재단법인 한 곡 의 학 장 학 회

Hankok Medical Science Foundation (since 1971)

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Contents

Time		Schedule		
10. 18 (Wen.)	14:00 ~	Registration		
	16:00 ~ 18:00	Committee activity (각 위원회 활동)		
10. 19 (Thu.)	08:45 ~ 09:00	Opening Ceremony (Rm 321–323)		
	09:00 ~ 10:30	Oral Presentation I (Rm 321–323) 좌장: 황승준(울산대), 한승호(중앙대)	Oral Presentation II (Rm 324–326) 좌장: 이종은(연세대), 이자경(인하대)	
	10:30 ~ 10:40	Coffee Break		
	10:40 ~ 11:20	Plenary Lecture I (5A홀) 좌장: 이왕재(서울대) Speaker: Lynne A. Opperman, PhD, Texas A&M University College of Dentistry (전 미국 해부학회 회장)		
	11:20 ~ 12:20	학회 창립 70주년 기념 Session (5A홀) 대한해부학회 70년 기념 특별 강연 좌 장: 이원복(중앙대) – 송창호 교수: 전북대 – 박형우 교수: 연세대		
	12:20 ~ 13:20	Photography & Lunch		
	13:30 ~ 14:30	Poster Presentation I – (P001–P089) (5A홀)		
	14:30 ~ 17:00	Symposium I (Rm 321–323) Obesity and Brain Function 좌 장: 유영현(동아대), 노구섭(경상대) 발표자: 박병현(전북대) 이동근(경상대) 김재근(인천대) 조동규(성균관대) 노구섭(경상대)	Symposium II (Rm 324–326) 해부학을 근간으로 하는 융합학문적 접근 좌 장: 이영일(단국대), 박정현(강원대의전원) 발표자: 이원준(국립과학수사연구원) 홍승모(울산대) 윤관현(인천가톨릭대학교대학원) 이수경(국립과학수사연구원) 반기원(City University of Hong Kong)	
	18:00 ~ 21:00	Gala Dinner (5A홀)		
10. 20 (Fri.)	09:00 ~ 10:30	Oral Presentation III (Rm 321–322) 좌장: 김희진(연세대), 이혜연(연세대)	Oral Presentation IV (Rm 323–324) 좌장: 윤 식(부산대), 김홍태(대구가톨릭대)	Oral Presentation V (Rm 325–326) 좌장: 강재승(서울대), 오세옥(부산대)
	10:30 ~ 10:40	Coffee Break		
	10:40 ~ 11:20	Plenary Lecture II (5A홀) 좌장: 최완성(경상대) Speaker: Inhee Mook–Jung, PhD, Seoul National University College of Medicine		
	11:20 ~ 12:05	해부학교육 심포지엄 (5A홀) 좌 장: 허영범(경희대) 발표자: 김홍태(대구가톨릭대) 송우철(건국대) 주경민(성균관대)		
	12:05 ~ 13:00	Lunch & Luncheon Workshop (Rm 321–323) – Prof. Brion Benninger – Western University of Health Science		
	13:00 ~ 14:00	Poster Presentation II – (P090–P178) (5A홀)		
	14:00 ~ 16:00	Symposium III (Rm 321–323) Biology of Urogenital System 좌 장: 한기환(이화대), 정채용(전남대) 발표자: 권태환(경북대) 김용균(가톨릭대) 오세옥(부산대) 서호경(국립암센터)	Symposium IV (Rm 324–326) Experimental System Simulating Human Body and Disease 좌 장: 강상수(경상대), 주경민(성균관대) 발표자: 주경민(성균관대) 정 석(고려대) 이동우(건양대) 조영재(분당서울대병원)	
	16:00 ~	67th General Meeting (Rm 321–323)		

학술대회장 배치도


상부주차램프
올라감
상부주차램프
나려옴
5A홀
[PL, 교육
심포지엄,
만찬]
포스터발표
5B 홀
5C 홀
5D 홀
5E 홀
전시업체
접수데스크
회의실
320
강의장
[회의실 321~326호]
2층진입
외부계단
야외데크

Plenary Lecture I

2017년 10월 19일(목) 10:40 ~ 11:20
5A홀

좌장 이왕재 서울대

PL-1 **10:40-11:20**

Pre-Clinical and Clinical Testing of a Novel Root-Shaped Implant

Lynne A. Opperman • Department of Biomedical Sciences, Texas A&M College of Dentistry, Dallas, Texas

PL-1

Pre-Clinical and Clinical Testing of a Novel Root-Shaped Implant

Opperman LA

Department of Biomedical Sciences, Texas A&M College of Dentistry, Dallas, Texas

Objectives: To test that using a Maryland-type bridge as a splint provides stability for a root-shaped implant and allows it to integrate similar to a control device. **Methods:** Preclinical Study: Six beagle dogs were subjected to a cone beam scan and silicone impressions were taken. Impressions and radiographs were used to custom-make root-form REPLICATE™ Tooth implants and crowns (RTI). Molars (P4) in the mandible and premolars (P3) in the maxilla were extracted and 24 RTI immediately placed in extraction sockets. Splint extensions of the crowns were bonded to mesial and distal teeth. As controls, twelve mandibular M2 molars were extracted and 3X8.5 mm DENTSPLY XiVE® implants (DXI) were immediately placed. Animals were placed on a soft diet post-surgery. Weekly intra-oral photos and radiographs were taken, calcein (C) and alizarin red (AR) flurochrome labels were injected intraperitoneally at 35 (C), 21 (AR) and 7 (C) days prior to sacrifice at 4 months. Measurements included clinical implant stability, vertical pull-out forces, loss of vertical bone height, bone-to-implant contact (BIC) percentage and mineral apposition rates (MAR) from undecalcified sections. Clinical Study: Ten patients were recruited in an FDA approved clinical study. All patients received preclinical radiographs, cone beam scans, and digital impressions. Impressions and radiographs were used to custom-make root-form REPLICATE™ Tooth implants and crowns. All patients received implants immediately after extractions, crowns were placed after 3 months, and final recall radiographs taken at 6 months. **Results:** Preclinical Study: Pull-out forces were 366.7+182.8 N for RTI. Average vertical bone loss, BIC and MAR were not significantly different between groups. Clinical Study: One implant was lost prior to placement of the crown. All other implants were fully integrated and gingival margins showed no vertical bone loss. **Conclusion:** REPLICATE™ Tooth implants and crowns appear to be acceptable alternatives to threaded implants for single tooth replacement.

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Plenary Lecture II

2017년 10월 20일(금) 10:40 ~ 11:20
5A홀

좌장 최완성 경상대

PL-2 **10:40-11:20**

The Molecular Pathogenesis of Alzheimer's Disease

Inhee Mook-Jung • Seoul National University, College of Medicine

PL-2

The Molecular Pathogenesis of Alzheimer's Disease

Inhee Mook-Jung

Department of Biochemistry & Biomedical Sciences, Seoul National University College of Medicine

Alzheimer disease (AD) is age-related neurodegenerative disorder and the most common form of dementia. It is characterized by senile plaques, neurofibrillary tangles, and neuronal cell death. In AD brains, intracellular and extracellular Aβ accumulation occurs because of the imbalance between the production of Aβ and its removal (clearance) from the brain. The lack of early diagnostic biomarker and therapeutic remedy hinders the prevention of increasing population of AD patients every year. In spite of accumulated scientific information, numerous clinical trials for candidate drug targets have failed to be preceded into therapeutic development, therefore, AD-related sufferers including patients and caregivers, are desperate to seek the solution. Also, effective AD intervention is desperately needed to reduce AD-related societal threats to public health. In this talk, I will summarize recent advances of studies on Molecular Pathogenesis of Alzheimer's disease. Also, various drug targets and strategies in recent preclinical studies and clinical trials for AD therapy will be discussed: Allopathic treatment, immunotherapy, Aβ production/aggregation modulator, tau-targeting therapy and metabolic targeting. Some has already failed in their clinical trials and the others are still in various stages of investigations, both of which give us valuable information for future research in AD therapeutic development.

Key Words: Alzheimer's disease, Amyloid β, Tau, Immunotherapy, Glucose metabolism, aggregation

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Symposium I

2017년 10월 19일(목) 14:30 ~ 17:00
Rm 321–323

Obesity and Brain Function

좌장 유영현 동아대 • 노구섭 경상대

S1-1 **14:30-15:00**
Hepatocyte-specific sirtuin 6 deletion predisposes to nonalcoholic fatty liver disease and nonalcoholic steatohepatitis
박병현 • 전북의대 생화학교실

S1-2 **15:00-15:30**
Hypothalamic regulation of feeding behavior and energy balance
이동근 • 경상의대 생리학교실

S1-3 **15:30-16:00**
Hypothalamus and muscle axis that controls energy homeostasis
김재근 • 인천대 생명과학부

S1-4 **16:00-16:30**
Mitochondrial dynamics in Alzheimer's disease
조동규 • 성균관약대

S1-5 **16:30-17:00**
Positive effects of caloric restriction in obesity or diabetic animal models
노구섭 • 경상의대 해부학교실

본 심포지엄 1은 경상의대 바이오항노화의과학연구센터(BAMRC)의 지원에 의해 진행되었습니다.

S1-1

Hepatocyte-specific sirtuin 6 deletion predisposes to nonalcoholic fatty liver disease and nonalcoholic steatohepatitis

Byung-Hyun Park /Department of Biochemistry, Chonbuk National University Medical School, Jeonju, 54896, Korea

Sirtuin 6 (Sirt6) has been implicated in negative regulation of inflammation and lipid metabolism, although its function in the development of nonalcoholic fatty liver disease (NAFLD) and the progression from NAFLD to nonalcoholic steatohepatitis (NASH) remain to be defined. To explore the role of hepatocyte Sirt6 in NAFDL and NASH development, we generated hepatocyte-specific Sirt6 KO mice and exposed to tunicamycin or fed a high-fat and high-fructose (HFHF) diet, respectively. I will discuss herein the possible molecular links between Sirt6 and metabolic phenotypes observed in hepatocyte-specific Sirt6 KO mice.

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S1-2

Hypothalamic regulation of feeding behavior and energy balance

Dong Kun Lee /Department of Physiology, Institute of Health Sciences, Gyeongsang National University School of Medicine, Korea

The homeostatic control of energy balance is associated with metabolic signals from the periphery and the neurons in several brain regions including the hypothalamus. Subset of neurons in the hypothalamus respond to nutritional and humoral signals, such as glucose, leptin and insulin. Among hypothalamic neurons, proopiomelanocortin (POMC) and neuropeptide Y (NPY)/agouti-related peptide (AgRP) in the arcuate nucleus and cholinergic neurons in the dorsomedial hypothalamus are play a critical role in regulating energy intake, energy expenditure and glucose metabolism. In this regard, the arcuate nucleus-based hypothalamic circuits is a critical coordinator of energy homeostasis by responding to metabolic signals. Therefore, here we suggest the experimental evidence of the function of hypothalamic neurons on feeding behavior.

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S1-3 Hypothalamus and muscle axis that controls energy homeostasis

Jae Geun Kim /Division of Life Sciences, College of Life Sciences and Bioengineering, Incheon National University, Incheon 406-772, Korea

A growing body of evidence has suggested that irisin, a myokine derived from skeletal muscle, gives rise to the beneficial effects on multiple human diseases. In particular, irisin improves the obesity pathogenesis via promoting browning of the white fat tissue. Although, irisin has been referred to a chemical messenger that mediates positive effects of exercise on metabolic disorders, potential impacts of irisin in the hypothalamic circuit that controls appetite are ill-defined. In this study, we observed that intracerebroventricular (icv) administration of irisin led to the reduction of food intake and body weight. In line with these behavioral results, we also found that central administration of irisin resulted in an increase of POMC neuronal activity and a decrease of AgRP neuronal activity. Furthermore, we found that icv injection of irisin triggered an elevation of energy expenditure. Collectively, the current study suggests that hypothalamus and muscle axis is an important component to maintain the whole body energy metabolism.

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S1-4 Mitochondrial dynamics in Alzheimer's disease

Dong-Gyu Jo /School of Pharmacy, Sungkyunkwan University

Excessive mitochondrial fission is a prominent early event and contributes to mitochondrial dysfunction, synaptic failure, and neuronal cell death in the progression of Alzheimer's disease (AD). However, it remains to be determined whether inhibition of excessive mitochondrial fission is beneficial in mammal models of AD. Mitochondrial fission relies on the evolutionary conserved dynamin-related protein 1 (Drp1). Drp1 activity and mitochondria fragmentation are significantly elevated in the brains of sporadic Alzheimer's disease (AD) cases. To determine whether Drp1, a key regulator of mitochondrial fragmentation, can be a disease-modifying therapeutic target for AD, we examined the effects of Drp1 inhibitor on mitochondrial and synaptic dysfunctions induced by oligomeric amyloid-β (Aβ) in neurons and neuropathology and cognitive functions in Aβ precursor protein/presenilin 1 double-transgenic AD mice. Inhibition of Drp1 alleviates mitochondrial fragmentation, loss of mitochondrial membrane potential, reactive oxygen species production, ATP reduction, and synaptic depression in Aβ-treated neurons. Furthermore, Drp1 inhibition significantly improves learning and memory and prevents mitochondrial fragmentation, lipid peroxidation, BACE1 expression, and Aβ deposition in the brain in the AD model. These results provide evidence that Drp1 plays an important role in Aβ-mediated and AD-related neuropathology and in cognitive decline in an AD animal model. Therefore, inhibiting excessive Drp1-mediated mitochondrial fission may be an efficient therapeutic avenue for AD.

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S1-5

Positive effects of caloric restriction in obesity or diabetic animal models

Gu Seob Roh /Department of Anatomy, Bio Anti-aging Medical Research Center, College of Medicine, Gyeongsang National University, Jinju, Korea

Caloric restriction (CR) reduces mortality in diverse species from age and other causes, including diabetes, cancer, cardiovascular disease, and brain atrophy. The effects of CR on lifespan and health span have been known for nearly a century. Generally, CR causes major metabolic reprogramming toward efficient fuel utilization and a reduction in oxidative damage to macromolecules. Although a range of putative mechanisms have been proposed, the precise molecular mechanisms underlying these effects remain unknown. Previous studies have shown that non-alcoholic fatty liver disease (NAFLD) changes the levels of metabolites, proteins and genes in the liver of human and animal models. In particular, NAFLD causes the accumulation of lipids in the liver and results in inflammation and mitochondrial dysfunction. It has also been reported that CR alters metabolism. Thus, we examined alterations in hepatic metabolism caused by CR treatment in the context of NAFLD of db/db mice, to investigate several metabolic pathways related to CR and NAFLD. We also investigated the hypothesis that long-term CR administration protects against NAFLD by inhibiting hepatic steatosis, autophagy, endoplasmic reticulum (ER) stress, mitochondrial fission, inflammation, and collagen deposition. In the brain, memory deficits associated with obesity and diabetes may be improved by weight loss. CR prevents some of the cognitive deficits associated with the aging process. CR may provide neuroprotective effects on hippocampal NMDARs in obese rats fed a high-fat diet (HFD). Here, we investigated the effects of CR on hippocampal O-GlcNAcylation, Ca^{2+} homeostasis, and memory in the ob/ob mice model of obesity-induced diabetes. In conclusion, the present study explored the therapeutic effects of CR on NAFLD and cognitive impairment in obese mice.

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Symposium II

2017년 10월 19일(목) 14:30 ~ 17:00
Rm 324-326

해부학을 근간으로 하는 융합학문적 접근

좌장 이영일 단국대 • 박정현 강원대의전원

S2-1 **14:30-15:00**
머리뼈의 형태 및 계측학적 분석을 통한 얼굴 예측
이원준 • 국립과학수사연구원 서울과학수사연구소 법의조사과

S2-2 **15:00-15:30**
암 병기(staging) 결정에서의 정상 조직 이해의 중요성
홍승모 • 울산대학교 의과대학 병리학교실

S2-3 **15:30-16:00**
의학 분야 교재 제작 및 연구에 필요한 〈해부학그림〉 만들기 과정
윤관현 • 인천가톨릭대학교대학원 조형예술학과 바이오메디컬아트 전공

S2-4 **16:00-16:30**
The Standardization of Korean Human Body Using Postmortem CT Scan – Estimation of stature from femur length in Korean cadavers
이수경 • 국립과학수사연구원 부산과학수사연구소 법의학과

S2-5 **16:30-17:00**
Development of novel strategies for promoting cardiac repair
반기원 • Department of Biomedical Science, City University of Hong Kong

S2-1

머리뼈의 형태 및 계측학적 분석을 통한 얼굴 예측

이원준[1], 이상섭[2], 노병윤[2], 서정욱[2], 최창운[1]

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법의학적 얼굴복원(Forensic Craniofacial Reconstruction/Approximation, 이하 '얼굴복원')이란 사후에 남겨진 사람의 머리뼈 위에 생존 당시의 얼굴모습을 예측하여 재구성 해내는 방법을 말한다. 얼굴복원은 머리뼈를 해부학적으로 분석하여 얻은 생체정보와 복원 제작에 필요로 하는 예술적 기법을 적용하여 만들어진다. 이렇게 완성된 얼굴복원의 궁극적 목적은 법의학 · 법과학 영역에서 신원이 아직 밝혀지지 않는 유해의 신원 확인에 도움을 주는 것이다. 따라서 얼굴복원은 어떤 사체의 신원확인 작업이 여러 법의학적 방법을 동원하고도 성과를 얻지 못하고, 머리뼈가 존재하는 경우에 적용해 볼 수 있는 유용한 방법이다. 최근 우리나라에서도 국립과학수사연구원의 법의학적 감정에 얼굴복원이 사용되기 시작하였고 신원 미확인 시신의 신원확인 작업에 활발히 적용되고 있다. 또한 고고학 관점에서 사료적 가치가 있는 역사적 유명인사나 옛사람 혹은 인류조상의 머리뼈를 얼굴복원에 적용하는 시도도 크게 늘어나고 있다. 얼굴복원의 정확성은 머리뼈의 해부학적 분석을 통해서 눈, 코, 입 등 얼굴형태소를 얼마나 정확하게 예측할 수 있느냐에 크게 달려있다. 따라서 19세게 후반 과학적인 얼굴복원이 유럽에서 시작된 이래로 머리뼈 형태분석 또는 머리뼈 계측법을 이용하여 얼굴형태소 예측 방법에 대한 많은 연구가 진행되어 왔다. 대표적인 예로 눈의 수평선(eye slit)의 기울기는 눈꺼풀인대(palpebral ligament)가 부착되는 광대결절(malar tubercle)과 눈물능선(lacrimal crest)의 위치로, 코 형태의 경우는 콧구멍뼈 주위의 주요 표지점간 측정치 연구로 얻은 회귀분석값을 통해 예측을 할 수 있다. 또한 입술의 크기와 위치는 송곳니와 입술 폭의 관계연구를 통해서 추정을 할 수 있다. 이렇게 연구된 결과들은 얼굴복원 전문가들에 의해 적용되어 사용되고 있다. 하지만 이들 방법들은 연구 된지 많은 시간이 흘렀거나 객관적인 근거가 부족하여 신뢰도에 의문이 가는 경우가 존재한다. 그리고 대개는 유럽계 백인을 대상으로 연구된 결과이다 보니 한국인이 포함된 동양인에 적용하기에는 아직은 불확실한 부분들도 많은 것이 사실이다. 이 같은 문제의식으로 최근 국내에서도 한국인을 대상으로 한 얼굴형태소 예측법에 대한 연구가 착실히 수행되고 있다. 그 중에서 얼굴의 인상에 큰 영향을 미치는 눈썹과 콧방울의 형태를 관련 머리뼈 주변 형태와 표지점 간 측정값을 사용하여 예측하는 연구가 진행되고 있다. 이번 발표에서는 현재 얼굴복원가들에 의해 사용되고 있는 대표적인 얼굴형태소 예측법에 대해서 전반적으로 살펴보고 얼굴형태소 예측 방법 개발을 위한 해부학적 연구방법론과 현재 진행되고 있는 연구 과정에서 도출된 결과를 소개하고자 한다.

Keywords: 해부학, 머리뼈, 얼굴복원, 신원확인, 얼굴형태소, 예측

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S2-2

암 병기(staging) 결정에서의 정상 조직 이해의 중요성

홍승모 /울산의대 병리학교실

암병기는 암환자의 예후 및 적절한 치료방침의 결정에 있어서 중요하고, 임상 시험에 있어서 환자의 포함 및 배제 기준으로 중요한 요인이며, 연구자간 정보의 교환을 촉진시키는데 사용되고, 임상 및 중계종양연구에서의 기본이 된다. 현재 사용하는 미국암연합위원회 (American Joint Committee for Cancer, AJCC)의 암병기는 TNM 병기를 사용하며, 각 종양의 병기는 원발성 종양의 크기 또는 침윤 깊이 (T), 국소 림프절 침윤 여부 (N), 및 원격전이 여부 (M)의 조합에 의하여 결정된다. 본 연제를 통하여 간외담도암의 병기의 결정에 있어서 정상 담도 조직의 이해의 중요성에 대하여 논의하고자 한다. 기존에 사용하던 미국암연합위원회의 제5판~7판 간외담도암의 병기는 간외담도의 조직학적 특징과 간외담도와 주변 장기와의 복잡한 관계, 간외담도암의 병리학적 특징인 결합조직증식증(desmoplasia)을 고려하지 않고 만들어졌기 때문에 수술 후 간외담도암 환자의 예후를 정확하게 예측하는데 실패하였다. 간외담도에서의 평활근의 분포는 위장관에서의 균등한 평활근의 분포와 매우 상이한 불균등한 분포를 보인다 즉, 파터씨 팽대부 주변의 하부 총담관에서 주로 두터운 평활근 묶음의 양상으로 관찰되지만, 담낭관 수준의 상부 총담관에서는 주로 평활근이 관찰되지 않거나 또는 얇은 평활근 섬유로 분포한다. 이러한 불균일한 평활근 분포에 의하여, 위장관 종양의 암병기에 사용하는 점막–점막하–고유근층–장막하 등 분류에 의한 T병기를 간외담도암에 적용 할 수 없다. 또한 간외담도의 신경섬유 및 혈관 분포는 담도 내외와 경계연 모두에 분포하기 때문에 신경섬유 와 혈관을 담도의 내외부로 나누는 기준으로 사용할 수가 없고, 담도 안팎의 경계를 평활근과 섬유화 조직이 관찰되는 가장 바깥 부분과 지방세포가 나타나는 가장 안쪽의 경계로 보는 것이 타당하다. 담도암의 종양세포의 침윤 깊이에 따라 환자의 예후가 차이가 나며, 이를 토대로 담도암의 침윤 깊이 5mm와 12mm의 두 개의 기준점으로 기준으로 하여, 종양세포의 침윤 깊이에 따른 T병기를 T1 (종양세포 침윤 깊이, 5mm 이내), T2 (종양세포 침윤 깊이, 5–12mm), T3 (종양세포 침윤 깊이, 12mm초과)로 분류하였고, 새로운 분류에 따른 병기가 기존에 사용하던 간외담도암의 병기보다 보다 정확하게 간외담도암 환자의 예후를 나누는 것을 증명하였고, 후속 논문들에 의하여 상기의 내용들이 검증되어서 2017년 개정되어 2018년부터 적용하는 제8판 미국암연합위원회의 간외담도암 병기에 종양세포 침윤 깊이 측정법이 담도암 병기의 표준으로 채택이 되었다. 이러한 간외담도암병기의 변화과정에서 보이듯, 평활근 섬유의 분포양상 등 정상 담도 조직에 대한 이해가 간외담도암의 병기의 결정에 있어서 매우 중요하다.

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S2-3

의학 분야 교재 제작 및 연구에 필요한 〈해부학그림〉 만들기 과정

Kwan-Hyun Youn /Division in Biomedical Art, Department of Fine Art, Incheon Catholic University Graduate School

해부학그림은 인체의 해부학적 구조를 설명, 강조, 보충하기 위해 본문 사이에 끼워 넣는 그림을 말하지만 아틀라스처럼 그림이 주된 경우도 있다. 우리나라의 경우 1906년 이마다의 ≪실용해부학≫을 기본으로 출간 된 최초의 ≪해부학≫ 교과서에 그림이 삽입되었다. 1980년 이전까지는 해부학 교과서에 들어가는 그림이 드물게 제작되었고, 1980년대 후반부터는 저작권법의 적용에 따라 해부학그림 제작에 대한 관심이 증대되었다. 이전에는 주로 해부학교육을 목적으로 그려졌지만 1990년대 중반 이후에는 연구나 홍보를 위한 상업적 목적으로도 제작되기 시작했다. 사진이나 3D영상이 발달한 오늘날에도 생략과 강조를 통한 시각적 표현이 가능하다는 장점 때문에 해부학그림은 여전히 유효하게 사용되고 있으며 또한 전자책 등의 새로운 매체와 결합하여 보다 발전할 것으로 예상된다. 해부학그림은 작가의 개성이나 창의성을 드러내기 보다는 내용의 정확성과 객관적 표현이 매우 중요하며 해부학적 이해와 예술적 표현능력이 요구되는 분야이다. 때문에 서양에서는 1900년대 초부터 북아메리카와 유럽을 중심으로 이 분야를 가르치는 정규과정이 개설되어 전문적인 메디컬일러스트레이터들을 육성하고 있는 실정이다. 국내에서는 그 동안 미술전공자들에 의해 주로 그려졌는데 대개의 경우 해부학적 이해가 부족하여 외국의 그림들을 모사하는 형편이었다. 2016년에 인천가톨릭대학교대학원에 바이오메디컬아트 전공이 개설되었으며 해부학을 바탕으로 전통적 방식의 2D일러스트와 3D모델링 및 영상제작 등을 가르치고 있다. 재학생들의 이전 전공은 미술, 생물학, 간호학, 수의학 등 다양하며 때문에 앞으로 보다 수준 높고 다양한 그림들이 제작될 수 있는 토대가 될 것으로 기대된다.

Keywords: Anatomical Illustration, Medical Illustration, Education

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S2-4

The Standardization of Korean Human Body Using Postmortem CT Scan - Estimation of stature from femur length in Korean cadavers

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The use of postmortem computed tomography(PMCT) is common process in the field of autopsy, although PMCT is only being used in the National Forensic Service(NFS) Seoul Institute. CT images can help the forensic pathologist to understand not only abnormal findings related to the cause of death, but also various anatomical characteristics. As the estimation of stature is a basic and important forensic procedure in identifying decomposed or skeletonized bodies, the authors tried to obtain the stature estimation formula for Korean using PMCT after the analysis of three-dimensional characteristics of femur bone in cadavers. Digitalized data will be a good tool for the understanding of human body and be essential elements for the 'Digital Bone Collection.'

