscle protein expression related to protein synthesis and PQC. However, since we did not analyze the influence of PPAR β on the protein synthesis ratio and PQC function, further studies are necessary to identify PPAR β -induced effects on protein synthesis and PQC.

P-16

TRPC6 deficiency drives adipocyte hypertrophy and mitochondria dysfunction in mice

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Lipid metabolism, regulated by adipose tissues, is a critical factor in the pathophysiology of obesity. For proper functioning, adipose tissues expand in response to lipid storage demands through adipogenesis. While excessive adipogenesis can contribute to obesity, a sustained level is essential for the normal function of adipose tissues. In this study, we identified the transient receptor potential cation channel canonical member 6 (TRPC6), as a crucial regulator of adipogenesis in adipose tissues' precursor cells. The TRPC6 deficiency in mice resulted in systemic metabolic disorders resembling obesity phenotypes characterized by reduced insulin sensitivity and impaired glucose tolerance. Ablation of TRPC6 expression in adipocytes reduced adipogenesis but increased lipid droplet size, indicating a preference for hypertrophic rather than hyperplastic expansion. Transcriptomic analysis identified that the cAMP signaling pathway is the major downstream effector pathway of TRPC6 in preadipocytes, which is critical for adipogenesis. The loss of TRPC6 reduces cAMP response, resulting in dysfunctional adipocytes. Additionally, healthy adipocytes rely on mitochondria to maintain their metabolic activities. Consistent with the observed obese phenotype, TRPC6 knock-out (TRPC6 KO) mice exhibited a significant reduction in mitochondrial size and oxidative phosphorylation proteins in the white adipose tissues (WAT). Moreover, the oxygen consumption rate was decreased, and mitochondrial ROS production was elevated in TRPC6 KO white adipocytes. In summary, our findings identify TRPC6 as a novel key regulator of white adipocyte function, linking Ca²⁺ signaling to lipid metabolism and mitochondrial functions. [This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and the BK21 FOUR program through the NRF under the Ministry of Education)]

P-17

The Role of Ei24 in Fine-tuning STIM1-Driven SOCE and Mitochondrial Ca2+ Dynamics

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Store-operated calcium entry (SOCE) plays a crucial role in maintaining Ca2+ homeostasis in non-excitable cells by facilitating Ca2+ influx following the depletion of the endoplasmic reticulum (ER) Ca2+ stores. This mechanism involves stromal interaction molecules 1 (STIM1) acting as ER Ca2+ sensors and Orai1 proteins forming Ca2+ release-activated Ca2+ (CRAC) channels in the plasma membrane. Although the mitochondria-associated membrane (MAM) protein Ei24 (etoposide-induced gene 2.4 kb) is known to interact with ER Ca2+ channels directly, its effect on plasma membrane Ca2+ channels, particularly the CRAC channel, remains unclear. This study explores the role of Ei24 in modulating SOCE-mediated Ca2+ uptake into ER and mitochondria through its interaction with STIM1. Patch-clamp experiments revealed that Ei24 overexpression reduces CRAC current, while Ei24 knockout in HeLa cells significantly increased Ca2+ influx via the SOCE pathway, an effect that is reversible upon Ei24 reintroduction. Furthermore, SOCE- and histamine-stimulated MAM-mediated mitochondrial Ca2+ uptake was elevated in Ei24 knockout cells. Co-immunoprecipitation and NanoBit assays demonstrated a physical interaction between Ei24 and the CRAC activation domain (CAD) of STIM1. Fluorescence recovery after photobleaching (FRAP) assays further showed that Ei24 overexpression slows the kinetics of STIM1 mobilization. These findings illuminate the critical role of Ei24 in regulating the ER Ca2+ sensor STIM1 and its essential function in fine-tuning Ca2+ dynamics between ER and mitochondria. This research advances the understanding of Ca2+ homeostasis and provides valuable insights into the mechanisms of Ca2+ regulation, offering hope for potential therapeutic interventions in the future. [This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and BK21 FOUR program through the NRF under the Ministry of Education)]

Keywords: STIM1, CRAC channel, Mitochondria, ER-PM contact site, Ei24

P-18

Regulation of TRPML1-mediated lysosomal Ca2+ release and mitochondria function by WNK1 kinase in autophagy