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S2-5

Development of novel strategies for promoting cardiac repair

Kiwon Ban /Department of Biomedical Sciences, City University of Hong Kong, Kowloon, Hong Kong

Ischemic heart disease (IHD) is the one of the major causes of death worldwide. Particularly, in the case of myocardial infarction (MI), patients ultimately advance to heart failure and die within short period from the onset of symptoms. Since the adult human heart has limited regenerative capacity[3], the infarcted areas by MI are rarely regenarated[7] and are easily converted to non-contractile fibrotic scar, which lead eventual heart failure. Despite its high clinical significance, currently available therapeutic options including surgical and pharmacological interventions for treating heart failure are not very efficient as these strategies cannot directly repair the damaged hearts, rather only delay the progression of this detrimental disease. Therefore, significant efforts has been made in order to develop alternative strategies that can efficiently repair the failing heart. Recently, stem cell-based therapy has emerged as a promising therapeutic option. Particularly, cardiomyocytes derived from pluripotent stem cells (PSCs) including both embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) are regarded as one of the most promising sources for multiple applications such as development of new treatments for heart diseases, establishment of platforms for drug discovery and predictive toxicology, creation of *in vitro* models of human disease, and cardiac tissue engineering. While cardiomyocytes derived from hPSC (hPSC-CMs) are attractive sources for the use of heart repair and many other applications, numerous hurdles stand in the way of their clinical use. Their applicability is significantly limited by a number of major reasons such as i) low yields, ii) heterogeneity of differentiated hPSC-CMs, iii) immaturity of hPSC-CMs, and v) lack of optimal methods to deliver hPSC-CMs into the hearts. Hence, in my presentation, I will discuss my studies that have been designed and performed to solve the current limitations in the use of hPSC-CMs for cardiac repair.

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Symposium III

2017년 10월 20일(금) 14:00 ~ 16:00
Rm 321–323

Biology of Urogenital system

좌장 한기환 이화대 • 정채용 전남대

S3-1 **14:00 -14:30**
Vasopressin–regulated aquaporin–2 in kidney collecting duct
권태환 • 경북의대 생화학교실

S3-2 **14:30 -15:00**
Defining the development of podocytes using kidney organoids derived from human iPSC
김용균 • 가톨릭의대 신장내과

S3-3 **15:00 -15:30**
Expression and prognostic significance of zinc fingers and homeoboxes family members in renal cell carcinoma
오세옥 • 부산의대 해부학교실

S3-4 **15:30 -16:00**
The developement and verification of efficacy for a new durg of bladder cancer using in–vivo bladder cancer model
서호경 • 국립암센터 생체표지자연구과

S3-1

Vasopressin-regulated aquaporin-2 in kidney collecting duct

Tae-Hwan Kwon /Department of Biochemistry and Cell Biology, School of Medicine, Kyungpook National University

The connecting tubule and collecting duct are important renal tubular segments for the regulation of body water homeostasis, where vasopressin regulates water reabsorption. Water reabsorption in these renal tubular segments is controlled by vasopressin, a peptide hormone which induces the osmotic water transport across the epithelia through regulation of water channel proteins aquaporin-2 (AQP2) and aquaporin-3 (AQP3). In particular, vasopressin induces both intracellular translocation of AQP2-bearing vesicles to the apical plasma membrane and transcription of *Aqp2* gene to increase AQP2 protein abundance. The signaling pathways, including AQP2 phosphorylation, RhoA phosphorylation, intracellular calcium mobilization, and actin depolymerization, play a key role in the translocation of AQP2. Moreover, long-term regulation or adaptation of AQP2 is presented by changing AQP2 protein abundance and a number of studies demonstrated that dysregulation of AQP2 protein expression plays a critical role in the pathophysiology of both water-losing disorders with polyuria and water retention disorders with dilutional hyponatremia. Mutations in the *AQP2* gene also lead to autosomal recessive nephrogenic diabetes insipidus in human patients. This talk will summarize recent data demonstrating the regulation of AQP2, as the underlying molecular mechanisms for the homeostasis of water balance in the body.

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S3-2

Defining the development of podocytes using kidney organoids derived from human iPSC

김용균 /가톨릭의대 신장내과

A critical event during kidney organogenesis is the differentiation of podocytes, specialized epithelial cells that filter blood plasma to form urine. Podocytes derived from human pluripotent stem cells (hPSC-podocytes) have recently been generated in nephron-like kidney organoids, but the developmental stage of these cells and their capacity to reveal disease mechanisms remains unclear. Here we show that hPSC-podocytes phenocopy mammalian podocytes at the capillary loop stage (CLS), recapitulating key features of ultrastructure, gene expression, and mutant phenotype. hPSC-podocytes in vitro progressively establish junction-rich basal membranes (nephrin+podocin+ZO-1+) and microvillus-rich apical membranes (podocalyxin+), similar to CLS podocytes in vivo. Ultrastructural analysis of gene-edited hPSC-podocytes, generated using CRISPR/Cas9, reveals that podocalyxin is essential for the assembly of microvilli and lateral spaces between developing podocytes. These defects are phenocopied in CLS glomeruli of podocalyxin-deficient mice, which cannot produce urine, thereby demonstrating that podocalyxin has a conserved and essential role in mammalian podocyte maturation.

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S3-3

Expression and prognostic significance of zinc fingers and homeoboxes family members in renal cell carcinoma

Ryuk-Jun Kwon[1,2,†], Yun Hak Kim[1,2,†], Dae Cheon Jeong[3], Myoung-Eun Han[1,2], Ji-Young Kim[1,2], Liangwen Liu[1,2], Jin-Sup Jung[4], Sae-Ock Oh[1,2,*]

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Zinc fingers and homeoboxes (ZHX) is a transcription repressor family that contains three members; ZHX1, ZHX2, and ZHX3. Although ZHX family members have been associated with the progression of cancer, their values as prognostic factors in cancer patients have been poorly examined. Renal cell carcinoma (RCC) is a highly heterogeneous, aggressive cancer that responds variably to treatment. Thus, prognostic molecular markers are required to evaluate disease progression and to improve the survival. In clear cell RCC (ccRCC), ZHX1 and ZHX3 expression were found to be down-regulated but ZHX2 was up-regulated, and the expressions of ZHX1 and ZHX3 were significantly associated with pathological stage. Furthermore, Kaplan-Meier and multivariate regression analysis showed that reduction in the mRNA expression of ZHX1 was associated with poorer survival. Taken together, the present study shows loss of ZHX1 is correlated with ccRCC progression and suggests it is an independent prognostic marker in ccRCC.

Keywords: ZHX1, renal cell carcinoma, prognosis

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S3-4

The developement and verification of efficacy for a new durg of bladder cancer using in-vivo bladder cancer model

Ho Kyung Seo /Center for Prostate Cancer, Hospital and Biomarker Branch, Research Institute, National Cancer Center, Goyang, Korea

The prognosis and treatment of bladder cancer have hardly improved in the last 20 years, with the exception of immunotherapy using a PD-1/PD-L1 blocker, which was approved by the United States Food and Drug Administration in 2016. Hence, bladder cancer remains a debilitating and often fatal disease, and among one of the most expensive cancer to treat. Preclinical models that are more representative of human cancer are urgently needed to improve our understanding of bladder cancer progression, as well as advance its diagnosis and treatment.

Non-muscle-invasive bladder cancer (NMIBC) accounts for >70% of all newly diagnosed bladder cancer cases. The gold standard of treatment for patients with NMIBC is transurethral resection. A major problem in the treatment of this cancer is the high incidence of tumor recurrence and progression to muscle invasive disease.

Intravesical administration of chemical and/or immunological agents is often utilized to prevent recurrence and progression; however, such treatments are limited in their efficacy and have adverse side effects. When currently available intravesical agents fail to control disease, radical cystectomy remains standard treatment. However, many patients are medically unfit and refuse this operation because radical cystectomy is also associated with significant morbidity and reduced quality of life. For this subgroup of patients, there are limited alternatives, so that there is an active investigation to understand bladder cancer oncogenesis for other intravesical therapy development.

Oncogenes, or the loss of tumor suppressor genes, may promote bladder carcinogenesis by modulating cell cycle progression or apoptosis. Recent genome-wide association studies confirmed that genetic variations in genes such as MYC, TP63, and PSC might be associated with bladder cancer risk. In addition, human bladder tumor tissue shows elevated expression of genes involved in the HIF-1α and c-MYC pathways, which are detected simultaneously with MYC gene amplification in high-grade, recurrent cases.

The transcription factor, c-MYC, dimerizes with Max and subsequently binds to the E-box sequence of its target gene promoters. The c-MYC gene is often amplified and/or its expression is up-regulated in many tumors including bladder cancer. Constitutive activation of c-MYC does not just drive normal cell transformation and genomic instability, but also induces EMT (epithelial-mesenchymal transition) and metastasis by inhibiting cell-cell and cell-substratum interactions. For example, amplification of CCND1 or alterations in c-MYC/cyclin D1 early in bladder carcinogenesis may have clinical relevance in promoting and predicting progression to muscle invasive bladder cancer. The c-MYC-dependency of cancer cells suggests that c-MYC can be a good target for cancer therapy.

c-MYC is a promising target for cancer therapy but its inhibition is expected to elicit unwanted and devastating side effects, since it is essential for proliferation in hematopoietic stem cells and pluripotency maintenance in adult somatic stem cells. Therefore, c-MYC inhibitors must be selectively used against tumors that are amenable to local treatment. We explored whether c-MYC inhibitor, KSI-3716, could be administered intravesically to suppress the growth of tumor in orthotopic bladder cancer model.

Immunotherapy now holds the promise of a new age in the battle against bladder cancer in late-stage and metastatic disease accompanied with poor prognosis. The discovery of immune checkpoint proteins such as CTLA-4, PD-1, TIM-3, LAG-3, IDO, along with a better understanding of the role that they play in immune evasion mechanisms of tumors, has paved the roads toward inducing a significant anti-tumor immune response in patients with cancer. For example, using monoclonal antibodies to block the inhibitory signals of the programmed death-1 (PD-1)/ programmed death-ligand 1 (PD-L1) pathway has demonstrated the potential for chemotherapy-resistant patients. There are a number of other cancer immunotherapies under investigation, but there are a few of immune-competent mouse model for bladder cancer.

To evaluate the effects of new immunotherapeutic modalities, it is critical to use suitable immune-competent animal model which mimics the behavior of human disease. There have been introduced a few of strategies when the studies focus on immune response or gene therapy. First, the genetically engineered mouse (GEM) enables bladder tumors available in immune-competent mouse. A number of GEM models of UCC (urothelial cell carcinoma) employed the uroplakin II (UPII) promoter of the mouse UPII gene. By placing the UPII promoter upstream to drive the urothelium-specific expression of SV40-T antigen, the GEM develops UCCs that bear a strong resemblance with human UCCs. However, cancer cells in GEM models are less heterogeneous than human bladder cancer due to similar origin and as a result, block GEM from being applied in testing the efficacy of novel immunotherapeutic agents. Alternatively, syngeneic tumors can be established by implanting bladder tumor cells that are established by carcinogen exposure. All studies that utilized syngeneic models have included either MBT-2 or MB49 or AY-27 cells. Such syngeneic models have quite good tumor take-rates and human bladder cancer mimicries. However, after tumors inside bladder are detected with non-invasive in vivo imaging such as MRI or bioluminescence imaging, mouse expires in just two to three weeks due to azotemia. It makes difficult to observe the long-term tumor responses upon intravesical immunotherapeutic treatments thereafter. It needs further development of bladder mouse tumor model to have the appropriate growth rate for reflecting durable and slowly ascending effect.

We established that novel orthotopic bladder cancer model in C3H/He mice using modification of c-myc expression level in MBT-2 murine bladder cancer cells for the evaluation of novel intravesical immunotherapy.

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Symposium IV

2017년 10월 20일(금) 14:00 ~ 16:00
Rm 324-326

Experimental System Simulating Human Body and Disease

좌장 강상수 경상대 • 주경민 성균관대

S4-1 **14:00 -14:30**
Translational animal model of human cancer
주경민 • 성균관대 해부학교실

S4-2 **14:30 -15:00**
Hydrogel incorporating tissues on chips
정 석 • 고려대학교 기계공학부

S4-3 **15:00 -15:30**
3D PDC (Patient Derived Cells)-based Drug Screening for Simulating Cancer Patients
이동우 • 건양대학교 의료공대 의공학부

S4-4 **15:30 -16:00**
Microengineered Physiological Biomimicry: Lung-on-a-chip
조영재 • 분당서울대병원 호흡기내과

본 심포지엄4 는 성균관대학교 단일세포 네트워크 연구센터의 지원에 의해 진행되었습니다.

S4-1 Translational animal model of human cancer

Kyeung Min Joo /Department of Anatomy and Cell Biology, Sungkyunkwan University School of Medicine

Frequent discrepancies between preclinical and clinical results of anticancer agents demand a reliable translational platform that can precisely recapitulate the biology of human cancers. Another critical unmet need is the ability to predict therapeutic responses for individual patients. Toward this goal, we have established a library of cancer xenograft models using surgical samples of glioblastoma, non-small cell lung cancer, renal cell carcinoma, and bladder transitional cell carcinoma patients. These patient-specific xenograft tumors recapitulate histopathological properties and maintain genomic characteristics of parental tumors in situ. Furthermore, in vivo irradiation, chemotherapy, and targeted therapy of these xenograft tumors mimic the treatment response of parental cancers. We also found that single-cell level genomic analysis of xenograft tumors could predict multiple drug target pathway activation of the parental tumors. Combinatorial regimen co-targeting mutually exclusive pathways of the tumors shows significant treatment efficacy in animal models or patients. Together, the patient-specific xenograft library represent the preclinically and clinically valuable "patient tumor's phenocopy" that represents molecular and functional heterogeneity of GBMs and is able to be utilized to design personalized cancer therapies.

주경민 | 성균관대 해부학교실 • kmjoo@skku.edu

S4-2 Hydrogel incorporating tissues on chips

Seok (Sid) Chung /School of Mechanical Engineering, KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, Korea

A simple microfluidic device for three-dimensional (3D) and heterotypic cell culture has been developed by incorporating hydrogel between micro channels. The novel microfluidic device constructs well-defined biochemical and biophysical stimuli to be applied to multiple cell types interacting each other, thereby replicating many aspects of various tissues and diseases. Capabilities exist for time-dependent manipulation of microflows and chemical gradients as well as high-resolution real-time imaging for observing spatial-temporal single cell behavior, cell-cell interactions and communications and cell-matrix interactions. The developed device can be used to study of blood microvasculatures, including angiogenesis, vasculogenesis and lymphangiogenesis. It also expands on transmigration and interaction studies of microvessels with immune cells and cancer cells. Robust barrier structures of blood brain barrier, glomerular filtration barrier or other tissue barriers can be reconstituted with direct and visual permeability measurements of target molecules. The device can explore complex and heterogeneous conditions of cancer progress, including survival, proliferation and collective migration under precisely controlled cancer microenvironments. Applications include the study of previously unexplored aspect of cancer metastasis, and have already provided new insights into how microenvironmental factors represent characteristics of a specific cancer patient.

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S4-3

3D PDC (Patient Derived Cells)-based Drug Screening for Simulating Cancer Patients

Dong Woo Lee /Biomedical Engineering, Konyang University

In this seminar, I will introduce new 3D cell culture technology, which is suitable to high throughput screening (HTS) with patient derive cells. Monolayer (2D) cell-based assays with human primary cells and immortalized cell lines have been used extensively for *in vitro* drug efficacy/toxicity testing, and indeed have become routine in drug discovery processes. However, many cells of normal and malignant origin lose some of their phenotypic properties when grown *in vitro* as 2D monolayer. Compared to 2D monolayer cell cultures, many researchers have already reported that three-dimensional (3D) cell cultures show different morphologies and protein/gene expressions and drug responses. Therefore, for mimicking human body or simulating cancer patients, there have been enormous efforts toward 3D cell cultures that can maintain specific biochemical and morphological features of human cells similar to the corresponding tissues *in vivo*, including human cells grown within the 3D structure of hydrogel such as alginate, matrigel, and collagen or human cells grown on 3D polymer scaffolds. However, conventional 3D cell cultures in hydrogels on the traditional multi-well plate platforms are difficult and daunting task to dispense highly viscous hydrogel/cell mixtures into multiple wells and change growth media by aspirating old media out and dispensing new media without disturbing the cell-containing hydrogels. Moreover, primary human cells are expensive and difficult to obtain in large quantities with uniform cell function for conventional high-throughput efficacy/toxicity screens. Therefore, assay miniaturization is an important issue for personalized cancer therapy research due to limited amounts of primary cells from invasive biopsy available for large combinations of therapeutic drugs. To address these technical issues, our group developed a novel micropillar/microwell chip platform (Fig. 1), on which 40 nL of cell spots in alginate are dispensed, and then immersed it into microwells filled with growth media for miniaturized 3D cell cultures. This approach easily exchanges media without any damage of 3D cell or hydrogels by replacing microwell chips. To verify the micropillar/microwell chip platform, we screen 24 drugs with three human primary brain cancer cells from patients and compare those results with gene expressions, which will eventually provide a valuable insight into personalized therapy research of each cancer patient.

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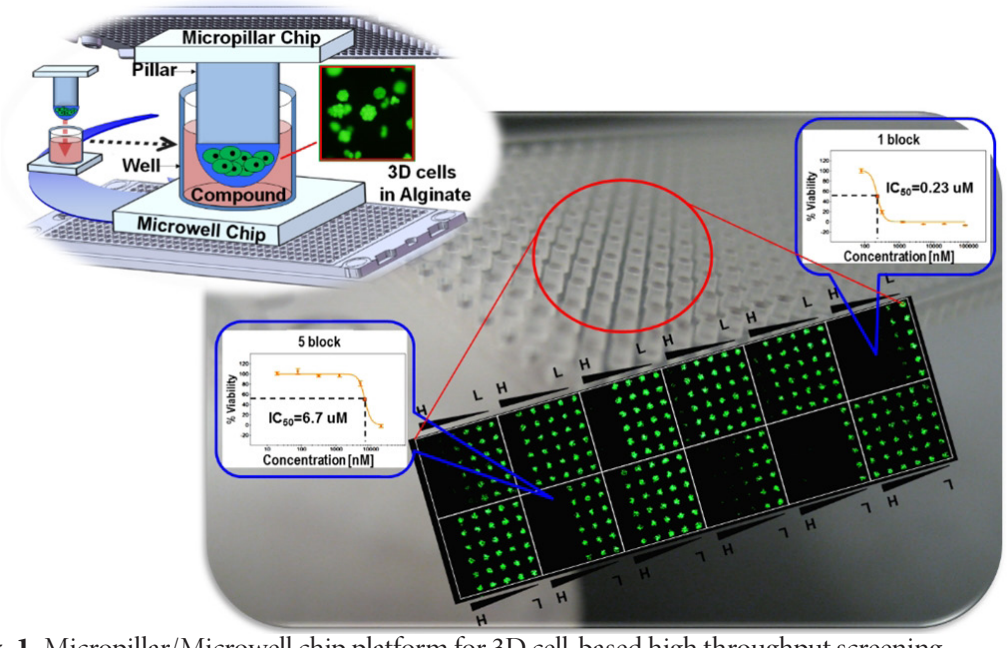

Fig. 1. Micropillar/Microwell chip platform for 3D cell-based high throughput screening.

S4-4

Microengineered Physiological Biomimicry: Lung-on-a-chip

Young-Jae Cho /Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University Bundang Hospital

Recently, personalized and precision medicine has become a hot topic of new medical research, and this is also true in the area of pulmonary disease. If standardized tissue dissociation techniques are developed to separate and cultivate epithelial cells, endothelial cells, and immune cells constituting tissues in normal or cancerous lung tissues derived from patients, and microelectromechanical systems with a 3D printing technique-based microelectromechanical system (MEMS) and microfluidics are applied, a lung-on-a-chip in which a human lung is three-dimensionally biologically imitated can be realized. The use of such organ chips can be an opportunity to establish a new research-based tool for the search for new drug candidates for acute lung injury, which is not easy for clinical trials. In case of commercialization, low cost effectiveness and shortening of research time can be expected. In addition, when simulating the tumor microenvironment, a patient-tailored metastatic lung cancer model can be generated and used to assess the efficacy of candidate drug candidates to block remote metastasis.

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해부학교육 심포지엄

2017년 10월 20일(금) 11:20 ~ 12:05
5A홀

좌장 허영범 경희대

ES-1 **11:20-11:35**
미래의학과 해부학교육
김홍태 • 대구가톨릭대학교 의과대학 해부학교실

ES-2 **11:35-11:50**
해부학 교육시간과 기초의학종합평가
송우철 • 건국대학교 의학전문대학원 해부학교실

ES-3 **11:50-12:05**
전국 의과대학 해부학, 조직학, 신경해부학 실습 현황 및 변화 양상
주경민 • 성균관대학교 의과대학

ES-1

미래의학과 해부학교육

김홍태 /대구가톨릭대학교 의과대학 해부학교실

인공지능과 빅데이터 활용, 3차원영상을 기반으로 한 가상현실, 증강현실, 융합현실이 미래 의학에 있어서 매우 중요한 역할을 하게 될 것이라고 예측하고 있다. 미래의 의료에서 의사는 교과서적 지식의 깊이보다는 의사와 환자의 개인적인 관계와 공감을 통한 소통능력과 비판적사고, 문제해결능력, 창의력 등의 능력이 보다 더 중요해 질 것이다. 미래 의학교육 현장은 주입식 암기교육이나 경쟁학습이 아니라 학생참여 협력학습이 필요하며, 기본개념을 이해한 다음에 바로 문제 해결을 위하여 기존의 지식과 정보를 어떻게 불러내고 변형하여 적용하는지 스스로 익히도록 하는 것으로 교육 개념이 바뀌고 있다. 미래 의료와 의학교육 환경 변화에 맞춰 지금부터 해부학교육을 어떻게 바꿔나갈 것인가를 논의하고 준비하여야 할 것이다. 미래 의학은 지금 의학을 전공하고 있거나 앞으로 의학을 전공하게 될 학생들에게는 곧 닥칠 현실이기 때문이다.

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ES-2

해부학 교육시간과 기초의학종합평가

송우철 /건국대학교 의학전문대학원 해부학교실

2016년 해부학교육시간 조사에 따르면 해부학관련 모든 과목의 평균 교육시간은 283시간으로 이 중 강의가 약 147시간, 실습은 약 135시간이었다. 기초의학종합평가는 KAMC 의학교육평가사업단에서 주관하여 주요 7개 기초의학과목의 문제를 출제, 정리, 검토, 선정하여 매년 시행하고 있다. 이 시험에는 1학년 29개, 2학년 22개 의과대학 및 의학전문대학원이 참여하고 있다. 그동안 약간의 변화가 있었지만 문항의 출제는 해부학회 교육위원회에서 논의하여 각 계통별로, 그리고 해부학, 조직학, 신경해부학, 발생학 등 각 과목별로 학습목표에 따라 고르게 출제되도록 조율하고 있다. 기초의학종합평가는 여러 단계를 거쳐 출제되고 검토되고 있기 때문에 각 대학에서 치르는 교내시험에 비해 비교적 공신력이 있다고 평가된다. 따라서 각 대학에서 진행되는 해부학 교육의 성취도를 평가하고 비교할 수 있는 참고자료로 활용될 수 있겠다. 학생들의 학업성취도에 영향을 미치는 요인으로는 교육과정(통합과정 또는 비통합과정), 교수법, 교육시기(의예과 또는 의학과), 교육시간(강의와 실습), 참여인력(교수와 조교) 등 여러가지가 있겠지만 여기에서는 기초의학종합평가의 해부학 성적과 해부학 교육시간과의 관계를 분석하여 어떤 상관관계가 있는지 보고자 한다.

Keywords: 해부학 교육시간, 기초의학종합평가

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ES-3

전국 의과대학 해부학, 조직학, 신경해부학 실습 현황 및 변화 양상

Kyeung Min Joo /Department of Anatomy and Cell Biology, Sungkyunkwan University School of Medicine

최근 성과바탕교육 등으로 의학교육이 점차 체계화, 표준화 되고 있다. 전통적으로 해부학교실이 담당하는 해부학, 조직학, 신경해부학, 발생학 과목도 의학교육 발전 추세에 발맞추어 나갈 것으로 예상된다. 이와 같은 상황에서 국내 의과대학의 교육현황과 그 동안의 변화양상을 정리하면 앞으로의 발전방향과 전략을 세우는데 큰 도움이 될 것이다. 강의와 실습 중에서 강의 시간 등은 몇 번의 전국적 조사가 있었으나 실습은 그렇지 못하였다. 강의뿐만 아니라 실습에도 많은 인력과 시간 그리고 노력이 투자되어야 한다는 점에서 실습교육 현황을 조사하는 것이 중요하다. 이에 전국 40개 의과대학 해부학교실을 대상으로 2017년, 2012년, 2007년 해부학, 조직학, 신경해부학 실습현황을 조사, 분석하였다. 대부분의 의과대학이 발생학 실습은 따로 진행하지 않을 것으로 예상하여 제외하였다. 조사 항목 중에서 실습시간, 실습교재(동영상 활용여부), 실습참여 인력 등을 중점적으로 비교분석하였다.

Keywords: Medical education, anatomy, histology, neuroanatomy, laboratory class

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젊은과학자 구연 발표

2017년 10월 19일(목) 09:00 ~ 09:15
Rm 324–326

좌장 이종은 연세대, 이자경 인하대

Y-1
(O-7)

09:00-09:15
The role of adiponectin in the central nervous system
Juhyun Song • Department of Anatomy, Chonnam National University Medical School, Gwangju, Korea

2017년 10월 20일(금) 09:00 ~ 09:15
Rm 323–324

좌장 윤 식 부산대, 김홍태 대구가톨릭대

Y-2
(O-19)

09:00-09:15
Fluorescence bioimaging of disease biomarkers and its applications in anatomy
Dokyoung Kim • Kyung Hee University, College of Medicine, Department of Anatomy and Neurobiology

2017년 10월 20일(금) 09:00 ~ 09:15
Rm 325–326

좌장 강재승 서울대, 오세옥 부산대

Y-3
(O-24)

09:00-09:15
Understanding Tumor Reversion: Searching for novel TCTP functions using a *Drosophila* model
Sung–Tae Hong • Department of Anatomy & Cell Biology, College of Medicine, Chungnam National University, Daejeon, Korea

Y-1

(0-7)

The role of adiponectin in the central nervous system

Juhyun Song /Department of Anatomy, Chonnam National University Medical School, Gwangju, Korea

Adiponectin as one of the adipocytes has been known that it controls glucose metabolism and inflammatory responses through a variety of cell signaling. The beneficial role of it has been demonstrated in diabetes and obesity models. Recently, adiponectin has been highlighted the role of it in central nervous system (CNS) diseases as well as metabolic diseases such as diabetes. In present study, we investigated the role of adiponectin in CNS through *in vitro* and *in vivo* studies. In neural stem cells (NSCs) culture, we confirmed that adiponectin could regulate the proliferation and survival of NSCs in high glucose *in vitro* condition. Based on our results after silencing TLX gene, adiponectin inhibits NSC's damage and promotes neurogenesis by controlling TLX genes. Moreover, we checked the effect of adiponectin in brain endothelial cells, consisted of brain blood barrier (BBB) under Amyloid beta induced oxidative stress condition. Adiponectin blocks the loss of tight junction proteins such as claudin 5 in Amyloid beta toxicity. Our western blotting and image data supported that adiponectin could protect the BBB breakdown by rescuing the brain endothelial cell's damage. Additionally, we observed that adiponectin regulates the polarization and function of microglia in *in vitro* oxidative stress condition. Moreover, we found that the anti-inflammatory effect of adiponectin on microglia is directly linked to PPAR-gamma signaling. Taken together, we suggest that adiponectin inhibits the neual stem cell damage and protects the BBB breakdown and suppresses inflammatory responses on microglia in inflammatory condition. Thus, we highlight that adiponectin may be a crucial target to attenuate inflammation in CNS.

Keywords: Adiponectin, Inflammation, Brain endothelial cells, Microglia, Neural stem cells, Blood brain barrier (BBB)

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Y-2

(0-19)

Fluorescence bioimaging of disease biomarkers and its applications in anatomy

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Understanding the molecular interactions in biological systems is of fundamental importance. Various types of assay and imaging tools have been developed for studying diverse biological processes as well as for diagnosis/imaging of disease. Among these tools, fluorescence methods have received great attention as they enable sensitive *in vivo* detection and imaging by relatively simple operation.

Fluorescent probes are molecules that absorb light of a specific wavelength and emit light of a different, typically longer, wavelength (a process known as fluorescence). Fluorescent probes with desirable sensing properties (analyte selectivity, sensitivity, bioimaging capability, etc.) are essential for the investigation of molecular interactions and thus have been extensively used in biochemical, clinical and environmental research areas. Recently, the fluorescence method is also widely used in anatomy and neuroscience. In this talk, speaker will introduce recent studies of fluorescent probes that can monitor biomarkers in disease such as Alzheimer's disease(AD) and cancer.

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Y-3

(O-24)

Understanding Tumor Reversion: Searching for novel TCTP functions using a *Drosophila* model

Sung-Tae Hong /Department of Anatomy & Cell Biology, College of Medicine, Chungnam National University, Daejeon, Korea

Tumor reversion is the biological process by which highly tumorigenic cells lose their malignant phenotype, thus it could be applied for one of the possible cancer treatment. However, the exact nature of tumor reversion is still largely unknown. TCTP (Transnationally controlled tumor protein) is a small protein of 25 kDa and the most critical protein out of several proteins to regulate tumor reversion. Although TCTP has many binding partners in cytoplasm, the nuclear functions of TCTP and its physiological (or *in vivo*) roles remains unclear.
To find novel TCTP function and its physiological roles, thereby expanding the knowledge to understand tumor reversion, I utilized two screen systems (phage display and yeast-two-hybrid using TCTP protein as a bait) and *Drosophila* as a model animal. From these screen, ATM (ataxia-telangiectasia-mutaed) kinase and Brm (Brahma) chromatin remodeling protein were obtained as a novel TCTP binding partner in cell nucleus. ATM kinase repairs DNA breaks and Brm promotes gene transcription. TCTP protein directly binds to these proteins and regulates their enzymatic activities. TCTP facilitates ATM kinase activity to repair DNA breaks and negatively regulates excess Brm activity to suppress ectopic gene transcription as well as to protect heterochromatin structure, biochemically and genetically. Altogether, these studies provides insights into novel TCTP functions in cell nucleus for the maintenance of genome stability.

Key words: Tumor reversion, TCTP (Transnationally controlled tumor protein), *Drosophila*, ATM (ataxia-telangiectasia-mutaed) kinase, Brm (Brahma) chromatin remodeling protein, DNA repair, Heterochromatin, Genome stability

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Oral Presentation

2017년 10월 19일(목) 09:00 ~ 10:30
Oral Presentation I (O1~6) Rm 321–323
Oral Presentation II (O7~12) Rm 324–326

2017년 10월 20일(금) 09:00 ~ 10:30
Oral Presentation III (O13~18) Rm 321–322
Oral Presentation IV (O19~23) Rm 323–324
Oral Presentation V (O24~29) Rm 325–326

01~6 **육안해부학**
좌장 황승준 울산대 • 한승호 중앙대

07~12 **신경과학**
좌장 이종은 연세대 • 이자경 인하대

013~18 **육안해부학**
좌장 김희진 연세대 • 이혜연 연세대

019~23 **조직 및 발생**
좌장 윤 식 부산대 • 김홍태 대구가톨릭대

024~29 **면역 및 종양**
좌장 강재승 서울대 • 오세옥 부산대

Oral Presentation I 육안해부학 (O1~6)

2017년 10월 19일(목) 09:00~10:30, Rm 321–323

좌장: 황승준 (울산대), **한승호** (중앙대)

O1 ---------- 34

Morpholog ical study of the subdeltoid bursa and its innervation

Chang Min Seo[1], Anna Jeon[1], Je-Hun Lee[2], Seung-Ho Han[1]
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O2 ---------- 34

Morphological Classification of the Temporalis Muscle Focusing on the Attachments on the Coronoid Process

Sun-Kyoung Yu, Heung-Joong Kim
Department of Oral Anatomy, College of Dentistry, Chosun University

O3 ---------- 35

작은광대근의 힘살 구성과 부착에 대한 해부학적 연구

허미선, 김호정, 이규석
Department of Anatomy, Catholic Kwandong University College of Medicine

O4 ---------- 35

Oblique thyroarytenoid muscle in humans: an independent muscle or an ac cessory belly?

Shin-Hyo Lee, Tae-Jun Ha, Ki-Seok Koh, Wu-Chul Song
Department of anatomy, Research Institute of Medical Science, Konkuk University School of Medicine, Seoul, Korea

O5 ---------- 35

Novel Structure Related with the Superficial Perineal Muscle

Hyun-Min Choi[1], So-Young Jung[1], Soo-Jung Kim[1], Jin Yoo[1], Hyeon-Joo Kim[1], Hee-Jun Yang[2], Hye-Yeon Lee[1]
[1]Department of Anatomy, Yonsei University Medical College, [2]Department of Anatomy, Gachon University Medical College

O6 ---------- 36

윗눈꺼풀의 감각신경 Sensory Innervation of the Upper Eyelid

Kun Hwang, Xiajing Wu
Department of Plastic Surgery, Inha University School of Medicine

Oral Presentation II 신경과학 (O7~12)

2017년 10월 19일(목) 09:00~10:30, Rm 324–326

좌장: 이종은 (연세대), **이자경** (인하대)

O7 ---------- 36

The role of adiponectin in the central nervous system

Juhyun Song
Department of Anatomy, Chonnam National University Medical School

O8 ---------- 37

Habenular cholinergic signaling dysfunction drives anhedonia-like behavior

Seungrie Han[1], Soo Hyun Yang[1], Jin Yong Kim[1], Seojung Mo[1], Esther Yang[1], Ki Myung Song[1], Byung-Joo Ham[2], Naguib Mechawar[3], Gustavo Turecki[3], Hyun Woo Lee[1], Hyun Kim[1]
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[3]Department of Psychiatry, McGill University, Douglas Mental Health University Institute, Montreal, QC H4H 1R3, Canada

O9 ---------- 37

Inhibition Of Microglial Activation Via P38 MAPK SiRNA-Encapsulated PLGA Nanoparticles Relieves Neuropathic Pain Induced By Spinal Nerve Ligation In Rats

Juhee Shin[1,2], Jinpyo Hong[1], Yuhua Yin[3], Hyewon Park[1], Dong woon Kim[1]
[1]Department of Anatomy, School of Medicine, Chungnam National University, [2]Department of Medical Science, Chungnam National University School of Medicine, [3]Department of Anesthesia and Pain Medicine, Chungnam National University Hospital

O10 ---------- 38

Perivascular adventitial cells expressing nestin contribute to fibrotic scar formation in striatum of 3-NP intoxicated rats

Tae-Ryong Riew[1], Jeong-Heon Choi[1], Hong Lim Kim[2], Xuyan Jin[1], Mun-Yong Lee[1]
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Oral Presentation III 육안해부학

(O13~18)
2017년 10월 20일(금) 09:00~10:30, Rm 321–322

좌장: 김희진 (연세대), **이혜연** (연세대)

Oral Presentation IV 조직 및 발생

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2017년 10월 20일(금) 09:00~10:30, Rm 323–324

좌장: 윤 식 (부산대), **김홍태** (대구가톨릭대)

020 ---------- 44
Three Theories on the Mechanism of Hair Graying
Seong Kyeong Jo[1], Ji Yeon Lee[1], Chang Deok Kim[2], Jeung-Hoon Lee[2], Young Ho Lee[1]
[1]Department of Anatomy, College of Medcine, Chungnam National University, [2]Department of Dermatology, College of Medcine, Chungnam National University

021 ---------- 44
The expression of androgen receptor on the kidney with ischemia and reperfusion injury
Sang Hong Bak, Min Jung Gong, Kwon Moo Park
Department of Anatomy, Kyungpook National University School of Medicine, Daegu, Korea

022 ---------- 45
Ancient Helicobacter pylori DNA found in Joseon mummies
Chang Seok Oh[1], Jong Ha Hong[1], Hyejin Lee[1,2], Soong Deok Lee[3,4], Eunju Lee[5], Dong Hoon Shin[1,4]
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023 ---------- 45
Genetic Study of Ancient Trichuris trichiura Eggs in Joseon Dynasty Specimens
Jong Ha Hong[1], Chang Seok Oh[1,2], Min Seo[3], Dong Hoon Shin[1,2]
[1]Laboratory of Bioanthropology, Paleopathology and History of Diseases, Seoul National University College of Medicine, Seoul, Korea, [2]Institute of Forensic Science, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Parasitology, Dankook University College of Medicine, Cheonan, Korea

Oral Presentation V 면역 및 종양
(O24~29)
2017년 10월 20일(금) 09:00~10:30, Rm 325-326

좌장: 강재승 (서울대), **오세옥** (부산대)

024 ---------- 46
Understanding Tumor Reversion: Searching for novel TCTP functions using a *Drosophila* model
Sung-Tae Hong
Department of Anatomy & Cell Biology, College of Medicine, Chungnam National University. Daejeon 35015, Korea

025 ---------- 46
Fish Scale Collagen Peptides Protect Against CoCl2/TNF-α-Induced Cytotoxicity and Inflammation via Inhibition of ROS, MAPK, and NF-κB Pathways in HaCaT Cells
Ye Seon Lim[1,5], Fazli Subhan[1,5], Muhammad Ikram[1,5], Seon Yeong Hwang[1,5], Yejin Ok[1,5], In Hwa Cho[1,5], Song Wan Jin[2,5], Young Hun Jeong[3,5], Jong-Young Kwak[4,5], Sik Yoon[1,5]
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026 ---------- 47
Ethanol extract of Dryopteris Crassirhizoma alleviates allergic rhinitis via modulation of cytokines and histamine release from mast cells
Chun Hua Piao, So Ri Sim, Suhwan Choi, Hyoung-Tae Kim, Eui-Hyeog Han, Chang Ho Song, Ok Hee Chai
Department of Anatomy, Chonbuk National University Medical School

027 ---------- 47
Rosae Multiflorae Fructus Extract Alleviates Ovalbumin-induced Allergic Rhinitis via Regulation of Th1/Th2 Imbalance
Thi Tho Bui, Chang Ho Song, Ok Hee Chai
Department of Anatomy, Chonbuk National University Medical School

028 ---------- 47
Identification of heterogeneity ac cording to progression in bladder cancer by single-cell RNA-seq
Da Eun Jeong[1,4], Hye Jin Song[3,4], Hee Jang Pyeon[3,4], Sung Soo Kim[1,4], Yoon Kyung Bae[1,4], Jeong Sup Won[1,4], Ji Yoon Hwang[3,4], So Yeong Cho[3,4], Hyun Nam[2,4], Kyeung Min Joo[1,3,4], Young Eun Choi[4]
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029 ---------- 48
Co-Targeting of Tiam1/Rac1 and Notch Ameliorates Chemoresistance Against Doxorubicin In A Biomimetic 3D Lymphoma Model
Muhammad Ikram[1,2], Ye Seon Lim[1,2], Seon Young Hwang[1,2], Yejin Ok[1,2], In Hwa Cho[1,2], Hae Yeong Kang[1,2], Sun-Yong Baek[1], Sik Yoon[1,2]
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01

Morphological study of the subdeltoid bursa and its innervation

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The subdeltoid bursa is one of the main structures that cause shoulder pain. Previous studies have discussed the locations and innervation of sensory nerve of the subacromial bursa at large, and there was no detailed study focusing on the subdeltoid bursa. The aim of this study was to accurately identify the distribution of sensory nerve branches running to subdeltoid bursa with mesoscopic dissection and the sizes, and locations after injecting gelatin into the bursa. Eighteen shoulders of 11 Korean soft cadavers were dissected (average age 65, age ranged 43 - 88 years). The most prominent point of greater tubercle of the humerus(GT) were used reference point. The horizontal line passing through GT was used as x-axis and the vertical line passing through the GT was used as y-axis. The average width and height of subdeltoid bursa were 4.6 ± 2.1 cm and 5.3 ± 1.2 cm, respectively. The size of the subdeltoid bursa was varied among specimens. The mean volume of subdeltoid bursa was 6.0 ± 1.0 ml (volume ranged 5 – 7 ml). The mean distances from GT were 2.6 ± 1.5 cm superiorly, 3.0 ± 1.4 cm inferiorly, and 1.9 ± 1.2 medially, 2.7 ± 1.1 cm laterally. The most common shape of subdeltoid bursa was oval shape. In 15 cases of 18 shoulders, the anterior branch of the axillary nerve distributed to subdeltoid bursa with running posteriorly. The muscular branch of anterior and middle parts of the deltoid distributed to the branch of nerve that into the subdeltoid bursa. A branch of the posterior cord of brachial plexus was distributed to the subdeltoid bursa with running anteriorly in 3 cases. These results might be helpful for the prevention of the residual pain on the anterior shoulder region after injection for relief the shoulder pain. Acknowledgement: This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning(2017R1A2B4005787).

Keywords: Subdeltoid bursa, Axillary nerve, Posterior cord of brachial plexus, Shoulder pain

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02

Morphological Classification of the Temporalis Muscle Focusing on the Attachments on the Coronoid Process

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Recently, it is reported that temporalis muscle is divided into three parts and acts as one structural unit. Insertion of temporalis muscle continues onto the retromolar triangle, so it is required caution during surgical treatment. The aims of this study were to classify the temporalis muscle by fascicle and to identify its attachments on the coronoid process for providing their anatomical characteristics and clinical significance. The temporalis muscle acquired 26 cadavers were examined. It was distinguished by fascicle and each attachment region on the coronoid process was measured based on the inferior border of the mandible and the lingula level. In all specimen, temporalis muscle was separated into 3 layers; zygomaticomandibularis part (outermost), proper temporalis muscle part (superficial), and sphenomandibularis part (deep). The zygomaticomandibularis part inserted into only a small part of the mandibular notch and the lateral coronoid process. The proper temporalis muscle part ran along the coronoid process anteriorly converting into the superficial tendon and made a lateral boundary of the retromolar triangle. The sphenomandibularis part inserted into the medial coronoid process, ran along the lingual margin of the temporal crest converting into the deep tendon, and made a medial boundary of the retromolar triangle. These research results are expected to provide the anatomical knowledge on morphology of the temporalis muscle related to its insertion on the coronoid process during the surgical procedure such as extraction, anesthesia, implant placement, and TMJ reduction at the retromolar region.

Keywords: Temporalis Muscle, Coronoid Process, Zygomaticomandibularis, Sphenomandibularis, Temporalis Tendon

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03

작은광대근의 힘살 구성과 부착에 대한 해부학적 연구

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이 연구의 목적은 작은광대근의 힘살 구성과 부착부위를 명확히 하기 위함이다. 재료는 한국성인시신 얼굴 20쪽을 사용하였다. 작은광대근의 구성과 부착부위를 확인하기 위하여 작은광대근을 구성하는 힘살 다발들을 분리하여 추적하였다. 작은광대근은 모든 예에서 광대뼈에서 일어나는 근육섬유와 눈둘레근에서 계속된 근육섬유로 구성되었다. 광대뼈에서 일어난 근육섬유와 눈둘레근에서 계속된 근육섬유의 양은 표본마다 다르게 관찰되었다. 작은광대근의 구성은 광대뼈에서 일어난 근육섬유가 눈둘레근에서 계속된 근육섬유보다 많은 경우는 50%, 눈둘레근에서 계속된 근육섬유가 광대뼈에서 일어난 근육섬유 보다 많은 경우는 35%, 광대뼈에서 일어난 근육섬유와 눈둘레근에서 계속된 근육섬유의 양이 비슷한 경우는 15%였다. 작은광대근은 모든 예 (100%)에서 위입술의 근육과 피부에 닿았으며, 광대뼈에서 일어나는 작은광대근의 근육섬유가 눈둘레근의 아래섬유와 합쳐지는 경우는 55%였다. 이 근육섬유들은 위턱뼈의 이마돌기, 위입술콧방울올림근, 눈썹내림근에 부착되었다. 이 연구 결과들은 작은광대근의 작용을 눈확과 입 부위의 움직임과 관련하여 이해하고, 다양한 얼굴 수술을 하는데 도움이 되는 자료가 될 것으로 생각된다.

Keywords: 작은광대근, 눈둘레근, 광대뼈, 위입술, 눈확

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04

Oblique thyroarytenoid muscle in humans: an independent muscle or an ac cessory belly?

Shin-Hyo Lee, Tae-Jun Ha, Ki-Seok Koh, Wu-Chul Song
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The thyroarytenoid (TA) muscle is known to play important roles in controlling the equality and intensity of phonation. The TA muscle draw the arytenoid cartilages toward the thyroid cartilage, thereby rotating the arytenoid cartilage medially and relaxing the vocal ligaments. Occasionally an anomalous muscle belly lies on the lateral surface of the main mass of the TA muscle. This study aimed to determine the prevalence and variations of anomalous muscle bellies superficial to the TA muscle in humans. One-hundred hemilarynges from 50 formalin-embalmed cadavers were dissected to investigate the morphology of muscle fibers of the TA muscle. 36% of hemilarynges (n = 36) were found to have distinct oblique belly superficial to the TA muscle. In 28 cases the belly had a relatively constant origin and an insertion that extended straight onto the TA muscle from the anterosuperior area of the internal surface of the thyroid lamina to the base of the muscular process of the arytenoid cartilage. Eight cases were located in a similar area, but with some differences in the origin or insertion features. We nominate this muscle as an oblique TA muscle. This muscle has a high prevalence, and it probably acts on closing and relaxing of the vocal cords. It remains to be determined whether the oblique TA muscle is an independent muscle or an accessory belly of the main TA muscle.

Keywords: arytenoid cartilage, oblique TA, thyroarytenoid muscle, vocal cord

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05

Novel Structure Related with the Superficial Perineal Muscle

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전립샘암의 수술은 고전적으로는 샅부위로 접근하는 수술을 하였으나, 내시경의 발달로 인해 로봇팔을 이용하여 골반으로 접근하는 새로운 수술법의 시대를 열게 되었다. 그러나 근래 들어 이의 개선방법으로 'perineal single port RP'로 림프절 절제까지 시도되고 있으나, 정작 비뇨생식삼각의 해부학 구조에 대한 발전은 없는 상태이다. 이에 연구자들은 29구의 남성시신(79.6세)을 이용하여 수술을 위해 필요한 해부학적 표지구조를 수립하고,

perineal body에 대한 새로운 구조적 정의를 확인하고자 이 연구를 시행하였다. 연구에 사용한 시신은 통상적 방법으로 포르말린 고정한 시신을 사용하였다. 모든 표본에서 피부밑조직에 위치한 fibrous band가 anal sphincter muscle의 cutaneous fiber에서 bulbocavernosus muscle의 raphe와 이어지는 것을 관찰하였으며, 그 두께는 표본에 따라 다양하였다. 이는 수술 시 perineal body의 위치를 찾을 수 있는 중요한 표지자로 활용할 수 있는 구조이며, 이전에 다른 연구자들이 흔히 perineal boby 와 혼동하던 구조임을 확인하였다. 연구자들은 이를 cutaneous central band로 명명하고 central perineal body 등으로 혼동되어 부르지 않아야 할 것을 제안한다. Perineal membrane 보다 표면에 위치하며, superficial transverse perineal muscle과는 달리 ischial tuberosity에서 일어나 사선방향으로 달려서 bulbospongiosus의 distal portion의 표면에서 끝나는 accessory superficial perineal muscle을 61.5 %의 표본에서 관찰하였다. 이 덧근육은 양쪽에 모두 나타나는 경우(38.4%)가 더 많았다. 이 덧근육은 주로 띠 모양이었으나, 삼각돛 모양으로 superficial perineal muscle과 연결된 것도 관찰하였다. 이 덧근육의 평균길이는 35.6 mm 였다. 이 근육은 음경을 지지해 주며 음경의 elevation 과 backward retraction 에 관여하는 것으로 추정하였다. Accessory superficial perineal muscle은 있으나 superficial transverse perineal muscle이 없는 경우는 4쪽에서 관찰하였다.

Keywords: New central fibrous band Superficial perineal muscle Accessory superficial perineal muscle

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06

윗눈꺼풀의 감각신경 Sensory Innervation of the Upper Eyelid

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목적: 윗눈꺼풀에서 삼차신경의 신경분포영역을 밝히는데 있다.
재료 및 방법: 한국인 성인시신 8구의 8쪽 얼굴을 해부하였다. 이마신경, 눈확위신경, 도르래위신경, 도르래아래신경 및 눈물신경을 추적하였다.
결과: 이마신경의 종말 가지들은 안쪽눈구석으로부터 눈틈새의 1/6에서 2/5 사이에, 눈꺼풀 가장자리에서 눈썹 높이의 1/6 이내에 분포하였다. 눈확위신경의 종말 가지들은 안쪽눈구석으로부터 눈틈새의 2/5에서 9/10 사이에, 눈꺼풀 가장자리에서 눈썹 높이의 1/3 이내에 분포하였다. 도르래위신경의 종말 가지들은 안쪽눈구석으로부터 눈틈새의 −1/4에서 −1/5 사이에, 눈꺼풀 가장자리에서 눈썹 높이의 1/5 이내에 분포하였다. 도르래아래신경의 종말 가지들은 안쪽눈구석으로부터 눈틈새의 −1/4에서 1/10 사이에, 눈꺼풀 가장자리에서 눈썹 높이의 1/5 이내에 분포하였다. 눈물신경의 종말 가지들은 안쪽눈구석으로부터 눈틈새의 3/5에서 13/10 사이에, 눈꺼풀 가장자리에서 눈썹 높이의 1/4 이내에 분포하였다. 이마신경과 눈확위신경의 주가지들은 위눈확틈새로부터 눈꺼풀판의 윗모서리까지 눈둘레근 밑으로 주행하다가, 눈꺼풀판 앞에서 눈둘레근과 눈꺼풀판 사이로 지나갔다. 도르래위신경과 도르래아래신경은 눈둘레근과 피부 사이에 있었다. 눈물신경은 눈둘레근과 눈꺼풀판 사이에서 관찰되었다.
결론: 주로 눈확위신경과 이마신경이 윗눈꺼풀에 분포하였다. 안쪽 끝은 도르래위신경과 도르래아래신경이, 가쪽 끝은 눈물신경이 분포하였다.

Keywords: Eyelids; innervation;

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07

The role of adiponectin in the central nervous system

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Adiponectin as one of the adipocytes has been known that it controls glucose metabolism and inflammatory responses through a variety of cell signaling. The beneficial role of it has been demonstrated in diabetes and obesity models. Recently, adiponectin has been highlighted the role of it in central nervous system (CNS) diseases as well as metabolic diseases such as diabetes. In present study, we investigated the role of adiponectin in CNS through in vitro and in vivo studies. In neural stem cells (NSCs) culture, we confirmed that adiponectin could regulate the proliferation and survival of NSCs in high glucose in vitro condition. Based on our results after silencing

TLX gene, adiponectin inhibits NSC's damage and promotes neurogenesis by controlling TLX genes. Moreover, we checked the effect of adiponectin in brain endothelial cells, consisted of brain blood barrier (BBB) under Amyloid beta induced oxidative stress condition. Adiponectin blocks the loss of tight junction proteins such as claudin 5 in Amyloid beta toxicity. Our western blotting and image data supported that adiponectin could protect the BBB breakdown by rescuing the brain endothelial cell's damage. Additionally, we observed that adiponectin regulates the polarization and function of microglia in in vitro oxidative stress condition. Moreover, we found that the anti-inflammatory effect of adiponectin on microglia is directly linked to PPAR-gamma signaling. Taken together, we suggest that adiponectin inhibits the neual stem cell damage and protects the BBB breakdown and suppresses inflammatory responses on microglia in inflammatory condition. Thus, we highlight that adiponectin may be a crucial target to attenuate inflammation in CNS.

Keywords: Adiponectin, Inflammation, Brain endothelial cells, Microglia, Neural stem cells, Blood brain barrier (BBB)

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08

Habenular cholinergic signaling dysfunction drives anhedonia-like behavior

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Dysfunction of cholinergic signaling in the brain has long been believed to be associated with depressive disorders. However, the functional impact of habenular cholinergic signaling on the specified depressive behaviors is not well understood. Here, we demonstrated that the expression levels of cholinergic signaling genes (CHAT, VACHT, CHT, CHRNA3, CHRNB3 and CHRNB4) were down-regulated in a chronic restraint stress (CRS) rat model of depression, in which rats display depression-like behaviors such as anhedonia and mood despair. Moreover, knockdown of CHAT in the rat habenula was sufficient to evoke anhedonia-like behavior. The anhedonia-like behavior induced by CHAT knockdown was not reversed by chronic administration of the selective serotonin reuptake inhibitor fluoxetine. To determine whether habenular cholinergic signaling is associated with regulation of dopamine neurons in the ventral tegmental area (VTA) and serotonin neurons in the dorsal raphe nucleus (DRN), we used CHAT::cre transgenic mice expressing the Designer Receptors Exclusively Activated by Designer Drugs (DREADD). Pharmacogenetic activation of habenular cholinergic neurons induces the excitation of dopamine neurons in the VTA and reduces the immunoreactivity of 5-hydroxytryptamine (5-HT) in the DRN. Habenular cholinergic gene down-regulation was recapitulated in the postmortem habenula of suicide victims diagnosed with major depressive disorder (MDD).