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Autophagy is a significant cellular degradation pathway essential for maintaining cellular physiology and adapting to metabolic stress. Mitophagy, a specialized form of autophagy, recycles damaged mitochondria and regulates the biogenesis of new healthy mitochondria. TRPML1, a lysosomal Ca2+ release channel, plays a vital role in both autophagy flux and mitochondria Ca2+ uptake. While, WNK kinases are known regulators of ion channels and transporters, their role in TROML1 regulation in the context of autophagy remains unexplored. This study demonstrates that WNK kinases suppressed TRPML1, leading to inhibition of autophagy. Using HEK293 cells and HeLa cells expressing GCaMP3-labelled TRPML1, the overexpression of WNK1 or 4 suppressed TRPML1-mediated peri-lysosomal Ca2+ release. Additionally, mitoKeima- transfected HeLa cells, used as an indicator of mitophagy, showed increased red fluorescence under low pH conditions during mitophagy. Activation of TRPML1 by the agonist MLSA1, stimulated mitophagy, as evidenced by FITC fluorescence, indicating that TRPML1-mediated Ca2+ release regulates both mitophagy and autophagy. Notably WNK1 knock-down resulted in increased mitophagy, suggesting that WNK1 regulates mitophagy through TRPML1 Ca2+ release. The suppression of Ca2+ release and subsequent nuclear translocation of TFEB by WNK1 was rescued by a catalytically inactive mutant of WNK1 (kinase-dead mutant, K233M), highlighting the critical role of catalytic activity of WNK1 in TRPML1 regulation. Furthermore, insulin, an endogenous activator of WNK1, suppressed TRPML1-mediated Ca2+ release, an effect that was effectively reversed by pretreatment with WNK463, a WNK inhibitor or diC-16-Pi(3,5) P2. These results suggest that WNK1 inhibits TRPML1 activity via the suppression of class III phosphoinositide-3-kinase. Overall, our findings provide novel insights into the role of WNK kinase signaling in the regulation of both autophagy and mitophagy, specifically targeting TRPML1-mediated Ca2+ regulation and lysosomal biogenesis. [This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and the BK21 FOUR program through the NRF under the Ministry of Education)]

Keywords: TFEB, lysosomal biogenesis, lysosomal Ca2+

P-19

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

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Dysregulated intracellular Ca2+ 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 Ca2+ entry (SOCE) also plays a role in maintaining Ca2+-dependent filtration and protecting podocyte damage. In diabetic nephropathy, elevated podocyte Ca2+ 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 Ca2+ signaling, podocyte actin dynamics, and filtration, leading to proteinuria in CKD, are not fully understood. Our research demonstrates that Pi enhances mitochondrial Ca2+ 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 Ca2+ 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:Orai1fl/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 Ca2+ 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 Ca2+ regulation and filtration integrity.

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Keywords: SOCE, STIM1, Orai1, Ca2+ signaling, actin cytoskeleton, proteinuria, ROS

P-20

Development of MitoRAISE, real-time assessment of mitochondrial ATP synthesis response against inhibiting and stimulating substrates (Oral Presentation - 7)

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The primary role of mitochondria is to synthesize adenosine triphosphate (ATP) through oxidative phosphorylation. Understanding and accurately measuring mitochondrial ATP synthesis rate provides crucial insights about the mitochondrial function and its contribution to the overall energy homeostasis of the cell. Unlike traditional methods that estimate mitochondrial function by measuring ATP levels at a single time point or through oxygen consumption rates, this study introduces a novel approach to detect real-time relative change in ATP levels as cells respond to substrates that either activate or inhibit specific mitochondrial complexes. Mitochondrial complex I was activated using a mixture of glutamic and malic acid and inhibited by rotenone. Mitochondrial complex II was activated with succinate and inhibited by malonate. The sensitivity and specificity of the mitochondrial ATP synthesis response against inhibiting and stimulating substrates (MitoRAISE) assay were validated using isolated mitochondria and multiple cell lines. Functions of mitochondrial complex I and II showed positive correlation with both cell differentiation status and the quantity of mitochondria and cells. Following this validation, the mitochondrial function of peripheral blood mononuclear cells (PBMCs) from 19 females breast cancer patients were compared with PBMCs of 23 healthy females. Basal ATP levels, responses to rotenone and malonate, as well as mitochondrial DNA copy numbers were found to be significantly lower in breast cancer females. Since the MitoRAISE assay has demonstrated its efficacy in measuring the mitochondrial functional status of mitochondrial complexes I and II, we propose MitoRAISE assay as a potential tool for monitoring changes in the mitochondrial metabolic status associated with various diseases.