Keywords: Habenula, Cholinergic, Depression, Chronic restraint stress

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09

Inhibition Of Microglial Activation Via P38 MAPK SiRNA-Encapsulated PLGA Nanoparticles Relieves Neuropathic Pain Induced By Spinal Nerve Ligation In Rats

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Neuropathic pain from the damage or dysfunction of the nervous system leads complex and various chronic pain state to patients, and its therapeutics are still not clear. It has been well known that p38 MAPK signaling cascade in microglia plays a pivotal role in the development and progression of neuropathic pain. Thus, p38 MAPK

inhibitors are frequently tried as drugs for curing neuropathic pain. However, it has low efficiency at large due to poor specificity to microglia. In this study, to overcome this limit, we used p38 MAPK siRNA-loaded PLGA nanoparticles to target p38 MAPK microglia-specifically to reduce neuropathic pain induced by spinal nerve ligation (SNL) in rats. Most of all, the physical characteristics of the nanoparticles were analyzed by Zeta potential measurement and TEM imaging. Then, the loss of p38 MAPK expression in BV2 cells with incubating the PLGA nanoparticles was also examined by immunoblotting. Moreover, LPS-induced pro-inflammatory gene expression including TNF-alpha and IL-1 beta was decreased dramatically in the nanoparticles-treated BV2 cells compared to control. Furthermore, SNL-induced pain was alleviated for five days in von Frey filament test by one intrathecal injection of the nanoparticles at day 7 following surgery. Likewise, microglial inactivation in dorsal horns of spinal cords of rats supplemented with the nanoparticles was investigated by immunostaining with Iba1 antibodies. Taken together, these results suggest that p38 MAPK siRNA-encapsulated PLGA nanoparticles attenuates SNL-induced neuropathic pain by suppressing microglia activation via p38 MAPK targeting, and it would be a feasible therapeutic tool for treating neuropathic pain.

Keywords: neuropathic pain, nanoparticle, p38, microglia

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010

Perivascular adventitial cells expressing nestin contribute to fibrotic scar formation in striatum of 3-NP intoxicated rats

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Perivascular cells expressing platelet-derived growth factor receptor beta (PDGFRβ) has recently been proposed to contribute the fibrotic scar, which is characterized by excess deposition of fibrous extracellular matrix in the lesion core, after brain insults. In the present study, we investigated a detailed characterization of PDGFRβ-positive perivascular cells in the striatum of rats treated with the mitochondrial toxin 3-nitropropionic acid (3-NP). We also determined whether these perivascular cells require intermediate proteins nestin and vimentin in order to acquire their scar-forming phenotypes. Cells expressing PDGFRβ were observed only in vascular profiles of larger caliber in control striatum, but expression on vascular profiles had increased in the lesion core 3–7 days after 3-NP injection: PDGFRβ was only partially noted on 62.8 % of the vasculature at day 3, but was associated with most (99.6%) vessels by day 7. By 14 days post-lesion, highly branched processes of PDGFRβ-positive cells formed a network within or around the vascular profiles and even in the intervascular area. The expression profiles of PDGFRβ and collagen IV shared overlapping expression patterns in the lesion core. In particular, PDGFRβ and collagen IV in the intervascular areas was distinct on days 7–14 after reperfusion and thereafter increased progressively throughout the 28-day experimental period. This observation was confirmed by quantitative comparison of time-dependent expression of PDGFRβ and collagen IV. Immunoelectron microscopic findings demonstrated that in saline-treated control, constitutive PDGFRβ-positive cells invariably lay outside the smooth muscle cells and had scarce cytoplasmic organelles, while in the lesion core starting from 3 days post-lesion, they had large euchromatic nuclei with a prominent nucleolus, and expanded cytoplasm with abundant and frequently dilated cisternae of granular endoplasmic reticulum and associated extracellular collagen, indicating that the cellular profile of PDGFRβ-positive cells changed dramatically from the resting fibrocyte-like cells to active fibroblast-like cells over time. The spatiotemporal distribution pattern of PDGFRβ expression within both perivascular and intervascular space closely matched those of nestin and vimentin in the lesion core, although both proteins were induced in almost all of vasculature earlier (3 days) than PDGFRβ. In addition, a correlative light- and electron-microscopic approach confirmed that PDGFRβ-positive cells expressed nestin. These findings show in the lesion core after 3-NP injection that PDGFRβ-positive cells originating from vascular adventitial fibrocyte-like cells could transform into cells with fibroblast-like cellular morphology and these reactive phenotypes expressed nestin and vimentin, suggesting that nestin and vimentin may allow for the dynamic structural remodeling in these cells that contribute to the fibrotic scar formation in response to brain insults. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2017R1A2B4002922).

Keywords: Fibrosis, Fibroblast, PDGFRβ, Nestin, 3-nitropropionic acid

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011

Role of Mitochondrial NADP+ dependentIsocitrate Dehydrogenase Obesity-induced Hypertension And Renal Dysfunction

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Obesity is a major risk factor for essential hypertension, diabetes, and other comorbid conditions that contribute to development of chronic kidney disease. Oxidative stress is an important pathogenic mechanism of obesity-induced hypertension. Mitochondrial NADP+-dependent isocitrate dehydrogenase (IDH2) catalyzes the oxidative decarboxylation of isocitrate to α-ketoglutarate, synthesizing NADPH, an essential factor for the maintenance of mitochondrial redox balance. Here, we investigated the role of IDH2 in obesity-induced hypertension using IDH2 gene-deleted (IDH2-/-) mice. Eight-week-old IDH2-/- and wild-type (IDH2+/+) littermates were fed a normal diet (ND) or a high fat diet (HFD) for 13 weeks. After 13 weeks HFD, mRNA levels of renin, angiotensinogen, angiotensin-converting enzyme, and angiotensin receptor type1 in the kidney increased in both of HFD mice, and these increases were greater in the IDH2-/- mouse kidneys than in the IDH2+/+ mouse kidneys. Angiotensin levels in the serum increased after HFD, and these increases were greater in the IDH2-/- mice than in the IDH2+/+ mice. After 13 weeks HFD, RNA levels of Na+-K+-ATPase, Na+-Cl- cotransporter, and Na+/H+ exchanger 3 increased both in the IDH2-/- and IDH2+/+ HFD mouse kidneys when compared with those of ND mice and these increases were greater in the IDH2-/- mouse kidneys than in the IDH2+/+ mouse kidneys. These results indicate that obesity-mediated hypertension and renal dysfunction are worsened by IDH2 gene deletion, suggesting that mitochondrial redox balance is associated with obesity-induced hypertension and renal diseases.

Keywords: Obesity, Isocitrate Dehydrogenase, Renin-Angiotensin-Aldosterone System, Hypertension

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012

Retinoic acid and CTCF induce the collinear expression of the Hoxa cluster in a competitive manner

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During the development of an embryo, the initiation of the collinear expression of Hox genes is essential for the proper formation of the anteroposterior body axis. Retinoic acid (RA), a natural derivative of vitamin A, plays a role in vertebrate development by regulating Hox gene expression. CCCTC-binding factor (CTCF), an insulator protein that controls gene transcription, also regulates the expression of Hox genes by binding to CTCF-binding sites (CBSs). It has been reported that upon RA signaling, retinoic acid response elements (RAREs) located in the Hox clusters become occupied. Interestingly, RAREs exist in close proximity with CBSs, and so when RA is bound, CTCF cannot bind. Without CTCF and its insulator activities, the repressive domain in the chromatin becomes open for transcription. Here, we examine the relationship between RA and CTCF during the RA-induced expression of the Hoxa cluster genes, using F9 murine embryonic teratocarcinoma cells as a model system. We time-dependently treat F9 cells with RA, confirm the collinear expression of Hoxa genes, and validate CTCF-binding in F9 cells as well as in CTCF-overexpressing F9 cells, in the presence of RA. The present study suggests that RA and CTCF pose antagonistic effects on each other during vertebrate development to attain Hox gene collinearity.

Keywords: Hox genes, RA, RAREs, CTCF, F9

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013

Professional identity formation of medical students through anatomy dissection and related rituals

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Gaining the values of medical professionalism is a critical issue in medical education. It is recognized that anatomy dissection can contribute to early professional identity formation by encouraging medical students to develop the fundaemental values of humanism and professionalism. The purpose of this study was to understand the change of attitude and acquired values through anatomy dissection and related rituals. A paper survey was conducted at the beginning and end of cadaver dissection to 235 first-year medical students for two consecutive years. Additional qualitative responses were collected on the first day of encounter with cadaver and on the day of annual cadaver memorial ceremony. Our results indicated that cadaveric dissection significantly improved students' attitude towards patients, believing a donor as their first patient. Students also responded that sign of last word, silence tribute, and annual ceremony for donors have positively influenced on humanistic values such as honesty, trustworthiness, and altruism. Several students expressed a sense of heaviness after encountering cadavers and donors' families; however, the feeling was converted into a sense of duty to become a doctor. Our findings suggested that cadaveric dissection and related rituals enables medical students to consider the humanity of donors and begin to contemplate one's attitude towards a career in medicine, which contributes to the formation of early professional identity.

Keywords: professional identity formation, anatomy dissection, donor, humanism

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014

The Distribution of Great Auricular Nerve on the Tympanoparotid Fascia and Earlobe Relating to Face and Neck Lift

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The tympanoparotid fascia has been reported that it is an effective and safe anchoring structure in performing platysma suspension and platysmaplasty. Surgeons are careful to avoid damaging the great auricular nerves during the rhytidectomy in the face and neck region. These nerve injuries result in a pain and paresthesia of the earlobe and preauricular region. The aim of this study was to elucidate the sensory distribution of the earlobe close to the tympanoparotid fascia and provide the safest point to fixate the platysma during neck lift procedures. Twenty hemifaces from Korean cadavers (5 males and 8 females; mean age 77.0 years) were used in this study. The intertragal notch point, otobasion inferioris, otobasion superioris were used as reference points. A line connecting the intertragal notch point and the otobasion inferioris was used as the y-axis; a line drawn perpendicular to this plane through the intertragal notch point was used as the x-axis. A line connecting the otobasion superioris and otobasion inferioris was a reference line and the otobasion superioris was the starting point for measuring the location of tympanoparotid fascia. The following measurements are obtained: the entering point and curved point of the lobular branch of great auricular nerve into the earlobe (x and y coordinates); the location of tympanoparotid fascia; the depth of tympanoparotid fascia from the skin; the depth of sensory nerve into the tympanoparotid fascia from the skin. And, the entering pattern of lobular branch was classified according to the Y axis. The average entering point into the earlobe was 1.6 ± 2.8 mm on the x-coordinate and 8.5 ± 2.4 mm on the y-coordinate. The average curved point in the earlobe was 2.7 ± 1.5 mm on the x-coordinate and 7.4 ± 1.6 mm on the y-coordinate. With regard to the entering pattern of the lobular branch, the centrally entered was the most common (50.0 %), followed by the laterally entered (33.0 %); the medially entered (17.0 %) was noted in only three specimens. The average distance of the superior border and inferior border of the tympanoparotid fascia on the reference

line as a percentage of the total reference line were 58.4 % and 72.9 %, respectively. The average value about the depth of tympanoparotid fascia from the skin was 10.8 ± 2.0 mm; the depth of the sensory nerve passing through the tympanoparotid fascia from the skin was 4.4 ± 1.2 mm. Acknowledgement: This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning(2017R1A2B4005787).

Keywords: great auricular nerve, tympanoparotid fascia; earlobe; rhytidectomy

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015

Stereotactic Topography of The Greater and Third Oc cipital Nerves and Its Clinical Implication

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The occipital nerve block has been commonly used to diagnosis and treatment of the occipital neuralgia, also known as C2 neuralgia. The aim of the present study was to provide the three-dimensional locations of emerging points of the greater occipital (GON) and third occipital (3ON) nerves on the back muscles (60 sides, 30 cadavers) and their spatial relationship with muscle layers, using a 3D digitizer (Microscribe G2X, Immersion Corp, San Jose CA, USA). With reference to the external occipital protuberance (EOP), GON pierced the trapezius at a point 22.6±7.4 mm lateral and 16.3±5.9 mm inferior and the semispinalis capitis (SSC) at a point 13.1±6.0 mm lateral and 27.7±9.9 mm inferior. With the same reference, 3ON pierced, the trapezius at a point 12.9±9.3 mm lateral and 44.2±21.4 mm inferior, the splenius capitis at a point 10.0±5.3 mm lateral and 59.2±19.8 mm inferior, and SSC at a point 11.5±9.9 mm lateral and 61.4±15.3 mm inferior. Additionally, GON arose, winding up the obliquus capitis inferior, with the winding point located 52.3±11.7 mm inferior to EOP and 30.2±8.9 mm lateral to the midsagittal line. Knowing the course of GON and 3ON, from their emergence between vertebrae to the subcutaneous layer, is necessary for reliable nerve detection and precise analgesic injections. Moreover, stereotactic measurement using the 3D digitizer seems useful and accurate for neurovascular structure study.

Keywords: Greater occipital nerve, Third occipital nerve, Occipital nerve block, Occipital neuralgia

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016

초음파를 이용한 위, 아래입술동맥의 위치관계

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입술에는 얼굴동맥의 가지인 위입술동맥과 아래입술동맥이 주행한다. 해부학적으로 입술은 피부, 피부밑조직, 입둘레근의 얕은부분, 입둘레근의 깊은부분, 입점막 등, 5층으로 구분할 수 있으며, 선행연구에 따르면 입술동맥은 입점막층에 가장 많이 분포하는 것으로 알려져 있다. 임상적으로 입술에 필러를 주사하는 lip contouring 또는 lip augmentation의 미용술식 등이 다양하게 시행되고 있으며, 여러 임상술식에서 동반되는 부작용을 예방하기 위하여 해부학적으로 다양한 임상 가이드라인이 제시되어 왔다. 본 연구에서는 피험자를 대상으로 초음파 촬영을 실시하여, 기존에 제시된 가이드라인의 안정성을 확인함과 동시에, 시신을 이용한 연구에서 획득할 수 없는 혈관의 깊이정보 등을 제시하고자 하였다. 본 연구를 위하여 한국인 30명 (남: 15명, 여: 15; 평균나이: 25.2세)을 대상으로 임상실험을 진행하였다 (IRB No. 2-2017-0023). 초음파 검사 장비는 E-Cube 15를 사용하였으며, 두 가지의 transducer (L8-12X, I08-17)를 사용하였다 (ALPINION MEDICAL SYSTEMS Co., Ltd., Seoul, Korea). 입술의 층을 명확하게 관찰하기 위하여 홍순경계를 따라 수평하게 촬영하였으며, 구조물의 위치 및 깊이정보를 계측하기 위하여 양쪽의 입꼬리와 정중선, 그리고 두 점의 사이를 1/3로 나누어 모두 7 개의 선상에서 수직하게 촬영하였다. 이 때, transducer의 압력으로 인해 입술조직이 변화하는 것을 막기 위하여 검사 부위

에 두껍게 젤을 도포하고 transducer를 피부로부터 띄워서 촬영을 진행하였다. 입술동맥이 위치하는 층을 관찰하기 위하여 입술을 피부밑조직 층, 근육 속 층, 입점막 층으로 구분하여 관찰하였으며, 입점막 층의 경우 이행부분 (dry mucosa), 점막부분 (wet mucosa)으로 다시 구분하여 관찰하였다. 촬영된 초음파 사진을 분석한 결과, 홍순경계에서 위입술의 전체 두께는 8.2±0.6mm, 아래입술의 전체 두께는 9.2±0.7mm였다. 위입술동맥이 피부밑조직 층에 위치하는 경우는 한 예도 없었으며 (0 %), 근육 층 속에 위치하는 경우는 57 %에서 관찰하였다. 나머지 43 %의 경우에서는 입점막 부위에 혈관이 위치하였으며, 이행부분과 점막부분의 점막밑층에 위치하는 경우는 각각 7 %와 36 %로 관찰하였다. 한편, 아래입술동맥이 피부밑조직 층에 위치하는 경우는 2%에서 관찰되었으며, 근육층 속에 위치하는 경우는 15 %로 관찰하였다. 대부분의 아래입술동맥은 입점막 부위에 위치하였으며 (83 %), 아래입술동맥이 이행부분과 점막부분의 점막밑층에서 관찰된 경우는 각각 37 %와 46 %로 관찰되었다. 위입술과 아래입술의 피부에서 위, 아래입술동맥의 위치까지의 평균 깊이는 각각 4.7±0.8mm, 3.7±0.7mm였다. 초음파촬영은 실제 임상에서 쉽고 안전하게 적용할 수 있는 검사방법으로, 본 연구자들은 피부 표면에서 관찰할 수 있는 구조물인 홍순경계를 기준으로 근육 및 혈관의 위치관계에 대한 자료를 구축하고자 한다. 이 결과를 바탕으로 한 "초음파를 이용한 주사법 (US–guided injection procedures)에 대한 해부학적 가이드라인"은 다양한 미용술식에서 발생할 수 있는 부작용을 최소화하는 안전하고 효율적인 시술의 기초가 될 것이다.

Keywords: 위입술동맥, 아래입술동맥, 초음파, lip augmentation, non–invasive treatment

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017

Architectural Feature of the Superficial Part of the Masseter Muscle by Ultrasonography

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Masseter muscle consist of three layers with the superficial part being the biggest among them. The three layers of the masseter muscle fiber interweave at the inferior region, therefore, thickens it. However, it has recently been reported that the superficial part of the superficial muscle belly of the masseter muscle is composed not only of the muscle belly but also of the strong deep tendon within the muscle belly at the inferior region of the masseter muscle. But previous studies lacked information regarding the depth of the deep tendon structure. Therefore, the aim of this study was to examine the deep tendon structure in humans and to compare the deep tendon structure with those of cadavers. In addition we aimed to identify the depth of the deep tendon in order to propose most effective treatment methods of botulinum neurotoxin type A injection. Twenty healthy volunteers participated in this study and the masseter muscle were scanned both longitudinally and transversely via ultrasonography (E-CUBE 15 EX, ALPINION, SEOUL, KOREA, IRB NO. 2-2017-0023). The deep tendon structure within the superficial part of the superficial muscle belly of the masseter was present in every subject. The deep tendon structure was located at anterior, middle, and posterior portion of the masseter muscle in 77.5%, 95%, 45% on the left side and 57.5%, 95%, 47.5% on the right side, respectively. The depth of the deep tendon was 5.0mm, 6.6mm, 3.6mm on the left side and 6.3mm, 7.6mm, 4.7mm on the right side at the anterior, middle and posterior portions from the mandible, respectively. The deep tendon of the masseter was confirmed via ultrasonography and can be regarded as a common structure in both human and cadavers. Based on the result of this study, both dual injections and ultrasound-guided injections are required in order for the treatment of botulinum neurotoxin type A injection to be most effective. Additional data regarding the depth of the deep tendon will become critical anatomic data and will be helpful in managing the masseteric bulging following the botulinum neurotoxin type A injection for masseteric hypertrophy, bruxism, or asymmetrical face.

Keywords: Masseter muscle, Superficial part of masseter muscle, Ultrasonography, Botulinum neurotoxin type A Injection

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018

The Optimal Incision To Avoid Sural Nerve Injury In Sinus Tarsi Approach For Calcaneal Fracture: A Cadaveric Study

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Calcaneal fractures are the most common fracture of the tarsal bones, yet controversy still exists on the best treatment for these disabling injuries. However, the optimal treatment for displaced calcaneal fractures involving the posterior facet is surgical. The extensile lateral approach is commonly preferred because it provides sufficient exposure of the subtalar facet. However, this technique has the risk of complications such as wound necrosis and sural nerve injury. There has been renewed interest in small incision surgery for calcaneal fractures to reduce possible complication, a small incision has been described with various modifications, such as the sinus tarsi approach. However, injury to the sural nerve has still been reported in the sinus tarsi approach. Sural nerve is vulnerable to injury during the incision for sinus tarsi approach, because the sural nerve runs superficially on the lateral aspect of the hindfoot. Although a relevant skin incision to avoid nerve damage is critical, there is no consensus with regard to skin incision for this approach. In present study, we hypothesized that identification of the anatomy of the sural nerve in accordance with easily identifiable bony land-marks may minimize the risk of nerve injury during sinus tarsi approach for calcaneal fracture. Twenty-four foot and ankle specimens in adult cadavers were dissected. Of the 24 specimens, 12 (50%) were from females and 12 (50%) from males. The lateral aspect of the foot of all cadavers showed intact skins and no signs of previous trauma or surgery, obvious deformities, and/or ulcers. The bony land-marks were used in the following reference points: A, the tip of the lateral malleolus; point B, the lateral border of the Achilles tendon on the collinear line with point A; point C, the posteroinferior margin of the calcaneus; point D, the inferior margin of the calcaneus on the plumb line through point A; and point E, the tip of the 5th metatarsal base. After careful dissection, the distances of the sural nerve to points A and B in the horizontal direction (lines D1 and D2, respectively), to points A and C in the diagonal direction (lines D3 and D4, respectively), to points A and D in the vertical direction (lines D5 and D6, respectively), to points A and E in the diagonal direction (lines D7 and D8, respectively) were measured. The identification of bony land-marks and measurement of the distance were performed by two independent researchers. All the measurements made by two independent researchers for each distance were used to assess the inter-rater reliability by calculating the intra-class correlation coefficients. The averages of the 2 researchers' measurements were recorded to describe each specimen. To evaluate the central tendency of all specimens, each distance (from D1 to D8) was presented using the mean ± 1.96 standard deviations. Moreover, the ratios of D1to D1+D2, D3 to D3+D4, D5 to D5+D6, and D7 to D7+D8 were calculated, and each ratio is presented as the median, range, and interquartile range. The Wilcoxon–Mann–Whitney test was performed to compare the ratio between males and females and the Pearson's correlation analysis was performed to evaluate the relationship between ratio and age. All statistical analyses were performed using the SPSS 24.0 software (SPSS, Chicago, IL). A p-value less than .05 was considered statistically significant. The median ratio of D1 to D1+D2, D3 to D3+D4, D5 to D5+D6, and D7 to D7+D8 were 0.37 (range 0.26 to 0.50), 0.23 (range 0.16 to 0.33), 0.35 (range 0.25 to 0.45), and 0.32 (range 0.20 to 0.45), respectively. There were no significant differences in all measurements by gender and age. Thus, we suggest that it is relatively safe to make a straight incision distally from just distal to the tip of the fibula and roughly horizontal to the sole of the foot.

Keywords: Sural Nerve, Sinus Tarsi, Calcaneus, Surgical Incision, Cadever

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019

Fluorescence bioimaging of disease biomarkers and its applications in anatomy

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Understanding the molecular interactions in biological systems is of fundamental importance. Various types of assay and imaging tools have been developed for studying diverse biological processes as well as for diagnosis/imaging of disease. Among these tools, fluores-

cence methods have received great attention as they enable sensitive in vivo detection and imaging by relatively simple operation.
Fluorescent probes are molecules that absorb light of a specific wavelength and emit light of a different, typically longer, wavelength (a process known as fluorescence). Fluorescent probes with desirable sensing properties (analyte selectivity, sensitivity, bioimaging capability, etc.) are essential for the investigation of molecular interactions and thus have been extensively used in biochemical, clinical and environmental research areas. Recently, the fluorescence method is also widely used in anatomy and neuroscience. In this talk, speaker will introduce recent studies of fluorescent probes that can monitor biomarkers in disease such as Alzheimer's disease(AD) and cancer.

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020

Three Theories on the Mechanism of Hair Graying

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Hair graying is an obvious sign of human aging. Although graying has been investigated extensively, the mechanism remains unclear. Here, we reviewed previous studies on the mechanism of graying and seek to offer some new insights. The traditional view is that hair graying is caused by exhaustion of the pigmentary potential of the melanocytes of hair follicles. Melanocyte dysfunction may be attributable to the effects of toxic reactive oxygen species (ROS) on melanocyte nuclei and mitochondria. A recent study suggests that bulge melanocyte stem cells (MSCs) are the key cells in play. Graying may be caused by defective MSC self-maintenance, not by any deficiency in bulbar melanocytes. Our study suggest that graying may be principally attributable to active hair growth. Active hair growth may produce oxidative or genotoxic stress in hair bulge. These internal stress may cause depletion of MSC in the hair follicles. Taken together, hair graying may be caused by MSC depletion by genotoxic stress in the hair bulge. Hair graying may be sometimes caused by dysfunction of the melanocytes by oxidative stress in the hair bulb. In addition, hair graying may be attributable principally to MSC depletion by active hair growth.

Keywords: Hair graying, Melanocyte, Melanocyte stem cell, Active hair growth

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021

The expression of androgen receptor on the kidney with ischemia and reperfusion injury

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Sex differences have been reported in many renal diseases including acute kidney injury (AKI). Recently we found that the presence of male hormone plays an important role for the sex differences on ischemia-reperfusion-induced AKI rather than the absence of estrogen. However, the expression and role of androgen receptor (AR) in the kidney tubules remain unclear. Here, we investigated the expression level and distribution of AR in the kidney tubular cells of mice. The strong expression of AR was detected distal tubules and collecting ducts, whereas the weaker expression was detected on the proximal tubules, and AR was merely expressed on the loop of Henle. AR expression pattern is not different significantly between male and female mouse kidney. The expression level of AR was higher on male mice kidney than female kidney. After ischemia/reperfusion surgery, the damage of outer medulla on male was more severe than that on female kidney. Blood urea nitrogen and plasma creatinine level after ischemia/reperfusion injury were also higher on male mice than female. The expression level of AR was reduced as the time passed after ischemia/reperfusion. These results indicate that the expression of AR is different between male and female, suggesting that sex difference in I/R-induced AKI may be associated different expression of AR and its signaling pathway.

Keywords: Androgen receptor, Sex difference, Ischemia reperfusion injury

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022

Ancient Helicobacter pylori DNA found in Joseon mummies

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Genetic study on Helicobacter pylori is of scientific interest because they can provide information about the history of human migration. However, there have been only a few studies of ancient H. pylori detection in the world, and furthermore, there was no report that this microorganism was detected in archeological samples in Asian countries including Korea. Considering that all of ancient H. pylori studies have been conducted in archaeological samples like mummies with soft tissues, the possibility of finding H. pylori be high if we analyze the well-preserved Joseon mummies. In this regard, we performed ancient DNA analyses to find the gene sequence of H. pylori, and succeeded in confirming the infection of H. pylori in two Joseon mummies by PCR and sequencing analyses. This study was the first case of ancient H. pylori infection found in ancient Asian people until now. Our discovery is expected to provide crucial information to study the history of H. pylori infection in Koreans and the migration route of Asians. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2013R1A1A2009688) and by the Seoul National University Hospital (SNUH) research fund (04-2017-0490). supported by the Seoul National University Hospital (SNUH) research fund (04-2016-0390).

Keywords: ancient DNA, Helicobacter pylori, Korea, Mummy

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023

Genetic Study of Ancient Trichuris trichiura Eggs in Joseon Dynasty Specimens

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We analyzed Trichuris trichiura (T. trichiura) ancient DNA (aDNA) extracted from the feces or precipitates of 15th to 18th century Korean mummies. After multiple T. trichiura genes in ancient samples were successfully amplified by PCR, consensus sequences were determined by the alignment of individual clone sequences. The obtained sequences of each gene were well matched with those of T. trichiura reported this far, but can be clearly differentiated from those of other Trichuris species. This can be further confirmed by phylogenetic tree though T. trichiura aDNA sequences were not clustered by their regions. To improve our knowledge in much detail about T. trichiura evolution, more ancient T. trichiura gene sequences should be obtained from the regions of much wider geo-historical scope. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (no. NRF-2016R1A2B4015669).

Keywords: Ancient DNA; Josoen; Trichuris trichiura; Mummy; Phylogenetic analysis

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024

Understanding Tumor Reversion: Searching for novel TCTP functions using a *Drosophila* model

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Tumor reversion is the biological process by which highly tumorigenic cells lose their malignant phenotype, thus it could be applied for one of the possible cancer treatment. However, the exact nature of tumor reversion is still largely unknown. TCTP (Transnationally controlled tumor protein) is a small protein of 25 kDa and the most critical protein out of several proteins to regulate tumor reversion. Although TCTP has many binding partners in cytoplasm, the nuclear functions of TCTP and its physiological (or *in vivo*) roles remains unclear.

To find novel TCTP function and its physiological roles, thereby expanding the knowledge to understand tumor reversion, I utilized two screen systems (phage display and yeast-two-hybrid using TCTP protein as a bait) and *Drosophila* as a model animal. From these screen, ATM (ataxia-telangiectasia-mutaed) kinase and Brm (Brahma) chromatin remodeling protein were obtained as a novel TCTP binding partner in cell nucleus. ATM kinase repairs DNA breaks and Brm promotes gene transcription. TCTP protein directly binds to these proteins and regulates their enzymatic activities. TCTP facilitates ATM kinase activity to repair DNA breaks and negatively regulates excess Brm activity to suppress ectopic gene transcription as well as to protect heterochromatin structure, biochemically and genetically. Altogether, these studies provides insights into novel TCTP functions in cell nucleus for the maintenance of genome stability.

Keywords: Tumor reversion, TCTP (Transnationally controlled tumor protein), *Drosophila*, ATM (ataxia-telangiectasia-mutaed) kinase, Brm (Brahma) chromatin remodeling protein, DNA repair, Heterochromatin, Genome stability.

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025

Fish Scale Collagen Peptides Protect Against CoCl2/TNF-α-Induced Cytotoxicity and Inflammation via Inhibition of ROS, MAPK, and NF-κB Pathways in HaCaT Cells

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Skin diseases associated with inflammation or oxidative stress represent the most common problem in dermatology. The present study demonstrates that fish collagen peptides (FCP) protect against CoCl2-induced cytotoxicity and TNF-α-induced inflammatory responses in human HaCaT keratinocyte cells. Our study is the first to report that FCP increase cell viability and ameliorate oxidative injury in HaCaT cells through mechanisms mediated by the down-regulation of key pro-inflammatory cytokines, namely, TNF-α, IL-1β, IL-8, and iNOS. FCP also prevent cell apoptosis by repressing Bax expression, caspase-3 activity, and cytochrome c release and by upregulating Bcl-2 protein levels in CoCl2- or TNF-α-stimulated HaCaT cells. In addition, the inhibitory effects of FCP on cytotoxicity and the induction of pro-inflammatory cytokine expression were found to be associated with suppression of the ROS, MAPK (p38/MAPK, ERK, and JNK), and NF-κB signaling pathways. Taken together, our data suggest that FCP are useful as immunomodulatory agents in inflammatory or immune-mediated skin diseases. Furthermore, our results provide new insights into the potential therapeutic use of FCP in the prevention and treatment of various oxidative- or inflammatory stress-related inflammation and injuries.

Keywords: Fish Collagen, HaCaT Cells, Cytotoxicity, Inflammation

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026

Ethanol extract of Dryopteris Crassirhizoma alleviates allergic rhinitis via modulation of cytokines and histamine release from mast cells

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Dryopteris crassirhizoma (DC) is used as a traditional herbal remedy to treat various diseases, the tapeworm infection, common cold, and cancer in Korea, Japan, and China. DC also has the antioxidant anti-inflammatory and antibacterial activities. However, anti-allergic inflammatory effect of DC and some of its mechanisms in allergic rhinitis model is unknown well. The purpose of this study is to investigate the anti-allergic inflammatory effect of DC on the allergic rhinitis model, mast cell activation and histamine release. Allergic rhinitis was induced in BALB/c mice by sensitization and challenge with OVA. Each various concentration of DC and Dexamethasone was administrated by oral gavage on 1 hour before OVA challenge. Mice of control group were treated with saline only. Then mice were evaluated for the presence of nasal mucosa inflammation, the production of allergen-specific cytokine response and the histology of nasal mucosa. DC significantly ameliorated the nasal symptoms and the inflammation of nasal mucosa. DC also reduced the infiltration of eosinophils and mast cells in these tissues and the release of histamine in blood. Meanwhile, DC evidently inhibited the overproduction of Th2 cytokine, and increased reduction of Th1 and Treg cytokines in nasal lavage fluid by OVA. DC also reduced the levels of OVA specific IgE, IgG1 and IgG2a in blood. This study suggests that DC has a significant anti-allergic inflammatory effect in nasal cavity. DC may have the therapeutic effect for allergic rhinitis.

Keywords: Dryopteris crassirhizoma (DC), Allergic rhinitis, Airway inflammation, Mast cell

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027

Rosae Multiflorae Fructus Extract Alleviates Ovalbumin-induced Allergic Rhinitis via Regulation of Th1/Th2 Imbalance

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Rosae Multiflorae fructus has potent antioxidative, analgesic, and anti-inflammatory properties. We investigated the immunomodulatory effect of Rosae Multiflorae fructus extract (RMFE) on allergic inflammation in an allergic rhinitis (AR) mouse model. Oral administration of RMFE inhibited the accumulation of eosinophils in nasal lavage fluid (NALF) and the nasal mucosa, goblet cells in the nasal epithelium, and mast cells in the respiratory region of the nasal cavity. Thus, the swelling of the nasal epithelium, nasal-associated lymphoid tissue (NALT), and lung tissue were ameliorated. Furthermore, the RMFE suppressed Th2-related cytokines, such as IL-4, IL-5, and IL-13 in NALF, NALT, and splenocytes, whereas the Th1-associated cytokine IL-12 was up-regulated by RMFE. We also reveal the active components of RMFE, such as ellagic acid, hyperoside, isoquercitrin, and miquelianin. They may inhibit IL-4 secretion in allergic responses. Therefore, RMFE may have therapeutic potential for treating allergic rhinitis by modulating the relationships between Th1/Th2 responses.

Keywords: Rosae Multiflorae fructus, Allergic rhinitis, Th2 cytokines, Miquelianin, Mast cells

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028

Identification of heterogeneity ac cording to progression in bladder cancer by single-cell RNA-seq

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To explore the correlation of intratumoral genetic and functional heterogeneity aboutcancer clinical prognoses, we applied single-cell RNA sequencing (RNA-seq) to isolatedcell from bladder cancer. In the single-cell RAN-seq analysis of the bladder cancer, there are many monocyte, fibroblast, T cell, muscle cell and endothelial cell as well as cancer cells. Interestingly, cancer cells are divided into two types, one of which is similar to the uroA type gene expression in bladder cancer, and the other has similar gene expression characteristicto the basal type. To analyze the mechanism of coexistence of uroA type and basal type cancer cells, also our study present how the ratio of two types of cancer cells changed as bladder cancer progressed. Basal type bladder cancer represents a poor prognosis not responding to treatment, genetic analysis of basal type cells was performed to establish a therapeutic strategy to target basal type cells. Thus, single-cell RNA-seq is a powerful approach for identifying unique tumor cell specific gene expression profiles which could overcome intratumoral heterogeneity for clinical anti-cancer strategies.

Keywords: Single cell analysis, Bladder cancer, Tumor heterogeneity

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029

Co-Targeting of Tiam1/Rac1 and Notch Ameliorates Chemoresistance Against Doxorubicin In A Biomimetic 3D Lymphoma Model

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Lymphoma is a heterogeneous disease with a highly variable clinical course and prognosis. Improving the prognosis for patients with relapsed and treatment-resistant lymphoma remains challenging. Current in vitro drug testing models based on 2D cell culture lack natural tissue-like structural organization and result in disappointing clinical outcomes. The development of efficient drug testing models using 3D cell culture that more accurately reflects in vivo behaviors is vital. Our aim was to establish an in vitro 3D lymphoma model that can imitate the in vivo 3D lymphoma microenvironment. Using this model, we explored strategies to enhance chemosensitivity to doxorubicin, an important chemotherapeutic drug widely used for the treatment of hematological malignancies. Lymphoma cells grown in this model exhibited excellent biomimetic properties compared to conventional 2D culture including (1) enhanced chemotherapy resistance, (2) suppressed rate of apoptosis, (3) upregulated expression of drug resistance genes (MDR1, MRP1, BCRP and HIF-1α), (4) elevated levels of tumor aggressiveness factors including Notch (Notch-1, -2, -3, and -4) and its downstream molecules (Hes-1 and Hey-1), VEGF and MMPs (MMP-2 and MMP-9), and (5) enrichment of a lymphoma stem cell population. Tiam1, a potential biomarker of tumor progression, metastasis, and chemoresistance, was activated in our 3D lymphoma model. Remarkably, we identified a novel synergistic combination of oncotargets, Tiam1 and Notch, as a strategy to combat resistance against doxorubicin in EL4 T and A20 B lymphoma. Therefore, our data suggest that our 3D lymphoma model is a promising in vitro research platform for studying lymphoma biology and therapeutic approaches.

Keywords: 3D Culture, Hydrogel, Tumor Spheroid, Lymphoma, Chemoresistance

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Poster

전시발표-1 (P001-P089)
2017년 10월 19일(목) 13:30 ~ 14:30 5A홀
■ 육안해부학: P1~P21
■ 조직 및 발생: P22~P36

전시발표-2 (P090-P178)
2017년 10월 20일(금) 13:00 ~ 14:00 5A홀
■ 면역 및 종양: P37~P62
■ 신경과학: P63~P145
■ 기타: P146~P178

P1

The Anterolateral Ligament of Korean Knee: Anatomical Study

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Anterolateral ligament (ALL) is a structure which is known as related with Second fracture and it is located at the anterolateral part of the knee. Several researchers have been investigating the existence of the ALL, and the frequency of the ALL has been reported inconsistently. Therefore, we checked whether or not the ALL is true ligament and studied morphological variation of the ALL. Twenty-nine Korean adult cadavers (56 sides) were used for this study. The skin and subcutaneous tissue were removed from the middle of the thigh to the middle of the leg at the lateral part. The iliotibial band was cut at the proximal part and reflected toward the Gerdy's tubercle. The insertion part of the biceps femoris tendon was also cut near the femoral head. The lateral part of the knee joint was carefully dissected maintaining internal rotation of the tibia. We checked the existence of the ALL and measured the dimensions (length, width and thickness). H&E stain was performed on one ALL and lateral collateral ligament (LCL) specimens for histologic analysis. The ALL was more identifiable with internal rotation of the tibia and found in 19.6% (11/56). The length of the ALL was 30.1 ± 2.1 mm in neutral position. The width and thickness at the joint line were 5.2 ± 1.5 mm and 1.0 ± 0.6 mm, respectively. Approximately a half of the ALL specimens had thickness thicker than 1 mm (5/11) and one specimen was thicker than 2 mm. Histologic analysis showed that the ALL was packed with dense collagen bundles organized in a parallel manner similar to the LCL. This study investigated the frequency and shape of the ALL using Korean adult cadavers. The ALL was rarely found, and even if it existed; only 1 side was thicker than 2 mm. However, the histologic analysis showed that the ALL had a typical ligament-like structure. Therefore, further histologic and biomechanical analysis on this structure should be conducted to clearly demonstrate the frequency of the ALL in Korean population.

Keywords: Anterolateral Ligament, Knee, Ligament, Anatomy, Korean

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P2

Ancient-to-Mdern Secular Canges of Canial/Cphalic Idex in Korean: Steady Bachycephalization and Rcent Drachycephalization

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The cranial index (and cephalic index) is a representative indicator of the head shape, and the value varies according to race or ethnicity. Macroscopically, this index has gradually increased (that is, brachycephalization) since Hominids ages to modern days. On a millennium basis, the cranial index has been changed differently depending on different regions. Of note is that there has been a worldwide phenomenon that the change has progressed rapidly during the last century, either brachycephalization or dolichocephalization. The change that has been occurred in Korean Peninsula during the last century also has been mentioned by some authors. However, no report has been done spanning millennium periods. In this study, we observed changes in the past 2,000 years based on all possible literatures and our own measurements. We also conducted a more precise analysis of the changes during recent decades. Literatures for the oldest skulls in Korea such as those from Shandong Shell mound, Jodo, and Jaeri showed that they were mesocephalic with the cranial index being below 80. In the Joseon Dynasty, the measured cranial index was about 82 for both sexes, and the values during the 20th century were around 84. Thus, it can be said that a steady brachycephalization has been progressed continuously in Korean Peninsula during the last 2,000 years. The progress of brachycephalization was particularly abrupt during the last century as was previously reported. Remarkably, the analysis of recent cephalic measurements, those done in 2003 and 2015, showed that this rapid brachycephalization stopped, or even possibly reversed to dolichocephalization since those born in the mid-1960's. Interestingly, this cessation of brachycephalization occurred in males and followed by females with about 5-year interval. This pattern of change - a long-term slow and steady, and a short-term rapid brachycephalization followed by stopping of the change in recent years - seems to be unique to Koreans, compared to those observed in other areas such as Central Europe, England, and Japan. This uniqueness presumably reflects the history of the Korean Peninsula, which should be further explored.

Keywords: cranical index, cephalic index, brachycephalization, debrachycephalization

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P3

해당 초록은 P-178로 번경되었습니다.

P4

Validation and Reliability of a Structured Light Scanner and Ultrasound Imaging System in Facial Skin Thickness Measurement

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This study was conducted to evaluate the validation and reliability of 3D scanning system comparing with ultrasound (US) imaging system and direct measurement of facial skin. Using ten embalmed adult Korean cadavers, facial skin thickness on 19 landmarks was measured by three different measuring methods. After acquiring the skin thickness by US device, 3D scanning of the skin surface of face were performed. And we dissected facial skin from the subcutaneous layer. The harvested facial skin was measured directly using a neck calipers. Dissected specimen was scanned again, and then, undissected and dissected faces were superimposed using MPS 3.0 software. Finally, the facial skin thickness was calculated on the superimposed images. The result of ICC between the 3D scanning system and the direct measurement showed excellent reliability (95% confidence interval 0.799-0.887). Bland-Altman analysis also showed 95% limit of agreement between the 3D scanning system and the direct measurement. Based on our study, it has been proven statistically that the 3D scanning system precisely reflects the structural changes of face. Therefore, through in-depth morphological study using this 3D scanning system, we can provide depth data of main anatomical structures of face, thereby providing crucial clinical anatomic knowledge in various clinical applications.

Keywords: Facial Skin Thickness; 3D Scanning System; Ultrasound Imaging system; Direct measurement; Reliability

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P5

Clinical Evaluation of the Ac cessory Foramina of the Mandible in Korean

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The mandible derives blood additionally from the accessory foramina as the nutrient vessel penetrates into there. The aim of this study was to evaluate the presence and location of the accessory foramina of the mandible in Korean, especially including the retromolar foramen and lingual foramen. At first, the retromolar neurovascular bundle in the retromolar canal originated from the inferior alveolar neurovascular bundle, and the mean areas of the neurovascular bundle and each artery and nerve contained within it were 0.59, 0.07, and 0.05 mm2, respectively. The mean horizontal and vertical diameters of the neurovascular bundle were 0.82 and 0.90 mm, respectively. The retromolar canal was detected more often on CBCT images (43.1%, 31 out of 72 patients). It mainly arose vertically (71.0%) from the mandibular canal and opened in the middle portion (57.9%) of the retromolar triangle at a mean distance of 13.13 mm from the second molar. The lingual foramen was detected in 86.7%. A single foramen was frequently found in 53.8% and in this case the superior lingual foramen above the mental spine was most present. The mean distances of the superior lingual foramen, mental spine, and inferior lingual foramen were 14.16±1.69, 12.09±1.66, 7.57±2.21 mm from the inferior border of the mandible, respectively. Finally, the accessory foramen on the lingual surface of the mandible was detected in 74.7% except in the lingual foramen located at the mandibular symphysis. They were classified into three groups: interalveolar foramen placed close to the alveolar crest between the central incisor and the lateral incisor, lateral lingual foramen located close to the inferior border of the mandible in the premolar region, and nonspecific accessory foramen in the molar region. These results on the accessory foramina might help to avoid both blood vessels and

nerves damage during surgical procedure in the mandible.

Keywords: Retromolar Foramen, Lingual Foramen, Lateral Lingual Foramen, Interalveolar Foramen

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P6

Ultrasonography-Based Forehead Soft Tissue Layer and Thickness

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Ultrasonography (US) has been widely used as a non-invasive imaging technique in various diagnostic procedures. With the exception of the face, most other normal structures of the human body have been observed and identified using US. Despite the clinical significance of the face, US was not used on the facial area due to a lack of detailed anatomical knowledge. Therefore, the purpose of this study was to identify the layered structure of the forehead region and to measure its soft tissue thickness. The US images were obtained from forty-four Korean volunteers (22 males, 22 females; mean age 26.0 years, IRB No. 2-2017-0023). We performed our US scans at 7 facial landmarks (only left side including midline) using linear transducers (IO8-17, E-CUBE15, ALPINION MEDICAL SYSTEM, Seoul, Korea), and all the images were scanned in transverse placements. The soft tissue thickness was measured using an image analysis program (Image J, National Institutes of health, Bethesda, MD, USA). The thickness of the medial part (point #3) of the frontalis muscle was 2.49±0.51mm. In the case of points #17 and #18 (the middle part), the thickness was 2.68±0.86mm and 2.39±0.81mm, respectively. At point #19 (lateral forehead), we observed the thickness of the frontalis to be slightly thinner (1.54±0.52mm). The skin thickness results reveal similar patterns in relation to frontalis thickness. Identifying target muscle layers, blood vessel locations, and soft tissue thicknesses maximize efficacy and minimize the complications of forehead procedures, making it extremely useful for US-guided injection procedures.

Keywords: Ultrasonography, Forehead, Frontalis, Thickness

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P7

Three-Dimensional Topography of the Emerging Point of Ophthalmic Artery

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The ophthalmic artery, the first branch of the internal carotid artery, emerges at the orbital region by piercing the orbital septum inferior to the medial part of the superior orbital rim. During the upper eyelid surgery, it runs risk of bleeding and hemorrhage at the emerging point of the ophthalmic artery. Therefore, the aim of this study was to determine the three dimensional location of emerging point of the ophthalmic artery by 3D scanner and ultrasound device and to facilitate procedure during upper eyelid surgery. Seventeen hemifaces of the emerging point of ophthalmic artery from 10 Korean and 7 Thai cadavers were dissected and scanned by 3D scanner (Morpheus3D®, Morpheus Company, Seongnam, Korea). The emerging point of the ophthalmic artery of 30 Korean participants was detected by ultrasound device (E-CUBE15, ALPINION, Seoul, Korea). The emerging point of ophthalmic artery where it emerges inferiorly to the medial part of the superior orbital rim was measured about its distance from the medial canthus and the facial sagittal midline, in addition to distance from the facial sagittal midline to the medial canthus by 3D scanner. It was measured the depth from the skin to the emerging point by 3D scanner. An image analysis program (Image J, National Institutes of Health, Bethesda, MD, USA) was used to measure the distance from the inferior margin of the medial part of the superior orbital rim to the emerging point of the ophthalmic artery. After removal of the upper eyelids skin and orbicularis oculi muscle, the emerging point of ophthalmic artery was exposed. The transverse distance was 3.8±1.0 mm from the medial canthus coordinate medially and the vertical distance was 14.0±2.9 mm from the medial canthus coordinate superiorly, respectively. It was 16.5±1.7mm from the midline to the emerging point of the ophthalmic artery and it was 20.0±2.0mm from the midline to the medial canthus, respectively. The depth from the skin

to emerging point of ophthalmic artery was 4.8±1.7 mm by 3D scanner and was 5.7±1.1mm by ultrasound device. The distance was 7.7±1.9mm from the inferior margin of the superior orbital rim to the emerging point of the ophthalmic artery. The emerging point of ophthalmic artery can be located one thumb finger – width above the medial canthus coordinate and 4mm medial to the medial canthus coordinate, respectively, in addition with its 5mm depth from the skin. Therefore, the aforementioned data can provide the clinical surgeon a practical method to avoid the iatrogenic injury as bleeding and hemorrhage complications during the upper eyelid surgical procedure.

Keywords: Emerging Point of Ophthalmic Artery, Three-Dimensional Location, Eyelid Surgery, Medial Canthus, Facial Sagittal Midline

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P8

3차원 모델링에 기반한 증강현실을 이용한 경질막정맥굴의 교육용콘텐츠 개발

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증강현실(Augmented Reality)은 실제 환경에 가상의 이미지를 덧씌워 보여주는 기술로 게임, 교육, 의료, 도시개발, 쇼핑, 예측, 훈련 등 각종 분야에서 사용 가능성이 높다. 특히 교육과 의료 분야에서의 활용 가능성은 매우 크며 실제로 증강현실을 이용한 다양한 콘텐츠가 접목되고 있다. 증강현실을 이용한 교육콘텐츠는 생생한 입체영상을 통해 보다 나은 교육효과를 제공하며, 간단한 조작을 통해 교과서만으로 학습하는 것보다 몰입과 흥미를 느낄 수 있는 장점이 있다. 해외에서는 증강현실기술을 이용한 해부학 교육콘텐츠가 이미 많이 개발되었지만, 국내는 이러한 교육콘텐츠가 아직 미비한 실정이다. 이에 증강현실을 활용한 학습에 익숙하지 않은 의학 및 보건계열 학생들을 위해 해부학 교육콘텐츠를 개발하였다. 본 연구에서는 경질막정맥굴(Dural Venous Sinus) 구조의 학습을 목적으로 증강현실 기반의 3차원 모델링 교육용 콘텐츠를 제작했다. 먼저 3D 스캐너를 이용해 한국인 머리뼈 모형을 디지털화 하여 기본 3차원 모델을 생성한 후 Cinema4D(Maxon, R17) 소프트웨어를 이용해 머리뼈 모델을 다듬었다. 이후 같은 소프트웨어로 뇌, 경질막, 경질막정맥굴의 3차원 모델을 제작했다. 더불어 경질막정맥굴의 3차원 모델 위에 정맥의 배출 경로를 애니메이션으로 추가했다. 완성된 3차원 모델과 애니메이션을 Unity3D(Unity, Unity2017.1) 게임엔진으로 다양한 인터페이스를 구성하였고, Vuforia(Vuforia, Vuforia6.2)를 이용해 증강현실로 구현하였다. 이를 스마트폰 또는 태블릿PC를 통해서 원하는 부위를 확대, 축소, 회전해서 관찰할 수 있게 하였으며, 각 구조물의 명칭도 확인할 수 있게 하였다. 또한 on/off 기능을 이용해 원하는 구조물만 선택할 수 있게 하여, 사용자가 디바이스와 상호작용을 통해 보다 직관적이고 실감나는 학습을 체험할 수 있게 하였다. 본 결과물을 바탕으로 해부학 교육에 증강현실을 활용한 연구가 더욱 활발히 되기를 바라고 증강현실이 접목된 교육콘텐츠가 학습자의 흥미를 유발하고 학습 능률을 효과적으로 높일 수 있기를 기대한다.

Keywords: Augmented Reality, Dural Venous Sinus, Education

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P9

Is There A Safe Zone To Avoid Sural Nerve Injury With Medial Displacement Calcaneal Osteotomy? A Cadaveric Study

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Medial displacement calcaneal osteotomy (MDCO) is a common choice for most surgeons when surgically treating any situation with hindfoot valgus. However, injury to the sural nerve has also been reported incidence with 7 to 16.7% after MDCO. Sural nerve is vulnerable to injury during the incision for MDCO, because the sural nerve runs superficially on the lateral aspect of the hindfoot. Thus, a relevant skin incision to avoid nerve damage is critical. In present study, we hypothesized that identification of the anatomy of the

sural nerve in accordance with easily identifiable bony land-marks may minimize the risk of nerve injury during surgical approach for MDCO. Twenty-four foot and ankle specimens in adult cadavers were dissected. Of the 24 specimens, 12 (50%) were from females and 12 (50%) from males. The lateral aspect of the foot of all cadavers showed intact skins and no signs of previous trauma or surgery, obvious deformities, and/or ulcers. The bony land-marks were used in the following reference points: A, the tip of the lateral malleolus; point B, the lateral border of the Achilles tendon on the collinear line with point A; point C, the posteroinferior margin of the calcaneus; and point D, the inferior margin of the calcaneus on the plumb line through point A. After careful dissection, the distances of the sural nerve to points A and B in the horizontal direction(lines D1 and D2, respectively), to points A and C in the diagonal direction (lines D3 and D4, respectively), and to points A and D in the vertical direction (lines D5 and D6, respectively) were measured. The identification of bony land-marks and measurement of the distance were performed by two independent researchers. All the measurements made by two independent researchers for each distance were used to assess the inter-rater reliability by calculating the intra-class correlation coefficients. The averages of the 2 researchers' measurements were recorded to describe each specimen. To evaluate the central tendency of all specimens, each distance (from D1 to D6) was presented using the mean ± 1.96 standard deviations. Moreover, the ratios of D1to D1+D2, D3 to D3+D4, and D5 to D5+D6 were calculated, and each ratio is presented as the median, range, and interquartile range. The Wilcoxon–Mann–Whitney test was performed to compare the ratio between males and females and the Pearson's correlation analysis was performed to evaluate the relationship between ratio and age. All statistical analyses were performed using the SPSS 24.0 software (SPSS, Chicago, IL). A p-value less than .05 was considered statistically significant.The median ratio of D1 to D1+D2, D3 to D3+D4, and D5 to D5+D6 were 0.37 (range 0.26 to 0.50), 0.23 (range 0.16 to 0.33), and 0.35 (range 0.25 to 0.45), respectively. There were no significant differences in all measurements by gender and age. Thus, we suggest that it is relatively safe to make an oblique incision for MDCO at the postero-inferior area of the point that is one third of the distance from the lateral malleolar tip to the posterior inferior margin of the calcaneus.

Keywords: Sural nerve, Calcaneus, Osteotomy, Cadever

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P11

Morphological Classification of the Moderator Band and its Relationship with the Anterior Papillary Muscle in the Right Ventricle

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Introduction: The aims of this study were to investigate and classify various type of moderator band in the right ventricle in relation with the anterior papillary muscle, as anatomical reference and fundamental knowledge of the clinical relevance about the conduction system or the congenital defects such as the defect of interventricular septum. Methods: The study has been carried out on 26 formalin fixed human hearts of both the sexes aged from 38~90 years. Results: Morphology of the moderator band and its connection with the anterior papillary muscle were various. Moderator bands were classified into three types according to its shape: cylindrical column, long and thin column, and wide and flat column types. The long and thin column type was the most commonly observed as 48%. The cylindrical column type and wide and flat column type were observed as similar proportion in 26% and 26%, respectively. In addition, the length of each type was varied. The moderator band usually originated from a single root, however it originated from two roots in three cases (11.5%). The moderator band was always attached to the anterior papillary muscle except in only one case. In 30 % of the specimens, the moderator band was divided into two or three parts before its attaching to the anterior wall of the right ventricle as well as the anterior papillary muscle. Conclusion: The findings of the present study provide fundamental anatomical and clinical information for designing cardiac surgical procedures.