P-21

Expression Analysis of Mitochondrial Calcium Uniporter Highlights its Critical Roles in the Transition from MASLD to Hepatic Fibrosis

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Not all patients with metabolic liver disease progress to metabolic acidosis-associated steatohepatitis (MASH); some remain in metabolic dysfunction-associated steatotic liver disease (MASLD). While the role of mitochondria in lipid metabolism and fibrosis, a key feature of MASLD and MASH is well-established, the dynamic changes in mitochondrial gene expression during the progression of hepatic metabolic disorders remain unclear. To investigate the changes, we analyzed four genome-wide transcriptome profiles from liver tissue samples associated with liver disease. We categorized the samples into two cohorts based on the fibrosis progression: (1) from control to MASLD and (2) from MASLD to MASH. Differential expression (DE) analyses were conducted for each cohort, including DESeq2 and Limma. Summary statistics indicated that genes related to mitochondrial signaling, particularly those involved in Ca2+ homeostasis, were differentially expressed in both pathological progressions. All mitochondrial calcium uniporter (MCU) complex genes were upregulated in the transition from control to MASLD, whereas half were downregulated in the progression of MASLD to MASH. Additionally, mitochondrial-associated membrane (MAM)-associated genes regulating ER- and mitochondria-mediated Ca2+ signaling- exhibited opposing expression patterns in MASLD and MASH. An inverse variance weighted (IVW) meta-analysis yielded identical findings by summarizing the overall gene signature across the dataset. To further explore the relationship between MCU complex genes and fibrosis, we conducted correlation analyses and identified a highly significant association between mitochondrial Ca2+ signaling and fibrosis-related genes. In conclusion, this study suggests that MCU complex genes and MAM-associated proteins, which regulate mitochondrial Ca2+ signaling, play distinct roles in the progression of MASLD and MASH.

[This study was supported by the National Research Foundation of Korea (NRF-2022R1A2C2011079 and BK21 FOUR program through the NRF under Ministry of Education)].

Keywords: Mitochondria, Ca2+ signaling, metabolic disorder, Liver

P-22

Ca²⁺-inhibited mitochondrial protein degradation in brown adipocytes

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Brown adipose tissue is involved in maintaining body temperature constant upon cold exposure or sympathetic stimulation. Furthermore, thermogenic induction of brown adipocytes improves insulin resistance, hyperlipidemia, and adiposity. This study focuses on the acute regulation of mitochondrial protein abundance in brown adipocytes by cytosolic and mitochondrial Ca2+ elevation due to adrenergic stimulation. In brown adipocytes, 1 hour incubation of norepinephrine (NE) elevated protein levels of uncoupling protein 1 (UCP1) and mitochondrial calcium uniporter (MCU) with increased mitochondrial respiration. Cycloheximide, a translation inhibitor, did not affect NE-induced upregulation of mitochondrial proteins, while MG132, a proteasome inhibitor, maintained high levels without further increases by NE. These results indicate that increased mitochondrial proteins by acute NE exposure result from inhibition of proteasomal degradation. We demonstrated that NE decreased proteasomal hydrolytic activities with accumulated ubiquitinated UCP1. Membrane-permeable cAMP recapitulated the upregulating actions of NE on mitochondrial proteins as well as the oxygen consumption rate (OCR). Conversely, H89, a protein kinase A (PKA) inhibitor, abolished NE-induced mitochondrial upregulations. Chelation of cytosolic Ca2+ using BAPTA-AM prevented NE-inhibited proteasomal degradation and, consistently, suppressed NE-induced mitochondrial protein and OCR upregulation. Knockdown of MCU, preventing mitochondrial Ca2+ uptake, abrogated NE-stimulated upregulation of mitochondrial proteins abundance and respiratory activities. Taken together, we suggest that Ca2+ elevation by NE-cAMP-PKA inhibits proteasomal degradation of mitochondrial proteins and elevates respiratory activities, providing a novel mechanism for acute thermogenesis in brown adipocytes.