Keywords: Moderator band; Right Ventricle; Anterior Papillary Muscle; Conduction System

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P12

Head Mount Display를 이용한 머리뼈 가상현실 3차원영상 만들기

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시신 해부의 어려움을 극복하기 위해서 온몸의 3차원영상이 개발되었다. 현재까지의 3차원영상은 2차원영상을 컴퓨터에서 재구성해서 만든다. 만들어진 결과는 3차원영상이지만 결과를 보는 방법은 2차원평면 모니터이기 때문에 3차원 생김새, 3차원 위치를 깨닫기에 많이 부족하였다. 또한 모니터의 경우 3차원 영상을 움직여서 구조물의 생김새를 파악하기 때문에 현실감을 느끼기에 부족하였다. 최근 들어 가상현실 기술과 Head Mount Display (HMD) 장비의 개발로 사용자가 가상의 공간 속에 들어가 3차원영상을 둘러봄으로써 실제와 비슷한 현실감을 느낄 수 있게 되었다. 이 연구의 목적은 HMD 가상현실 3차원영상을 만드는 방법을 알려서 해부 구조물의 가상현실을 필요로 하는 연구자가 쉽게 가상현실 3차원영상을 만들 수 있게 하는 것이다. 선행연구에서 만든 머리 절단면영상과 머리뼈 구역화영상을 써서 머리뼈 각각의 3차원영상을 FBX 파일로 만들었다. Unreal Engine (ver 4.17, Epic games)에서 FBX 파일을 불러와서 가상현실의 공간에 넣었다. 이 공간에서 가용자의 시점을 만들었고, 시점이 처음 만나는 3차원영상의 이름이 나타나게 하였다. 안드로이드 스마트폰에서 볼 수 있도록 APK 파일로 변환하였다. 안드로이드 스마트폰(갤럭시 S7 이상)에 APK 파일을 복사하고 실행한 다음에 갤럭시기어 HMD를 착용하여 가상현실에서 머리뼈 3차원영상을 볼 수 있게 하였다. 가상의 공간에 머리뼈는 고정되어 있고 사용자가 움직이면서 구조물을 둘러보았다. 시점이 만나는 구조물의 이름도 나타나게 하였다. 이 연구에서 쓴 재료(절단면영상)와 기술(가상현실 제작 소프트웨어, 제작 매뉴얼)을 공짜로 퍼뜨리고 있다. 이 연구를 바탕으로 해부학자가 필요한 구조물의 3차원 가상현실 소프트웨어를 제작하면 해부학을 쉽게 익히는 데 도움 줄 것이다.

Keywords: Three Dimensional Images, Visible Human Project, Skull

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P13

법의학적 얼굴복원을 위한 얼굴피부두께 작업 사례: 나주 정촌고분, 영동리고분 출토 인골

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법의학적 얼굴복원(forensic facial reconstruction)을 위한 과학적 자료 중 얼굴피부두께 자료는 얼굴의 윤곽을 결정짓는 가장 기초적인 자료이다. 연구자는 머리뼈에서의 수직거리를 측정하는 기존 얼굴피부두께 자료와 다르게 머리뼈의 표지점과 얼굴의 표지점 사이의 직접거리와 단위벡터로 구성하여 얼굴복원 시 피부두께의 크기와 방향을 고려한 한국인 얼굴피부두께 자료를 구축하였다. 20대부터 40대까지의 연령대와 성별에 따라 10개의 3차원 얼굴 및 머리뼈 모델을 사용하여 총 60개의 모델을 조사하였다. 정중시상면에서 20개의 표지점, 얼굴의 쪽 별로 39개의 표지점을 사용하여 총 98개의 표지점으로부터 얼굴피부두께의 크기와 단위벡터를 수집하였다. 연구자는 이러한 한국인 얼굴피부두께 자료를 이용하여 나주문화재연구소에서 발굴한 나주 정촌고분 출토 인골과 동신대학교에서 발굴한 나주 영동리고분 출토 인골에 대한 얼굴 복원 작업 중 얼굴피부두께를 표지하는 작업을 수행하였다. 정초고분 출토 인골은 인류학 감정 상 여성으로 추정하고 연령은 추정이 불가능하였다. 이 인골은 여러 개의 조각으로 분리되어 있어서 3차원 상에서 정합하는 과정을 거쳐 원해의 머리뼈를 복원하여 얼굴피부두께 작업을 수행하였다. 영동리고분 출토 인골은 2호석실의 2호 인골이었으며 동아대학교 김재현 교수의 인류학 분석을 바탕으로 한국인 여성의 얼굴피부두께 자료를 적용하였다. 연령은 고령층으로 추정되었으나 구축한 자료의 연령 범위가 20–40대로 한정되어있어 여성의 평균 두께 자료를 이용하였다. 얼굴피부두께를 적용한 결과 이마, 눈, 광대의 얼굴피부두께의 재현력은 좋았으나 코방울, 양쪽 측면 부위와 턱뼈각 부위는 과도하게 표현되는 경향을 보았다. 현재 60대를 포함한 한국인의 고령층 자료를 이용한 얼굴피부두께 자료 구축을 마무리하고 있으며 표현력이 떨어진 부위에 대한 얼굴피부두께 자료를 보완할 방법을 모색 중에 있다. 본 연구에 적용한 얼굴피부두께 자료는 표지점에서의 얼굴피부두께를 크기와 방향에 대한 수치값으로 표현하여 많은 정보량을 통해 얼굴복원의 정확도를 올릴 수 있을 것으로 기대하며 과거 사람의 얼굴복원 연구에도 활용되기를 바란다. 이 초록은 2017년도 문화재청 용역사

업으로 수행된 연구이며 2015년도 정부(미래창조과학부)의 재원으로 한국연구재단의 지원(No. 2015R1C1A1A01052630)을 받은 연구임.

Keywords: Forensic facial reconstruction, Facial thickness, Three-dimensional model, Human remains

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P14

Topographic Anatomy of the Neurovascular Structures around the foramen ovale

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Knowledge of the location of the branches of the maxillary artery (MA) and mandibular nerve (MN) in the infratemporal fossa around the foramen ovale (FO) is essential for adequate block anesthesia, mandibular condyle fracture, tumorectomy, maxillofacial trauma, orthognathia and foramen ovale puncture to avoid neurovascular injury. The precise anatomic data of these structures in relation to each other does not appear to have been determined, thereby the purpose of this study was to describe morphological and morphometric branching pattern of the accessary meningeal branch (AMbr), the pterygomeningeal artery (PMA), the relationship between neurovascular structures and the pterygospinous ligament (PSL). Thirty hemi-sectioned head specimens from 15 embalmed Korean cadavers (13 males and 2 females; mean age 63.3 y; range 42-85 y) underwent dissection of the region surrounding the FO. The courses of the MA that arises from the external carotid artery and extends to the maxillary tubercle were identified as well as its branches by removing adjacent muscles. Also the inferior alveolar nerve (IAN) and the lingual nerve (LN) were tracked upwards towards the FO in the infratemporal fossa. The whole process was carried out using a surgical microscope (Carl Zeiss, Germany) and micro surgical instruments. The topography of the neurovascular structures around the FO was observable after procedures, the AMbr was classified into three types according to its presence and further into two types according to the distribution patterns of the PMA. The variation of the communicating patterns between the MN branches was identified. Each branching point of branches of the MA and the MN were measured using digital calipers (Model CD-15CP; Mitutoyo, Kawasaki, Japan). The data are presented as mean ± SD values. In the classification of the AMbr, type A; the case where the AMbr arises from the middle meningeal artery (MMA), was found in 5 sides (16.7%), type B; the case of the AMbr arises from the MA, was found in 2 sides (6.7%), and Type C; the absence of the AMbr, was found in 23 sides (76.6%). In the classification of the PMA, type I; the PMA arose from the MA, was found in 9 sides (30%), and Type II; the PMA arose from the MMA, was found in 21 sides (70%). The distances from the origin of the MA to the MMA, inferior alveolar artery, AMbr and PMA were 10.8, 12.0, 21.2, and 13.3 mm, respectively. A total of 24 PSL were observed in 30 sides (80%). The relationship between the neurovascular structures and the PSL showed two patterns; 20 sides (83.3%) of the neurovascular structures were located laterally to the ligament, and 4 sides (16.7%) were located medially to the ligament. By discovering various morphology of the neurovascular structure around the FO, expected to provide valuable information for approaches of the infratemporal fossa to dentists, neurosurgeons and operators.

Keywords: Infratemporal fossa, Accessary meningeal branch, Pterygomeningeal artery, Pterygospinous ligament, Foramen ovale

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P15

Internal and external diameters of branches of the facial artery

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Facial filler injection are popular for facial rejuvenation and volume augmentation. Vision loss caused by hyaluronic acid filler embolism due to accidental injection of fillers into the facial artery and then retrograding into the ophthalmic artery system is a rare but medical emergency for which there is no proven rescue treatment. The diameter of the facial artery at various positions is important factor in the vulnerability to vascular complications following filler injection. Sixty-two facial arteries were harvested from 31 Korean formalin embalmed cadavers. The diameter of the facial artery was measured

at the level of the margin of the mandible, origin of the inferior labial artery, level of oral commissure, origin of the superior labial artery, and lateral nasal branch. The values of the means as follows; the internal diameter of arteries were 1.2±0.3, 1.2±0.3, 1.0±0.3, 0.9±0.2, and 0.7±0.2 mm, respectively. The external diameter of arteries were 1.9±0.4, 1.7±0.3, 1.5±0.4, 1.3±0.3, and 1.1±0.2 mm, respectively. ¬¬Some aesthetic surgeons empirically inject hyaluronidase to dissolve the peptide bonds of the long-chain proteins within hyaluronic acid. Information about the diameter of the related arteries is important for safe filler injections and effective management of devastating vascular complications.

Keywords: facial artery, diameter, hyaluronic acid, filler embolism

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맨눈해부학실습에서 협동학습의 의의

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통합의학교육과정의 도입으로 맨눈해부학실습 시간이 감소하면서 해부학실습 교육의 효율성을 높일 수 있는 방법의 개발이 필요해졌다. 실습교육의 효율성을 높이기 위해서는 학생들에게 자기 주도 학습을 장려하고, 상호간의 동료 학습을 통해 협동학습을 유도하는 것도 하나의 방안이라고 생각하여 본 연구를 실시하게 되었다. 2017년도 부산대학교 의과대학 1학년 121명(남 72명, 여 49명)의 학생을 대상으로 하였다. 해부학실습에서 한 조를 7~8명으로 나누어 16개 조를 만들고, 4구의 사전 해부시신을 제공하였다. 한 조 내에서 3~4명을 해부조 혹은 학습조로 편성하였다. 해부조는 직접 해부에 참여하고, 학습조는 강의실에서 주어진 학습과제를 수행하며, 당일 해부학실습 내용에 대한 공부를 하는 자기주도학습을 하도록 하였다. 해부학 실습 종료 1시간 전에 학습조가 합류하여 해부조는 학습조에게 당일 해부한 내용에 대한 설명하면서 체크리스트에서 제시한 구조물을 함께 표시하도록 하였으며, 학습조는 학습과제의 내용을 해부조에게 설명하는 과정으로 조원 간에 협동학습이 이루어지도록 하였다. 해부조와 학습조는 번갈아가면서 교대하여 동일한 해부학실습의 기회를 제공하였다. 체크리스트의 구조물을 채점하는 과정을 액션캠으로 촬영하여 다음 실습시간에 학습조에게 제공하여 평가과정을 동영상으로 확인할 수 있게 하였다. 해부조와 학습조로 나누어 실습하면서 모든 학생이 실습에 적극적으로 참여할 수 있었으며, 교수가 담당하는 학생의 수도 1/2로 줄어들어 보다 효율적인 실습지도와 여유로운 실습실 공간 활용이 가능하였으며, 체크리스트를 이용한 채점과정에 대한 의견을 나눌 수 있었다. 시신에 표지한 구조물의 이름을 기입하는 해부학실습시험을 3회 실시하였다. 해부조와 학습조가 분명히 구분된 등부위와 팔다리 부위의 77개 문항을 대상으로 해부조와 학습조의 정답률을 조사하여 통계학적 분석을 하였다. 해부조와 학습조간의 해부학실습 시험의 성적은 유의한 차이를 보이지 않았다. 77개의 문항 중에서 52개의 문항은 해부조와 학습조간의 정답률에서 유의한 차이를 보이지 않았지만, 11개의 문항은 해부조의 정답률이 더 높았고, 9문항은 학습조의 정답률이 더 높았다. 해부조에서 더 높은 정답률을 보인 문항은 혈관계 3문항(가슴봉우리동맥, 앞뼈사이동맥, 깊은넙다리동맥), 신경계 3문항(안쪽아래팔피부신경, 노신경의 얕은가지, 폐쇄신경), 근육계 5문항(위팔두갈래근널힘줄, 긴노쪽손목폄근, 깊은손가락굽힘근, 네모엎침근, 긴종아리근)이었다. 학습조에서 정답률이 더 높았던 문항은 혈관계 1문항(깊은손바닥동맥활), 신경계 3문항(팔신경얼기의 뒤다발, 아래팔뒤뼈사이신경, 정중신경의 되돌이가지), 근육계 5문항(넓은등근, 가장긴근, 엉덩갈비근, 팔꿈치근, 벌레근)이었다. 해부학실습을 해부조와 학습조로 나누어 협동학습을 실시하였을 때, 실습 진행에서는 보다 효율성을 높일 수 있었으며, 실습시험 성적에서 해부조와 학습조 사이에 유의한 차이를 보이지 않았다.

Keywords: 맨눈해부학실습, 해부조, 학습조, 협동학습

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P17

첫째에서 다섯째 갈비사이공간에서 관찰되는 교통가지에 대한 국소해부학적 연구

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손바닥땀과다증의 치료를 위한 수술 방법 중 하나인 교통가지절단술은 가슴교감신경절이나 줄기에 손상을 주지 않기 때문에 이

론적으로 가장 좋다고 알려져 있다. 수술 후 재발 또는 보상성 땀과다증과 같은 원치 않는 부작용을 줄이기 위해서는 위쪽 가슴교감신경절과 갈비사이신경 사이를 연결하는 교통가지에 대한 정확한 국소해부학적 이해가 필요하다. 따라서 이 연구는 첫째에서 다섯째 갈비사이공간에서 교통가지의 형태변이 및 위치 관계를 밝히기 위해 시도되었다. 재료는 한국 성인시신 26구 중 50쪽의 가슴을 사용하였다. 교통가지의 개수는 총 764개 였으며, 첫째에서 다섯째 갈비사이공간에서 각각 평균 4.6±1.3, 2.9±1.0, 2.5±1.1, 2.3±0.9, 2.2±0.8개가 관찰되었다. 교통가지는 가슴교감신경절과 갈비사이신경 사이를 연결하는 형태에 따라 세 유형으로 분류하였다. 첫째 유형은 교통가지가 교감신경절과 이에 상응하는 갈비사이신경 사이를 연결하는 경우였는데, 일부에서는 교통가지가 교감신경절 뒤쪽으로 짧게 연결되어 교감신경절을 가쪽으로 완전히 젖혀야만 관찰 가능하였다. 둘째과 셋째 유형은 교통가지가 각각 교감신경절과 하나 위쪽 또는 하나 아래쪽 갈비사이신경 사이를 연결하는 경우였다. 둘째 유형의 교통가지 중 일부는 교감신경절의 안쪽면과 갈비사이신경을 연결하고 있었는데, 이 경우 교통가지가 갈비뼈머리와 척추뼈고리뿌리 사이로 지나가기 때문에 갈비뼈머리를 제거해야 확인 가능하였다. 이를 바탕으로 첫째에서 다섯째까지 각 갈비사이공간에서 관찰되는 교통가지의 조합을 분석하였다. 첫째 갈비사이공간에서는 세 유형이 모두 존재하거나(28%), 둘째 또는 셋째 유형 중 하나가 없는 것이(72%) 관찰되었다. 둘째 갈비사이공간에서는 세 유형이 모두 존재하는 경우(14%)와 둘째 또는 셋째 유형 중 하나가 없는 경우(44%), 그리고 첫째 유형만 있는 경우(42%)가 관찰되었다. 셋째 갈비사이공간에서는 둘째 또는 셋째 유형 중 하나가 없는 경우(22%), 첫째 유형만 관찰되는 경우(74%)가 있었으며, 교통가지가 없는 경우도 있었다(4%). 넷째 갈비사이공간에서는 세 유형이 모두 존재하거나(2%), 둘째 또는 셋째 유형 중 하나가 없는 것(12%), 첫째 유형만 있는 것이(84%) 관찰되었으며, 교통가지가 없는 경우도 2% 있었다. 다섯째 갈비사이공간에서는 둘째 또는 셋째 유형 중 하나가 없는 경우(6%)와 첫째 유형만 관찰되는 경우(94%)가 있었다. 교통가지의 두께 및 폭의 계측값은 첫째 갈비사이공간에서 가장 컸으며, 아래로 내려갈수록 점점 작아지는 경향이 있었다. 이상의 결과를 바탕으로 수술 후 원치 않는 부작용을 일으킬 가능성이 있는 교통가지의 형태학적 변이에 대해 고찰하였다.

Keywords: 갈비사이공간, 가슴교감신경절, 갈비사이신경, 교통가지, 손바닥땀과다증

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Ac cessory Head of the Extensor Carpi Radialis Longus Muscle Merging with Extensor Carpi Radialis Brevis Muscle

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The retention and capture functions of hand can be achieved by the consistent manner work of the extensor and flexor muscles. Therefore, it is important to know variations of the extensor and flexor muscles. During an educational dissection, accessory heads of the extensor carpi radialis longus muscle were found on the right side in a Korean cadaver. The extensor carpi radialis longus muscle was originated from the lateral supracondylar ridge of the humerus and trifurcated into three heads as lateral, intermediated, and medial heads. The lateral and intermediated heads merged and inserted to the base of the second metacarpal bone. However, medial head of extensor carpi radialis longus muscle was merged with the extensor carpi radialis brevis muscle. The author describes this previously novel case report and discusses the clinical implications of such a variant.

Keywords: extensor carpi radialis longus muscle, extensor carpi radialis brevis, variation

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Topographic Anatomical Study of the External Branch of the Superior Laryngeal Nerve

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The external branch of the superior laryngeal nerve (eSLN), which provides the only efferent fibers to the cricothyroid muscle. Injury to the eSLN can cause a hoarse or weak voice with dysergia of the cricothyroid. The present study provided the topographic information of the eSLN in the Asian and verified anatomical validity of the landmarks previously recruited to localize the eSLN. The vertical distance between the eSLN and the apical pole of the thyroid gland (AP) was 8.2±4.2mm. It descended over the AP with ‹1cm distance in 51.7%, ›1cm distance in 27.6% and under the AP in 20.7%. The piercing point (PP) of the eSLN to the muscles located 26.0±5.5mm posterior and 14.7±5.0mm inferior to the laryngeal prominence. Generally, the PP located superoposterior to the midpoint of the joint between the joint of inferior constrictor and cricothyroid (ICJ). The distance between the PP and the midpoint was 8.7±5.1mm. We found that 1) the Asian had the eSLN located over the AP with ‹1cm distance about half cases, 2) the PP can be a consistent reference for the eSLN identification, 3) the ICJ can be a useful landmark to preserve the eSLN at the PP. Clinical implication of the eSLN anatomy in this study supposed necessity of routine eSLN identification during thyroid surgery.

Keywords: Cricothyroid muscle; External branch of superior laryngeal nerve; Superior thyroid artery; Larynx

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눈확아랫면 골절시 손상받기 쉬운 눈확아래신경의 해부학적 연구

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눈확아래고랑은 눈확의 아랫면 즉, 위턱뼈눈확면에 있으며 눈확아래신경은 아래눈확틈새를 통해 눈확아래구멍으로 나온다. 눈확아래고랑은 다양한 형태를 이루고 있으며 안구 손상 또는 눈확부위의 외과 수술시 눈확아래신경이 손상받기 쉽다고 알려져 있다. 이에 눈확아래신경이 주행하는 눈확아래고랑의 해부학적 형태와 위치를 관찰하는데 있다. 한국인 시신 20구 40쪽의 눈확을 대상으로 하였으며, 눈확아래고랑을 세 가지 유형으로 나누고 수술시 볼 수 있는 눈확아래가장자리에서 볼수 있는 눈물오목(Fossa for lacrimal sac), Frankfort horizontal plane을 잇는 눈확가장자리지점(FHP), 광대위턱봉합의 눈확가장자리지점(ZO) 등과 해부학적 표시점인 시각신경관(OC), 눈확아래고랑의 시작점(S), 눈확아래고랑의 끝점(C), 눈확아래구멍(SIOF) 등의 지점을 기준으로 길이를 계측하여 해부학적 위치를 확인하였다. 또한 각 길이의 남녀와 좌우 통계적 차이를 관찰하였으며, 또한 눈확아래신경이 지나는 눈확아래구멍외의 덧눈확아래구멍도 관찰하였다. 눈확아래신경은 아래눈확틈새를 통해 위턱뼈눈확면에서 눈확아래관 또는 눈확아래고랑을 지나 눈확아래구멍으로 나오는데 시작부위를 세가지 유형으로 나누었다. Type Ⅰ은 시작부위에서 완전한 눈확아래관으로 경우로 12.5% (5/40) 나타났고, Type Ⅱ는 시작부위가 눈확아래고랑의 형태이나 얇고 투명하며 작게 열려있는 경우로 65.0% (26/40) 이며, Type Ⅲ는 눈확아래고랑으로 형성되어 있는 경우로 22.5% (9/40) 이었다. 눈확아래틈새에서 눈확아래구멍까지의 길이는 평균 29.0±3.2 mm이며, 눈확눈확아래관의 길이는 평균 12.9±3.8 mm 이고 눈확아래고랑의 길이는 평균 16.2±2.9 mm이었다. 덧눈확아래구멍은 35% (14/40)에서 나타났으며 통계적으로 남자는 50%로 여자(20%)보다 많았다. 이러한 결과로 눈확의 아랫면의 외과 수술시 눈확아래신경 손상을 최소화 할 수 있는 방법을 제시할 것으로 사료된다.

Keywords: 눈확아래신경(Infraorbital nerve) 눈확아래고랑(Infraorbital groove) 눈확바닥골절(Orbital floor fractures)

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New Aspect of the Structure of the Perineal Body

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전립샘암의 수술은 고전적으로는 샅부위로 접근하는 수술을 하였으나, 내시경의 발달로 인해 로봇팔을 이용하여 골반으로 접근하는 새로운 수술법의 시대를 열게 되어 고전적 의미의 urogenital diaphragm의 해부학에 대한 중요도가 간과되어 왔다. 최근 retropubic space를 보존하는 것이 술후 비뇨생식 기능 유

지를 위해 중요하다는 의견이 제시되고, perineal single port RP가 시도됨에 따라 urogenital diaphram의 국소해부학과 perineal body(PB)의 구성에 대한 세밀한 해부학적 지식이 필요하게 되었다. 이에 PB를 구성하는 각 구조들에 대해 정확한 해부학을 수립하고자 이 연구를 하였다. 연구에 사용한 시신은 통상적 방법으로 포르말린 고정한 시신 15구를 사용하였다. Ischial tuberosity에서 central tendon까지의 평균길이는 왼쪽이 33.6 mm, 오른쪽이 38.6 mm 였다. 항문의 가장 앞쪽 모서리에서 bulbocavernosus m. 중앙의 가장 뒤쪽까지의 거리는 평균 15.8 mm였다. Bulbocavernosus m.은 bulb에서 dorsal side의 raphe로 닿는 것과 perineal body로 닿는 것이 구별되었다. 11.5% 의 표본에서 bulbar의 bulbospongiosus m.이 나란히 배열되지 않아 bulbar 전체를 덮지 못하고, 일부는 external anal sphincter m.의 fiber와 연결되는 것을 관찰하였다. Median raphe의 길이는 뿌리부터 46.9 mm 였다. PB는 얕은층의 근육과 깊은층의 근육이 부착되는 위치가 서로 구분되었다. 얕은층의 근육은 깊은층의 근육보다 좀 더 뒤쪽에서 표면구조를 이루며 합쳐졌으며, bulbocavernosus m., superficial transverse perineal m., superficial anal sphincter m.의 일부가 합쳐져서 구성되었다. Deep transverse perineal m.과 deep anal sphincter m.이 연결됨을 확인할 수 있었다. Deep transverse perineal m.과 deep anal sphincter m.은 이들보다 좀 더 앞쪽 깊은 곳에서 합쳐져서 합류하였다. 일부에선 superficial transverse perineal m.과 superficial anal sphincter m.의 muscle fiber 가 서로 cross 되어 연결되었고, 2예에서 deep anal sphincter m.의 일부가 bulbospongiosus m.의 옆쪽으로 연결되며, PB를 형성하는데 참여하지 않는 것을 관찰하였다. 이들이 PB를 이루는 형태는 prostate 수술은 물론 rectal cancer의 수술 시에도 고려해야 한다. 즉, prostate로 perineal approach시 이들이 이루는 삼각형 지표를 정확하게 아는 것이 중요하며, 이러한 구조들이 수술 후 배뇨와 생식기능은 물론 배변에도 영향을 줄 수 있으므로 유념해야 할 것이다.

Keywords: Perineal body Central tendon

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P22

RCANs Regulate The Convergent Roles Of NFATc1 In Bone Homeostasis

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Activation of calcineurin-dependent nuclear factor of activated T cells c1 (NFATc1) is convergent for normal bone homeostasis. NFATc1 regulates both osteoclastogenesis and osteoblastogenesis. Here we investigated the roles of regulator of calcineurin (RCAN) genes in bone homeostasis. RCANs function as potent physiological inhibitors of calcineurin. Overexpression of RCANs in osteoclast precursor cells attenuated osteoclast differentiation, while their overexpression in osteoblasts enhanced osteoblast differentiation and function. Intriguingly, opposing effects of RCANs in both cell types were shown by blocking activation of the calcineurin-NFATc1 pathway. Moreover, the disruption of RCAN1 or RCAN2 in mice resulted in reduced bone mass, which is associated with strongly increased osteoclast function and mildly reduced osteoblast function. Taken together, RCANs play critical roles in bone homeostasis by regulating both osteoclastogenesis and osteoblastogenesis, and they serve as inhibitors for calcineurin-NFATc1 signaling both in vivo and in vitro.