Keywords: brown adipose tissue (BAT); norepinephrine (NE); mitochondria; uncoupling protein 1 (UCP1); mitochondrial calcium uniporter (MCU)

P-23

JNK3, a Novel Therapeutic Target for Chronic Kidney Disease

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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 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 actions, 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 JNK3 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 either a pan JNK inhibitor or a JNK3 selective inhibitor. Both inhibitors protected against renal fibrosis, podocyte damage and albuminuria induced by Adriamycin. However, selective JNK3 inhibition showed more preservation of kidney function, while pan-JNK inhibition elicited hepatocyte injury, a side effect not observed in selective JNK3 inhibition. These results suggest that selective JNK3 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, JNK3 could be a novel and promising therapeutic target for the treatment of chronic kidney diseases.

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Genetic Suppression of Mitochondrial Ca2+ Uniporter Prevents Podocyte Ferroptosis and Glomerulosclerosis

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Mitochondrial Ca2+ uniporter (MCU) plays a critical role in regulating mitochondrial calcium homeostasis, and its dysregulation has been implicated in various pathological conditions. In this study, we investigated the therapeutic potential of MCU inhibition in renal fibrosis, focusing on its role in ferroptosis, a form of regulated cell death associated with Fe2+-dependent lipid peroxidation. In vitro experiments using siRNA-mediated knockdown in human kidney podocytes demonstrated that silencing of MCU protects against TGF- β -induced epithelial-mesenchymal transition and fibrogenesis. Additionally, BODIPY581/591 C11 staining revealed that knockdown of MCU suppressed Erastin- or Adriamycin-elicited lipid peroxidation, an indicator of ferroptotic progression. To validate these results in animal studies in vivo, we established tamoxifen-inducible whole-body MCU knockout mouse model subjected to Adriamycin-induced nephropathy. Consistent with the in vitro results, glomerulosclerosis with foot process effacement in podocytes by Adriamycin were markedly attenuated in MCU knockout mice. Furthermore, Adriamycin-induced albuminuria and deteriorated kidney function were prevented by genetic deletion of MCU, highlighting a protective role for MCU inhibition in glomerulosclerosis and proteinuria. 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



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뉴로셀텍은 엽산, 비타민A, 비타민B12, 비타민C, 비타민D, 비타민E 및 피로 회복에 필요한 비타민B군을 고함량으로 함유한 건강 100세 시대의 맞춤형 스마트 종합비타민제입니다.

- ① 뉴로셀텍은 호모시스테인 농도를 낮추는 엽산과 비타민B12 함유로 심혈관¹⁾ 및 신부전 환자의 동맥경화증 발생 위험²⁾을 낮추어 줍니다.

1) J Am Diet Assoc. 97(1997) 167-173

2) The Korean Journal of medicine 72(2007) 607-615

- ② 뉴로셀텍은 당뇨병 치료제(Metformin) 장기 복용 시 엽산과 비타민B12 결핍으로 인한 말초신경병증(Peripheral Neuropathy) 발생위험을 낮추어 줍니다.³⁾

3) British medical journal 340(2010) 1177-1183

- ③ 뉴로셀텍은 골다공증 골절 위험을 유발하는⁴⁾ 호모시스테인의 농도를 낮추고 비타민D는 필요한 혈중 칼슘 농도 유지로 골대사에 도움을 줍니다.⁵⁾

4) N Engl Med 2004 350 2033-41

5) Journal of American Medical Association 294(2005) 2336-2341

- ④ 뉴로셀텍 함유 비타민류를 복용 시 비만 여성의 HDL-C와 휴식기 에너지 소비량은 증가하고 지방량과 LDL-C는 감소하여 고지혈증 위험을 감소시킵니다.⁶⁾

6) International Journal of Obesity 34(2010) 1070-1077

- ⑤ 뉴로셀텍은 혈중 비타민D 농도 부족으로 인한 만성 피로증을 개선시키는 비타민D를 함유하고 있습니다.⁷⁾

7) Medicine (Baltimore) 95(52)(2017) 4985-5950



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SGLT2, sodium glucose cotransporter 2; TZD, thiazolidinedione

References. 1. 트루버디정 허가사항, 식품의약품안전처, 약품안전관리, Accessed on 2023.09.26. 2. 보건복지부 고시 제2023-58호. 요양급여의 적용기준 및 방법에 관한 세부사항.

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