Keywords: Osteoclast, Osteoblast, RCAN, Calcineurin, NFATc1

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P23

Autophagy-related Genes Are Crucial For Inner Ear Development And Hearing Function

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Autophagy is a catabolic lysosomal degradation pathway that plays critical roles in cell maintenance, expansion, and differentiation. Autophagy is activated during starvation and hypoxia to facilitate cell viability. Recent studies demonstrated that autophagy is associated with apoptotic cell clearance in aminoglycoside- or noise-induced hearing loss condition in mice. However, the specific role of autophagy in inner ear development and function has not been explored in mice lacking autophagy-related genes. In this study, we investigated the role of autophagy in inner ear development and hearing function by targeting Atg5, autophagy related 5, which acts as E3 ubiquitin ligase in autophagosome elongation and targeting Atg7, autophagy related 7, which acts as E1 like enzyme in autophagosome elongation. Due to the neonatal lethality of Atg5-and Atg7-null mice, we generated four different inner ear-specific Atg5 and Atg7 knockout models by crossing Gfi1Cre with Atg5lox/lox mice and Atg7lox/lox mice for hair cell-specific deletion and by crossing Pax2Cre with Atg5 lox/lox mice and Atg7lox/lox mice for inner ear-specific deletion. We observed disorganization of stereociliary bundles and hair cell loss in Atg5 and Atg7-deficient mice. These defects resulted in severe hearing loss, which was confirmed by auditory brainstem response and distortion product otoacoustic emissions test. We are currently investigating when and how the degeneration of hair cells and spiral ganglion neurons occur in the Atg5 and Atg7 cKO mice. Thus, we demonstrate that functional and morphological defects in the cochlea of Atg5 and Atg7 null mouse models. Our further study will provide insight into the mechanisms of autophagy in inner ear development and hearing function.

Keywords: Autophagy, Autophagy-related Gene, Innerear Development, Hearing

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P24

GlcNAc Kinase Increases O-GlcNAc Level and Beating Rate of NRVM and Reduces ROS in H9C2 Cells

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O-linked N-acetyl-β-D-glucosamine (O-GlcNAc) is a dynamic post-translational modification of serine and/or threonine residues in diverse nucleocytoplasmic and mitochondrial proteins. Since recent studies have indicated that the sugar moiety O-GlcNAc is further phosphorylated to produce O-GlcNAc-6-phosphate, we investigated the effects of GlcNAc kinase (NAGK) in cultured cardiomyocytes. Exogenous expression of DsRed-tagged NAGK in neonatal rat ventricular myocytes (NRVMs) increased GlcNAc immunocytochemial signals and the beating rate. The primary NRVM and L6 myogenic line were very resistant to hypoxia (12 hr in 1% O2, 37°C). In contrast, H9C2, a myocardiocyte cell line, was relatively susceptible to hypoxia and thus appropriate for assessing the cytoprotective effects of NAGK in hypoxia/reoxygenation (H/R) injury. Exogenous expression of NAGK reduced the reactive oxygen species (ROS) levels after H/R in H9C2 cells, and this effect was abolished by a short hairpin (sh) RNA to NAGK. Scatter plots revealed that the ROS levels of each cell was in a linear descending or ascending trend with the expression levels of DsRed-NAGK or shRNA, respectively. NAGK increases intracellular O-GlcNAc level and the beating rate of NRVM, which helps the H9C2 cells overcome hypoxic shocks by reducing ROS levels.

Keywords: H/R injury, NAGK, NRVM, O-GlcNAc, ROS

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P25

Autophagy in FOXD1 Stroma-Derived Cells Plays a Critical Role in Renal Tubulointerstitial Fibrosis

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Renal fibrosis is the final common pathway of various renal injuries and it leads to chronic kidney disease. The FOXD1 lineage pericyte has been recognized to plays a critical role in renal tubulointerstitial fibrosis (TIF), however the regulatory mechanism remains unclear. Autophagy is a cellular process of degradation of damaged cytoplasmic components that regulates cell death and proliferation. Here, we showed the induction of autophagy in platelet-derived growth factor receptor-β positive stromal cells of the obstructed kidney after unilateral ureteral obstruction (UUO) using green fluorescent protein-LC3 transgenic mice. FOXD1-lineage stromal cell-specific Atg7 deletion enhanced tubulointerstitial fibrosis through Smad-dependent transforming growth factor-β signaling after UUO. We also showed that FOXD1-lineage stromal cell-specific Atg7 deletion increased the accumulation of interstitial myofibroblasts and enhanced the differentiation of pericytes into myofibroblasts after UUO. Peritubular capillary rarefaction and apoptosis of interstitial cells were accelerated in FOXD1-lineage stromal cells-specific Atg7 deficient mice after UUO. Our data showed that autophagy in FOXD1 stroma-derived cells played a protective role in the development of renal TIF and the apoptosis of stromal cells, which may be a new therapeutic target for renal TIF.

Keywords: Autophagy, Kidney, Fibrosis, FOXD1, Stroma

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P26

Expression of cyclin-dependent kinases (CDKs) and CDK inhibitors in hypokalemic rat kidney

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Chronic hypokalemia induces proliferation and hypertrophy in renal tubular epithelial cells. Cell cycle regulatory proteins play an important role in renal hyperplasia and hypertrophy. The purpose of this study was to examine the expression of cyclins, cyclin dependent kinases (CDKs), and CDK inhibitors in the hypokalemic kidney. Sprague-Dawley rats received either K+-free or control diets for 2 week. Kidney tissues were processed for immunocytochemistry and immunoblot analysis. Rats receiving the K+-deficient diet developed hypokalemia and showed typical histopathology including hyperplasia and hypertrophy, especially in the outer medullary collecting ducts (OMCD). Hypokalemia significantly increased the expression of proliferating cell nuclear antigen (PCNA), cyclin D1 and D3, CDK 2, 4, and 6 in the OMCD. In contrast, hypokalemia decreased the expression of p18(INK4c), p21(WAF1/Cip1), and p27(Kip1) in the OMCD. No significant changes were observed in cyclins, CDKs, and CDK inhibitors expressions in the cortex. The OMCD consists of two different cell types, the principal cell and intercalated cell. Double immunolabeling with the principal cell marker, AQP2, and the intercalated cell marker, H+-ATPase, revealed that expression of CDK2 and p27 were changed mainly in principal cells. These findings suggest that CDKs and CDK inhibitors may play an important role in the regulation of OMCD principal cell proliferation in chronic hypokalemia. This work was supported by funds from the National Research Foundation of Korea (NRF-2013R1A1A2058028 & 2017R1D1A1B03030573).

Keywords: Kidney, Hypokalemia, Cell cycle

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P27

Topographical anatomy of the intestine and colon during physiological herniation: a study using histological sections of human embryos and fetuses

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Because most malrotations of the small intestine and colon are

thought to occur during the repackaging process, the positions of the intestine and colon should vary less during than after physiological herniation. Examination of serial sagittal sections of 27 embryos and fetuses (gestational age 6–9 weeks; crown-rump length 15–39 mm) during herniation showed that, in 16 specimens, the jejunum and ascending colon passed through a small opening of the hernia sack at the levels of the pancreas. Below the pancreas, a definite mesentery was found to extend between the ascending and descending colon in the abdominal cavity. In the other 11 specimens, the descending colon passed through an opening with a size almost same as the majority and ran posteriorly along the urinary bladder, resulting in the entire ilium, ascending colon and transverse colon entering the sack. In these specimens, the duodenojejunal junction was often situated in a window of the mesentery of the colon (internal herniation). The descending colon was observed at an outside location more frequently in earlier specimens. In contrast to our working hypothesis, the positions of the intestine and colon were abnormal in 40.7% (11/27) of samples. An outside location of the descending colon was not directly associated with malrotation because recovery was likely. However, the delayed development of the inferior mesenteric arterial branches might cause failure, including death in utero, during or after the repackaging process associated with physiological herniation.

Keywords: Malrotation, Colon, Physiological herniation, Repackage, Human embryos

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P28

Characterization of Psg Gene Expression and Function During Murine Placentogenesis

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Placenta is essential organ for sustaining survival and growth of fetus during gestation. It mediates maternal-fetal exchange and produces hormones that alter maternal physiology and protect the fetus against the maternal immune system during pregnancy. These placental roles are necessary for normal pregnancy outcomes, and defects in its functions lead to adverse pregnancy outcomes including intrauterine growth restriction (IUGR) and pre-eclampsia (PE), spontaneous preterm delivery, and abortion as well as long-term effects on health and behavior of adult offspring in sex-specific manners. The pregnancy-specific glycoproteins (PSGs), members of the immunoglobulin (Ig) superfamily, are the most abundant fetal proteins produced by placenta during pregnancy and play pivotal roles in anti-platelet, pro-angiogenesis and anti-inflammation. There is accumulating evidence that prenatal maternal stress or infection show differential effects on immune activation and inflammation depending on fetal sex. Especially, our previouswork demonstrated that administration of synthetic glucocorticoid, dexamethasone, on pregnant mice induces sex-specific activation of immune-related genes including many Psg genes. Therefore, we hypothesized that the placental Psg genes are regulated differently in a sex-dependent manner, contributing to immune response during pregnancy. Here we first examined differential Psg gene expression patterns atdifferent gestational days by RT-PCR and further determined the possible roles of Psg genes in sex-specificimmunoregulatory responses during pregnancy.

Keywords: Placenta, Pregnancy-Specific Glycoprotein

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P29

Sustained smoothened causes renal hypoplasia and hydronephrosis

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Sonic Hedgehog (Shh) signaling plays a major role and is essential for the regulating, patterning and proliferation during renal development. Smoothened (Smo) plays a pivot role in transducing Shh-glioma associated oncogene-Kruppel family member. However, the cellular and molecular mechanism underlying the role of sustained Smo activation in postnatal kidney development is still not clearly

understood. Using a conditional knock-in mouse model that expresses a constitutively activated form of Smo (SmoM2) upon Homeobox-B7 mediated recombination (Hoxb7-Cre), the effects of Shh signaling was determined in postnatal kidney development. The SmoM2;Hoxb7-Cre mutant mice showed growth retardation with the reduction of body weight. Constitutive activation of Smo in the renal collecting duct caused renal hypoplasia, hydronephrosis and hydroureter. The parenchymal area and glomerular numbers were reduced, but glomerular density was increased in SmoM2;Hoxb7-Cre mutant mice. The expression of Patched 1, the receptor of Shh and a downstream target gene of the Shh signaling pathway, was highly restricted and was upregulated in the inner medullary collecting duct of the kidney. The proliferative cells in the mesenchyme and collecting duct were decreased in SmoM2;Hoxb7-Cre mutant mice. This study showed for the first time that sustained Smo inhibits postnatal kidney development by suppressing the proliferation of mesenchyme and medullary collecting duct in mice.

Keywords: Sustained smoothened, Renal hypoplasia, Hydronephrosis

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P30

Expression pattern of Copine-7 (Cpne7), a preameloblast-derived factor, in developing mouse teeth

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Introduction: Interactions between the ectodermal tissue and mesenchymal tissue are at the basis of the central mechanism regulating the tooth development. We have previously reported that the diffusible signaling molecule Cpne7 is secreted by preameloblasts and that Cpne7-Nucleolin complex regulates the differentiation of mesenchymal cells of dental or non-dental origin into odontoblasts. However, the precise expression patterns of Cpne7 protein in tooth developmental stages is not elucidated yet. The aim of the present study was to establish the spatiotemporal expression pattern of Cpne7 during mouse tooth development.
Methods: To investigate the distribution of Cpne7 during odontogenesis, we performed immunohistochemistry and immunoflourscence of sectioned mice first molars at developmental stages.
Results: During the initial stage of developing teeth, Cpne7 stage-specific expression was found in dental epithelium but not in mesenchyme. At embryonic day 19 (E19), Cpne7 was expressed in inner enamel epithelium and stratum intermedium of the first molar, which was at the bell stage of development. At postnatal day 7 (PN7), Cpne7 was localized in differentiating odontoblasts; however, Cpne7 was no longer detected in ameloblasts. These findings suggest that Cpne7 secreted by preameloblasts was translocated to differentiating odontoblasts in response to epithelial-mesenchymal interaction.Cpne7 was expressed in differentiating odontoblasts and odontoblast apical cell surface during dentin formation, but was absent in mature functional odontoblasts. Our previous studies show that Cpne7 translocates from the ameloblasts to the odontoblasts via Nucleolin, a cell surface receptor of Cpne7. To provide further evidence for colocalization between Cpne7 and Nucleolin, we performed immunoflourscence analysis of MDPC-23 cells and sectioned mice tissues. Precisely, Cpne7 protein showed strong colocalization with Nucleolin protein in nuclei of odontoblasts and odontoblast apical cell surfaces. Furthermore, Cpne7 was expressed in cervical loop and HERS during root formation.
Conclusions: We suggest that Cpne7 regulates odontoblast differentiation through colocalization with Nucleolin at apical cell surface and root formation during tooth development.

Keywords: Cpne7, Odontoblasts, Ameloblasts, Tooth, Dentin

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P31

YAP Mediates Ca2+-dependent Adhesion and Migration of Ameloblastoma Cells

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Calcium (Ca2+) is a ubiquitous second messenger which is involved in the tuning of multiple fundamental cellular functions. Due to the multifunctional effects of the metal iron, abnormality in the Ca2+ homeostasis has been observed in various cellular disorders, including tumourigenesis. Tumour spread is a highly regulated process that usually starts with the loss of cell-cell contact and the epithelial-mesenchymal transition (EMT). The remodelling of Ca2+ signals during EMT processes has been reported for a variety of cancer cells. In this study, we examined that Ca2+ signals modulate EMT of a human ameloblastoma cell-line (AM-1). AM-1 cells in low Ca2+ condition showed low cell-cell contact and highly migratory behaviour. However, treatment of CaCl2 recovered cell-cell contract and suppressed cell migration of the ameloblastoma cells. Interestingly, numerous filopodia were observed in the membrane of AM-1 cells in low Ca2+ condition with nuclear localization of yes-associated protein (YAP), a transcriptional co-activator of various genes including cell adhesion related genes. We investigated that the nuclear YAP was essential for the low Ca2+ induced EMT and cell migration of AM-1 cells using YAP inhibitors. In conclusion, we suggest that YAP regulates Ca2+ dependent EMT and cell migration in ameloblastoma cells.

Keywords: AM-1, Calcium, YAP, Epithelial-Mesenchymal Transition(EMT)

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P32

Interaction Between Lgr5 and FGF10 is Necessary to Circumvallate Papillae Development

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Taste buds are developed in different regions of the oral cavity in mammals. Adult stem cells in various organs including tongue papillae are marked by Leucine-rich repeat-containing G protein-coupled receptor 5 (Lgr5) and its homologs, Lgr6. Recent studies have reported that adult taste stem/progenitor cells in circumvallate papillae (CVP) on posterior tongue are Lgr5 positive. In this study, we confirm the Lgr5 expression pattern during CVP development. Previous study has reported that mesenchymal Fgf10 is necessary for maintenance of epithelial Lgr5 positive stem/progenitor cells. To confirm the interaction between Lgr5 positive CVP epithelium and mesenchymal factor Fgf10, 180 degree reverse recombination was performed after detaching tongue epithelium. Moreover, FGF10 protein soaked bead implantation was performed after 180 degree reverse recombination. This study may suggest that interaction between epithelial Lgr5 and mesenchymal FGF10 would act pivotal roles in invagination of CVP formation during mouse tongue development.

Keywords: Lgr5, FGF10, Circumvallate Papillae(CVP), Tongue

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BMP4 controls specification of cuspal pattern during tooth development

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The enamel knot (EK), which is located in the center of bud and cap stage tooth germs, is a transitory cluster of non-dividing epithelial cells. The EK acts as a signaling center that provides positional information for tooth morphogenesis and regulates the growth of tooth cusps by inducing secondary EKs (sEK). There are two opinions about the fate of primary EK (pEK). One is that the pEK has been considered to have cellular continuity with the sEKs through the division of the surviving cells in the pEK and their migration into the sEKs. The other is that the pEK cells do not migrate to form sEKs. Still these opinions are controversial. Here, to eliminate enamel knot, the tooth germs at bud stage (the stage before pEK appear) and at early cap stage (the stage when pEK starts to appear) were divided lingual and buccal part by mechanical microdissection with mesiodistal direction. Then, we tried to transplant into kidney capsule for 4 weeks. The calcified teeth with flattened cusp were shown in only transplants of lingual (Bud- and Cap-lingual) tooth germ. The EK markers, such as Shh, Fgf4, and Bmp4, were identified in Cap-

lingual tooth germs. Bmp4 expression was not shown in divided tooth germs, as the expression in Gerbil's tooth germs with flattened cusp. To observe how to change the cusp shape, Bmp4 and Bmp4 inhibitors (Noggin, Chordin, and Follistatin) soaked beads were applied to not only tooth germs at bud and cap stage but also lingual tooth germs. Interestingly, the pointed cuspal shape of cap stage tooth germs was changed with Noggin protein, and with Bmp4 protein, the flattened cusp shape of Cap-lingual tooth was changed into pointed cusp. However, the pointed cuspal pattern of bud stage tooth germs and bud-lingual tooth were not changed. This study provides evidence that Bmp4 in pEK controls significantly to cuspal shape during tooth development.

Keywords: Cuspal pattern, Tooth, Bmp4, Enamel knot

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Regulation of IFITM5 related to Wnt signaling on cementoblast differentiation

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Introduction IFITM5 (also known as BRIL), a member of the interferon-induced transmembrane(IFITM) protein family, are ubiquitously expressed in osteoblast. In the mouse embryo, IFITM5 expression is specific to particular elements of the skeletal system and in vitro and in vivo studies consistently reveals a role of IFITM5 in early stage of osteoblast and bone mineralization. However, the molecular mechanism of IFITM5 and relating osteogenic signaling pathways remains unclear yet. Disruption of Wnt/beta-catenin signaling in osteoblasts and cementoblasts in a conditional knockout mouse arrests tooth root development. The fact that canonical Wnt signaling, including Wnt3a can promote dental follicle cell differentiation into cementoblast/osteoblast phenotypes, the relationship between IFITM5 and Wnt signaling in cementoblasts is not clearly delineated. Therefore, we hypothesized that IFITM5 would decisively regulate mineralized tissue-associated genes in ihCementoblasts. Materials and Methods To identify expression pattern of IFITM5 in developing mouse mandible, we performed immunohistochemistry for IFITM5 of first mandible molar tooth germs of ICR mice at E16, postnatal (PN) 2, and PN10. Immortalized human cementoblast cells were cultured in growth medium and Wnt3a expressing cell line was cultured in conditional medium according to the manufacture's instruction. Also, we investigate mRNA expression of osteogenic marker genes and protein expression of β-catenin through real-time polymerase chain reaction (RT-qPCR) and western blotting. Results At the bell stage, E16, IFITM5 was expressed in the dental follicle and the developing alveolar bone. At PN2 and PN10, IFITM5 expression showed in dental follicle, cementoblasts, odontoblasts in crown part, and osteoblasts in alveolar bone. Interestingly, IFITM5 was not expressed in odontoblasts in the root basal region. The overexpression of IFITM5 enhanced cementoblast-mediated mineralization as measured through alizarin red staining. The addition of IFITM5 overexpression lentivirus significantly increased the expression of the osteogenic transcription factors (Runx2 and Osterix), and cementum associated markers (BSP and OCN). Also, IFITM5 overexpression increased cementoblast differentitation and the mRNA levels of Col1a1 and Col1a2 increased more than 2-fold in ihCementoblasts. Moreover, Runx2, Osterix, BSP, and OCN were downregulated upon treatment with Wnt3a CM and upregulated with IFITM5 overexpression, but with both Wnt3a CM and IFITM5 overexpression, Runx2, Osterix, BSP, and OCN showed a tendency to be expressed at higher levels than Wnt3a but lower levels than IFITM5. By western blotting, we monitored the accumulation of β-catenin, an effector molecule of the canonical Wnt pathway, in the presence of Wnt3a and IFITM5 overexpression in ihCementoblast cells. Cells treated with Wnt3a CM showed accumulation of β-catenin. Conclusion We have shown for the first time that IFITM5 is expressed in dental follicle, crown odontoblast, cementoblasts, and the developing alveolar bone, and that IFITM5 acts on ihCementoblast differentiation in an inhibitory manner associated with Wnt signaling. Our study provides strong evidence that IFITM5 plays a role in tooth development associated with cementoblasts. Although the in vivo study of IFITM5 mutation on tooth development should be studied in the future, the findings of this study are expected to contribute to future research in periodontal regenerative engineering.

Keywords: IFITM5, Immortalized human cementoblast, Osteogenesis imperfact type V, Wnt signaling

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P35

The modulation of Sox2 and Cldn10 in cuspal shape via RhoA signaling

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The HMG-box transcription factor SOX2 plays a role in the self-renewal of stem cells as well as in proliferation and specific cell differentiation. Claudins (including Claudin10, Cldn10) are integral membrane proteins and components of tight junction strands, interact with cytoplasmic protein network which provides a bridge to the cytoskeleton and directly interact with actin filament. Actin filament structures play key roles in bending, molding, and sticking together the epithelial tissues to shape the embryo. However, the function of Sox2 and Cldn10 in the cuspal shape of tooth development is not yet known. Here, we used two rodents of different cusp shape, mice (pointed cusps) and gerbils (flat lophs cusps). This different cuspal shape occurs due to the invagination of inner dental epithelium in intercuspal region. First of all, to compare the localization of Sox2 amd Cldn10, immunofluorescence were performed. As a result, SOX2 and Cldn10 were co-localized in the lingual epithelium during tooth development in mouse. However, Cldn10 expression in the intercuspal region was shown higher in mice than in gerbil. Chromatin immunoprecipitation assays was revealed that SOX2 binds to Claudin10 promoter in the primary cells from E14.5 mouse tooth germ. Claudin10 regulates the RhoA signaling, which alters the cuspal shape by coordinating adhesion junctions and actin filament to drive inner dental epithelium invagination. Therefore, SOX2 and Claudin10 modulation might be able to convert the tooth shape through the RhoA signaling.

Keywords: Sox2, Cldn10, cuspal shape, tooth development, RhoA signaling

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P36

Rescue of craniofacial defects with therapeutic hedgehog target chemical in Endocrine-cerebro-osteodysplasia (ECO) syndrome mouse model

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Endocrine-cerebro-osteodysplasia (ECO) syndrome is a recessive genetic disorder in human associated with congenital defects in endocrine, cerebral, and skeletal systems that is caused by a missense mutation of the intestinal cell kinase (ICK) gene. ICK is important for ciliogenesis. Previous findings have shown that craniofacial defects with cleft palate/lip and tooth malformation in Ick mutant mice closely resemble ECO syndrome, similar with ciliary disorders. Cleft palate/lip is the most common congenital defect. Ick mutant results in cleft palate and reduced sonic hedgehog signaling, but not palatal adhesion and fusion. Ick deficiency affects palatal cell proliferation. However, regulatory effects of cilia on craniofacial development and therapeutic attempt have not yet been reported. Therefore, we intraperitoneally treated with smoothened agonist (SAG) into pregnant Ick mutant mice to examine its therapeutic effect. Exogenous stimulation of Hh signaling restored palate and tooth development. These data implicate that Hh agonist is a strong candidate for the development of novel therapies for cleft palate/lip and possibly other symptom of the ciliopathies.

Keywords: craniofacial defects, hedgehog, ciliopathy, Endocrine-cerebro-osteodysplasia (ECO)

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P37

Raman Spectroscopic Analysis of Non-Thermal Plasma-Treated Human Colon Cancer Cells

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Non-thermal atmospheric-pressure plasma has been introduced in various applications such as sterilization, wound healing, blood coagulation, and other biomedical applications. The most attractive application of non-thermal atmospheric-pressure plasma is in cancer treatment, where the plasma is used to produce reactive oxygen species (ROS) to facilitate cell apoptosis. We investigate the effects of different durations of exposure to dielectric-barrier discharge (DBD) plasma on colon cancer cells using measurement of cell viability and ROS levels, western blot, immunocytochemistry, and Raman spectroscopy. Our results suggest that different kinds of plasma-treated cells can be differentiated from control cells using the Raman data.

Keywords: Ramam Spectroscopy, Non-Thermal Plasma, Colon Cancer

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P38

Comparison of immunological characteristics of mesenchymal stem cells from the periodontal ligament, umbilical cord, and adipose tissue

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Mesenchymal stem cells (MSCs) are of therapeutic importance in the fields of regenerative medicine and immunological diseases. Accordingly, studies evaluating MSCs for clinical applications are increasing. In this study, we characterized MSCs from the periodontal ligament, umbilical cord (UC-MSCs), and adipose tissue, which were relatively easy to obtain with limited ethical concerns regarding their acquisition, and compared their immunological characteristics. Among MSCs isolated from the three different tissues, UC-MSCs grew the fastest in vitro. The three types of MSCs were shown to inhibit proliferation of activated peripheral blood mononuclear cells (PBMCs) to a similar degree, via the indoleamine 2,3-dioxygenase and cyclooxygenase-2 pathways. They were also shown to inhibit the proliferation of PBMCs using HLA-G, which was most prominent in UC-MSCs. Unlike the other two types of MSCs, UC-MSCs showed minimal expression of HLA-DR after activation, suggesting that they pose minimal risk of initiating an allogenic immune response when administered in vivo. These characteristics, the ease of collection, and the minimal ethical concerns regarding their use suggest UC-MSCs to be suitable MSC therapeutic candidates.
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Keywords: Immunological Characteristics, Mesenchymal Stem Cells, Periodontal Ligament, Umbilical Cord, Adipose Tissue

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P39

Rae1 regulates breast cancer progression and metastasis via epithelial-mesenchymal transition

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Breast cancer and its metastasis is one of the main causes of death in women around the world. Metastasis is the result of epithelial–mesenchymal transition (EMT), which is the loss of epithelial and the gain of mesenchymal characteristics. Therefore, many studies are being conducted to explain mechanisms involved in the process of EMT in breast cancer, ultimately leading to metastasis. RAE1, ribonucleic acid export 1, is one of the factors that is reported to be dysregulated in breast cancer. Some of the dysregulations include the up or downregulation of mRNA, missense mutations, and chromosome amplification. In our previous study, we investigated and demonstrated the role of RAE1 in inducing the aggressive phenotype of breast cancer cells through EMT under an in vitro system. In this study, we use three–dimensional (3D) culture system and mouse in vivo system to further validate RAE1 and its function in metastasis of breast cancer. Moreover, we show changes in EMT markers through RT–qPCR and immunocytochemistry. Taken together, this study shows that RAE1 indeed plays a key role in inducing EMT in breast cancer, and that RAE1 has the potential to be an effective therapeutic target against metastasis in breast cancer.

Keywords: RAE1, breast cancer, metastasis, EMT

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P40

Clinicopathological characteristics of TZAP expression in CRCs

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The zinc finger protein ZBTB48 is a telomere-associated factor and renamed it as telomeric zinc finger-associated protein (TZAP). It binds preferentially to long telomeres competing with TRF1 and TRF2. However, its expression in cancers has not been performed. In the present study, we analyzed TZAP expression in 59 colorectal cancers (CRC) and its association with telomere length was investigated. TZAP expression in CRC was significantly higher than that in paired non-cancerous tissues ($p = 0.033$). Higher expression of TZAP was found in CRCs with CEA positive (>5 ng/ml) ($p = 0.012$). Telomere length was shorter in CRCs with high TZAP expression than them with low TZAP expression ($p = 0.010$). According to quantitative correlation analysis, TZAP has a negative correlation with age ($r = -0.349$, $p = 0.007$) and telomere length ($r = -0.305$, $p = 0.021$). No prognostic significance was found in overall survival (OS) and disease free survival (DFS) between CRC with TZAP expression and CRC without TZAP expression. When stratifying for variables, TZAP expression was shown to be a statistically significant prognostic marker for OS: TZAP expression conferred a better prognosis in CRC with shorter telomere (HR 4.69; $p = 0.030$). This result suggested that TZAP expression appears to be a possible prognosis marker dependently with telomere length in CRC.

Keywords: TZAP, telomere, colorectal cancer, ZBTB48

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P41

Erdr1 induced anti-inflammatory-effects through the shedding off TREM-1 with MMP3 in microglial cells

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Erdr1, erythroid differentiation regulator 1, has been identified as a hemoglobin synthesis inducer but also has been demonstrated regulatory functions in anti-cancer effect and anti-inflammation. However, the functional mechanism of Erdr1 remains unknown. Here, we show that Erdr1exerts anti-inflammatory effect by regulation of surface Triggering receptor expressed on myeloid cells-1 (TREM-1) in BV2, murine microglial cells. Upon activation, TREM-1 can directly amplify an inflammatory response. TREM-1 receptor contributes to the pathology of several non-infectious acute and chronic inflammatory diseases. In this study, lipopolysaccharide (LPS) stimulation after Erdr1 transfection in BV2 cells down-regulated pro-inflammatory cytokines, IL-1b, IL-6, and TNF-a with up-regulation of anti-inflammatory cytokines, IL10 and TGF-b. Erdr1 conducts anti-inflammatory functions by shedding off the TREM-1 molecules on the microglial cell membrane by MMP3. With the action of induced MMP3, soluble TREM-1 molecules were liberated into the culture media of Erdr1 transfected BV2 cells, and cleaved

TREM-1 on BV-2 cells were defective for inflammatory response. Application of specific inhibitor for MMP3 suppressed soluble TREM-1 liberation and recovered the inflammatory effects of LPS. We discuss pre-clinical studies which show that TREM-1 inhibition, via Erdr1-induced shedding of TREM-1, can be an effective strategy to prevent inflammatory disorders. Further research aimed at identification of detailed functional mechanism involving signal pathways, is required to unravel the therapeutic potentials of Erdr1 for related diseases.

Keywords: ERDR1, TREM1, MMP3, inflammation, microglia

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P42

TZAP Mutation Leads to Poor Prognosis of Patients with Breast cancers via Telomere Lengthening

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The regulation of telomere length has been known be important mechanism for cancer development. Recent studies showed that telomeric zinc finger-associated protein (TZAP) induced rapid shortening from overly long telomere to normal length. However, genetic study about it has not been performed, therefore, we analyzed TZAP mutation and telomere length in 128 breast cancers (BCs). We found TZAP mutation in 7.0% (9/128) patients, and all mutation was c.1272G>A (L424L), as silent mutation. TZAP mutation was significantly associated with longer telomere (16.2% vs. 3.3%, $p = 0.017$) and N stage (11.4% vs 0%, $p = 0.049$). TL in BC was 1.1 ± 0.37, calculated as the ratio of TL in tumors to that of paired normal tissues. TL with TZAP mutation was significantly longer than TL without TZAP mutation (2.62 ± 1.71 vs. 0.98 ± 0.37, $p = 0.009$). Kaplan-Meier analysis demonstrated a decreased OS in patients with BC with TZAP mutations compared with wild-type TZAP (56.67 vs. 94.23 months; $\chi 2 = 9.88$; $P = 0.002$). This result suggested that TZAP may have an important role in the development and progression of BC.

Keywords: Breast cancer, TZAP, Telomere, ZBTB48

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Direct Conversion of Adult human neural stem cell into Glioblastoma multiform stem cell

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Glioblastoma multiform is the most aggressive brain tumor in adults. This tumor is highly lethal disease due to poor prognosis as well as resistance to chemotherapy and radiotherapy. Therefore, it is important to find enhanced treatment. Within tumor population, there is cancer stem cells that possess characteristics associated with normal stem cells, the ability of self-renewal and differentiation into other cell types. Cancer stem cells have effect on tumor relapse and metastasis by involving decreased cancer stem cell regeneration after cancer therapy. Therefore, we conducted the study to identify the essential genetic alteration to transform from normal adult multipotent neuronal cell to cancer stem cell in Glioblastoma. Typically, glioblastoma characterized by abnormalities in EGFR, IDH1, PDGFRA, and NF1 based on The Cancer Genome Atlas (TCGA) data. Aberrations of EGFR, NF1, and PDGFRA/IDH1 each typify the Classical, Mesenchymal, and Proneural subtypes, respectively. Additionally, tumor suppressor gene is inactivated concurrently with tumor formation gene overexpression. Therefore, we attempted to deletion of p14/p16, one of the tumor suppressor genes, using sgRNA, and overexpression of oncogenes simultaneously in adult human multipotent neuronal cells. Our data show mutated cells have a high level of clonogenic potential compared to wild type cells. In addition, genotypic variation as well as functional and phenotypic change could be analyzed after induction to cancer stem cell from

normal stem cell. Our research will be a starting point for developing novel therapeutic method targeting glioblastoma.

Keywords: Neural stem cell, Cancer stem cell, Glioblastoma

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P44

Roles of zinc-fingers and homeoboxes 1 during the proliferation, migration, and invasion of glioblastoma cells

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Zinc-fingers and homeoboxes 1 (ZHX1) is a nuclear transcription repressor and known to be involved in cell differentiation and tumorigenesis. However, the pathophysiological roles of ZHX1 have not been characterized in glioblastoma. We examined ZHX1 expression in glioblastoma patients' tissues and analyzed overall survival of the patients based on expression level of ZHX1. We also examined the effects of ZHX1 on proliferation and motility of glioblastoma cells.In silico analysis and immunohistochemical studies showed that the messenger RNA and protein expressions of ZHX1 were higher in the tissues of glioblastoma patients than in normal brain tissues, and that its overexpression was associated with reduced survival. In vitro, the downregulation of ZHX1 decreased the proliferation, migration, and invasion of glioblastoma cells, whereas its upregulation had the opposite effects. In addition, we showed ZHX1 could contribute to glioblastoma progression via the regulations of TWIST1 and SNAI2. Taken together, this study demonstrates that ZHX1 plays crucial roles in the progression of glioblastoma, and its findings suggest that ZHX1 be viewed as a potential prognostic maker and therapeutic target of glioblastoma.

Keywords: Glioblastoma, Zinc-fingers and homeoboxes 1, Proliferation, Migration, Invasion

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P45

Direct Interaction of CD40 on Tumor Cells with CD40L on T Cells Increases the Proliferation of Tumor Cells by Enhancing TGF-β Production and Th17 Differentiation

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It has recently been reported that the CD40-CD40 ligand (CD40L) interaction is important in Th17 development. In addition, transforming growth factor-beta (TGF-β) promotes tumorigenesis as an immunosuppressive cytokine and is crucial in the development of Th 17 cells. Th is study investigated the role of CD40 in breast cancer cells and its role in immunosuppressive function and tumor progression. CD40 was highly expressed in the breast cancer cell line MDA-MB231, and its stimulation with CD40 antibodies caused the up-regulation of TGF-β. Direct CD40-CD40L interaction between MDA-MB231 cells and activated T cells also increased TGF-β production and induced the production of IL-17, which accelerated the proliferation of MDA-MB231 cells through the activation of STAT3. Taken together, the direct CD40-CD40L interaction of breast tumor cells and activated T cells increases TGF-β production and the differentiation of Th 17 cells, which promotes the proliferation of breast cancer cells.

Keywords: Breast cancer, CD40, CD40L, TGF-β, IL-17

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The pathogenic role of interleukin-22 and its receptor during UVB-induced skin inflammation

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Recent studies show that IL-22, a cytokine produced by activated CD4+ T cells and NK cells, plays a pathogenic role in acute and chronic skin diseases. While IL-22 is produced by immune cells, the expression of IL-22Rα, the functional subunit of IL-22R, is mostly restricted to non-hematopoietic cells in organs such as the skin and pancreas. Although it is well known that ultraviolet B (UVB) radiation induces skin inflammation, there have been no reports regarding the effect of UVB on the expression of IL-22Rα. This study investigated IL-22Rα expression and IL-22-mediated proliferation and pro-inflammatory cytokine production by UVB-irradiated keratinocytes. IL-22Rα was increased in HaCaT and primary human keratinocytes after UVB irradiation through the translocation of IL-22Rα from the cytosol to the membrane. This increase in the expression of IL-22Rα was mediated by the PI3K/Akt pathway. Moreover, the suppression of keratinocyte proliferation by UVB irradiation was inhibited by treatment with IL-22. At the same time, IL-22 increased the production of IL-1α, IL-6, and IL-18 in UVB-irradiated HaCaT cells and primary human keratinocytes. Finally, IL-22Rα expression was increased in UVB-irradiated human and mouse skin by immunohistochemistry. The increased expression of IL-22Rα therefore promotes keratinocyte proliferation and pro-inflammatory cytokine production during UVB-induced skin inflammation, suggesting that UVB facilitates skin inflammation by increasing the responsiveness of keratinocytes to IL-22. This study provides a new insight into UVB-induced skin inflammation and the regulation of related inflammatory skin diseases.

Keywords: IL-22, IL-22R, UVB, Skin inflammation

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The Role of Interleukin-22 and Its Receptor in the Development and Pathogenesis of Experimental Autoimmune Uveitis

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IL-22 is a pro- and anti-inflammatory cytokine that is mainly produced by T cells and NK cells. Recent studies have reported the increased number of IL-22 producing T cells in patients with autoimmune noninfectious uveitis; however, the correlation between IL-22 and uveitis remains unclear. In this study, we aimed to determine the specific role of IL-22 and its receptor in the pathogenesis of uveitis. Serum concentration of IL-22 was significantly increased in uveitis patients. IL-22Rα was expressed in the retinal pigment epithelial cell line, ARPE-19. To examine the effect of IL-22, ARPE-19 was treated with recombinant IL-22. The proliferation of ARPE-19 and the production of monocyte chemoattractant protein (MCP)-1 from ARPE-19 were clearly elevated. IL-22 induced MCP-1 which facilitated the migration of inflammatory cells. Moreover, IL-22 increased the IL-22Rα expression in ARPE-19 through the activation of PI3K/Akt. Experimental animal models of uveitis induced by interphotoreceptor retinoid binding protein 1-20 (IRBP1-20) exhibited elevation of hyperplasia RPE and IL-22 production. When CD4+ T cells from the uveitis patients were stimulated with IRBP1-20, the production of IL-22 definitely increased. In addition, we examine the regulatory role of cysteamine, which has an anti-inflammatory role in the cornea, in uveitis through the down-regulation of IL-22Rα expression. Cysteamine eff ectively suppressed the IRBP1-20-induced IL-22Rα expression and prevented the development of IRBP1-20-induced uveitis in the experimental animal model. These finding suggest that IL-22 and its receptor have a crucial role in the development and pathogenesis of uveitis by facilitating inflammatory cell infiltration, and that cysteamine may be a useful therapeutic drug in treating uveitis by down-regulating IL-22Rα expression in RPE.

Keywords: Interleukin-22, Interphotoreceptor Retinoid Binding Protein, Experimental Autoimmune Uveitis

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Integrative Transcriptome and Secretome Analysis Developed a Prediction Model of Non-Small-Cell Lung Cancer

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Lung cancer is one of the most fatal malignancies, making screening tests needed for its early detection. In this study non-small-cell lung cancer (NSCLC), constituting 80% of all lung cancers and the remnant 20% small-cell lung cancers (SCLC), was targeted to detect serum proteins or markers in patients. First, we used 9 lung malignancy transcriptome datasets from publicly available D/B to find out differently expressed genes when compared to adjacent normal tissue, and then combined them with 6 secretome data that we prepared from purchased lung cancer cell lines to list up which proteins are secreted out of cancer cells. Secondly, with a pooled sample of human blood, we tested whether or not the candidate proteins are detected and quantified in there, and obtained 5 candidate (i.e., differently tissue-expressed, cell-secreted, and blood-detected) proteins. Finally, we compared means (medians) of the control and cancer (NSCLC) groups, resulting in BCHE (butyrylcholinesterase) and GPx3 (Glutathione peroxidase 3) selection, and made a logistic regression model in both MRM (cancer n=23, control n=23) and ELISA (cancer n=50, control n=50) measurements. The results of ROC assessment were as follows: For MRM, BCHE, GPx3 and BCHE/GPx3; AUC = 0.713, 0.673 and 0.773, respectively. For ELISA, BCHE, GPx3 and BCHE/GPx3; AUC = 0.630, 0.759 and 0.788, respectively.

Keywords: Transcriptome, Secretome, MRM, ELISA, Non-small-cell lung cancer, Blood marker

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Investigation of innate immune cells in the septic liver model using two-photon intravital microscopy

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Sepsis refers to systemic inflammatory condition caused by, for example, pathogens spreading in the blood. Sepsis shows mortality rate ranging from 30% for slight sepsis to 80% for septic shock leading to serious organ failure if not treated early. Therefore, it is expected to reduce significantly the mortality rate of sepsis if the immune responses can be controlled on time. In this study, we have developed a novel liver imaging protocol that can better detect acute inflammation using two-photon intravital microscopy. Using this two-photon intravial microscopy, we aimed to observe the activity of innate immune cells in real-time manner. Septic condition/environment was induced by intraperitoneal injection of lipopolysaccharide (LPS) to mice. Inside the septic liver, neutrophils exhibited a few distinct patterns of reactions: increase in number, reduced motility, and movement along the sinusoid to hepatic central vein. On the other hand, kupffer cells, which are resident macrophages of the liver, have little or no movement during inflammation and seem to affect the surrounding leukocytes. Since this methodology is easy to establish and can efficiently monitor the overall immune process inside the liver, it would be a useful tool to provide critical cues to unveil the possible treatment of sepsis.

Keywords: Two-photon microscopy, Sepsis, Kupffer Cell, Neutrophil, Lipopolysaccharide

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P50

Inhibitory effects of C. Tachibana leaves ethanol extract on airway inflammation

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Asthma is a chronic inflammatory disease of bronchial airway which is characterized by chronic airway inflammation, airway edema, goblet cell hyperplasia, the aberrant production of the Th2 cytokines, and eosinophil infiltration in the lungs. In the present study, the therapeutic effect and the underlying mechanism of C. Tachinaba leaves ethanol extract (CTLE) in the ovalbumin (OVA)-induced allergic asthma and compound 48/80-induces anaphylaxis were investigated. Oral administration of CTLE inhibited OVA-induced asthmatic response by reducing airway inflammation, OVA-specific IgE and IgG1 levels, and increasing OVA-specific IgG2a levels. CTLE restored Th1/Th2 balance through an increase in Th2 cytokines TNF-α, IL-4, and IL-6 and decreases in Th1 cytokines IFN-γ and IL-12. Furthermore, CTLE inhibited the total level of NF-κB and the phosphorylation of IκB-α and NF-κB by OVA. In addition, CTLE dose-dependently inhibited the compound 48/80-induced anaphylaxis via blocking histamine secretion from mast cells. The underlying mechanism of CTLE may involve to the modulation of Th1/Th2 imbalance via inhibiting the NF-κB signaling and histamine secretion. Taken together, we suggest that CTLE could be used as a therapeutic agent for patients with Th2-mediated or histamine-mediated allergic asthma.

Keywords: Airway inflammation, Airway edema, Goblet cell hyperplasia, Th2 cytokines

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P51

Anti-allergic effect of Fructus Amomi on nasal mucosa inflammation of allergic rhinitis

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Fructus Amomi Cardamomi is the mature fruit of Amomum villosum Lour of the family Zingiberaceae. It has been used in Chinese medicine for the treatment of a variety of gastrointestinal disorders, such as hyperchlorhydria, stomachache, diarrhea, abdominal distention, anorexia, gastric atony, nausea, and vomiting. However, the anti-allergic rhinitis effects of Fructus Amomi ethanol extract are less known. Allergic rhinitis was initiated in BALB/c mice by sensitized with ovalbumin (OVA) emulsified in aluminum on days 1, 8 and 15, then nasal installation challenged with OVA from days 22 to 26. Fructus Amomi (10, 20, 40 mg/kg) and Dexamethasone (1.5 mg/kg) groups were administrated by nasal installation (20μL per nasal cavity) on days 16 to 26, and from days 22 to 26, mice were received treatment 1 hour before OVA challenge. Mice of Naïve group were treated with saline and without sensitization and challenge. Then mice were evaluated for the presence of nasal mucosa inflammation, production of allergen-specific cytokine response and nasal mucosa histology. Fructus Amomi significantly ameliorated the nasal symptom and alleviated nasal mucosa inflammation. It also reduced the eosinophils, mast cells and histamine release. Meanwhile, Fructus Amomi treatment evidently decreased the high expression of Th2 cytokine, increased the Th1 and Treg cytokines in nasal lavage fluid. Fructus Amomi also reduce the both serum OVA specific IgE and anti-OVA IgG1. degranulation of rat peritoneal mast cells (RPMC) in a dose-dependent manner degranulation of rat peritoneal mast cells (RPMC) in a dose-dependent manner In this study, our data suggest that Fructus Amomi has a significant anti-allergic inflammation effect and it may proves to be an efficacious therapeutic regent on allergic rhinitis.

Keywords: Fructus Amomi, allergic rhinitis,

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P52

Improved Antitumor Activity of Trifluoperazine Derivatives in Xenograft Models of Glioblastoma Multiforme

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Recently, drug repositioning, which is a process of discovering, validating, and marketing of existing drugs to treat new diseases, has gained interests by many researchers and pharmaceutical industries. This is because drug repositioning could save time and costs in bringing new drugs to market by already proven drug's safety, efficacy and quality. Trifluoperazine (TFP), an FDA-approved antipsychotic and antiemetic drug used for treating schizophrenia. Interestingly, TFP has been recently reported to show a strong anticancer effect on lung cancer, hepatocellular carcinoma and T-cell lymphoma. In our previous study, TFP inhibited glioblastoma proliferation, migration, and invasion in vitro and in vivo. However, TFP showed no effect of increasing the survival rate in in vivo brain xenograft mouse model. Here we synthesized and screened several TFP derivatives as potential therapeutic drugs for glioblastoma treatment. Among the newly synthesized TFP derivatives, KCFC0051 showed the most improved Ca2+ increase in glioblastoma cells (34% enhancement compared to TFP), with 4-5 fold higher potency of anti-glioblastoma effect on cell viability than TFP. We further confirmed the in vivo brain xenograft mouse model, intraperitoneal injection of KCFC0051 significantly reduced the tumor size in the brain by 88%, and increased the survival time by 6 days. Our data proposes that newly constructed TFP derivatives are improved anti-glioblastoma activity better than TFP.

Keywords: Anti-tumor agent, Chemotherapy, Drug-repurposing, Glioblastoma, Trifluoperazine

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P53

Effect of an Antipsychotics on Glioma Cell Death

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Glioblastomas (GBM) are the most malignant brain tumors those originate from glial cells. The prognosis for GBM patients is very poor with a median survival less than 15 months. Patients with GBM have highly invasive brain area characteristics and, so survival rates are not high even with surgery, radiation therapy, and chemotherapy. Trifluoperazine (TFP) has been used as an antipsychotic drug and is widely used to treat schizophrenia. Recently, there have been reports that TFP exhibits anticancer effects in various types of cancers. The purpose of this study was to investigate the mechanism and effect of TFP on the GBM cell line. After TFP treatment, cell proliferation was inhibited and apoptosis-related protein expressions were changed. Also, COX-2 mRNA and protein expression were increased. In case of PPARγ, TFP treatment increased mRNA levels but not protein. Treatment with COX-2 inhibitor NS398 or PPARγ inhibitor GW9662 restored the TFP-induced inhibition of cell proliferation to a control level, respectively. In the flow cytometric analysis, TFP treatment increased the sub-G1 population, and COX-2 or PPARγ inhibitor treatment restored these phenomena. In conclusion, TFP, an antipsychotics, shows anticancer effect in GBM cell line through the activation of COX-2 and PPARγ dependent manner. This study provides that TFP can be used as a new therapeutic agent for patients with GBM.

Keywords: Glioblastoma, Trifluoperazine, Cell death, COX-2, PPARγ

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P54

Resveratrol demethylate tristetraprolin expression in lung cancer cells through suppression DNMT1

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Tristetraprolin (TTP) is an AU-rich element (ARE) binding protein in the 3'-untranslated regions and promotes the decay of target mRNAs. Downregulation of TTP expression is found with following stabilization of target mRNAs. The recent study suggests that downregulation of TTP expression in human liver cancer caused by an epigenetic mechanism. The purpose of this study is to investigate the potential of resveratrol to induce TTP expression. The expres-

sion profile and clinical importance of TTP were examined immunohistochemical analyses in normal and tumor patient samples. Promoter methylations were checked using methylation-sensitive restriction analysis and quantitative PCR, respectively. Resveratrol treatment induced TTP expression in lung cancer cells. Resveratrol also decreased the mRNA levels of TTP downstream genes. In addition, resveratrol decreased TTP promoter methylation levels at methyl site I by 30% and at methyl site III by 34%, respectively. Furthermore, resveratrol downregulated the mRNA levels and protein expression of DNMT1. Altogether, downregulation of TTP expression in lung cancer cells occurs through methylation and resveratrol may have an important role in the development of novel epigenetic therapy for the non-small cell lung cancer.

Keywords: Resveratrol, Demethylation, Tristetraprolin, Epigenetic, DNA (cytosine-5)-methyltransferase 1

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P55

O-linked-N-Acetylglucosamin Transferase enhance sCLU expression through O-GlcNAcylation of LXRs in cervical cancer cell line

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O-GlcNAcylation known as one of post-translational modifications is involved in many biological processes such as transcription and cell growth. Recently, hyper-O-GlcNAcylation has been reported in tumorigenesis and metastasis. Secretory clusterin (sCLU) is involved in cancer cell proliferation and drug resistance, and recently, liver X receptors (LXRs) and sterol response element binding protein-1 (SREBP-1) were reported to regulate sCLU transcription. However, relationship between O-GlcNAcylation and sCLU expression has not been elucidated, yet. In this study, we found that sCLU is significantly increased in cervical cancer cell lines, which have higher expression levels of O-GlcNAc and OGT than normal keratinocytes. OGT knockdown decreased expression of LXRs, SREBP-1, and sCLU through hypo-O-GlcNAcylation of LXRs; additionally, Thiamet G-induced O-GlcNAcylation enhanced sCLU expression. Treatment with thiamet G, O-GlcNAcase inhibitor, increased expression of O-GlcNAcylation and sCLU in HeLa cells, and HeLa cells exposed to high glucose concentrations had increased levels of LXRs, SREBP-1, and sCLU than cells grown in low glucose conditions. Moreover, OGT knockdown induced G0/G1 phase cell cycle arrest and late apoptosis in cisplatin-treated HeLa cells. Taken together, our study suggests that hyper O-GlcNAcylation enhances sCLU expression and the enhanced levels of sCLU may contribute to the drug-resistance and metastasis in cervical cancer.

Keywords: O-GlcNAcylation, OGT, LXRs, SREBP-1, Cisplatin

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P56

RPS27a enhances EBV-encoded LMP1-mediated proliferation and invasion by stabilizing of LMP1

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Epstein-Barr virus (EBV)-encoded latent membrane protein 1 (LMP1) is an oncoviral protein that plays a pivotal role in EBV-induced oncogenic transformation. The function of LMP1 in EBV-induced oncogenesis has been well studied. However, the molecular mechanisms underlying LMP1 protein stability remain poorly understood. In this study, we found that ribosomal protein s27a (RPS27a) regulates LMP1 stability by a tandem affinity purification analysis. RPS27a interacts directly with LMP1 in vitro and in vivo. Furthermore, overexpression of RPS27a increases the half-life of LMP1 in 293T cells, whereas downregulation of RPS27a using lentiviral shRNA technology accelerates the decrease in LMP1 protein level in EBV-transformed B cells. We show that LMP1 ubiquitination via the proteasome is completely inhibited by overexpression of RPS27a. RPS27a also enhances LMP1-mediated proliferation and

invasion, suggesting that RPS27a interacts with LMP1 and stabilizes it by suppressing proteasome-mediated ubiquitination. These results suggest that RSP27a could be a potential target in EBV-infected LMP1-positive cancer cells.

Keywords: EBV, LMP1, RPS27a, Proteasome, Ubiquitination

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P57

Regulation of MLKL on gastric cancer cells through EBV-miR-BART 18-3p

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Gastric carcinoma is one of the most common carcinoma and the third most lethal malignancy in Korea. The Cancer Genome Atlas(TCGA) Network suggested a molecular classification gastric cancer into four subgroups. Epstein-Barr virus (EBV), as well as Helicobacter pylori, has been admitted as an infective agent causing gastric carcinoma(GC). EBV encodes multiple non-coding RNAs during all types of latency, 44 mature miRNAs have been identified. EBV-encoded microRNAs showed that these small molecules function as post-transcriptional gene regulators and may play a role in the carcinogenesis process. MiR-BARTs regulate cellular genes mainly for preventing apoptosis and escaping the host immune system. Although the crucial roles of anti-apoptosis in EBV infection cells have previously been reported, few studies about the necroptosis, another cell death pathway in EBV infected host cells has been reported. We examine the relationship between microRNAs and necroptosis in EBV positive/negative gastric cancer cells. Incubation with EBV particles and exosome purified from EBV positive cells reveal that MLKL as a regulator of necroptosis were decreased in EBV negative gastric cells. EBV infection resulted in alteration of cellular and viral miRNA. We selected EBV-miR-BART18-3p(BART18-3p) as a possible regulator of MLKL, because BART18-3p was highly expressed in EBV positive cells and sequence of BART18-3p was match to MLKL. Unexpectedly, mimics for BART18-3p increased MLKL in EBV negative KATOIII, but inhibitor for BART18-3p decreased in EBV positive SNU719. Taken together, we suggested that EBV infection resulted in escaping from necroptosis of host cells against virus. BART18-3p seems not to be involved in direct regulation of MLKL, but reverse effect through other regulators of MLKL. For solving the discrepancy, further studies will be needed. Thus, our study might suggest novel mechanistic insights into the role of EBV-related miRNA in programmed cell death on gastric cancer.

Keywords: EBV,BART18-3p,Necroptosis,MLKL

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P58

Epstein-Barr virus-encoded latent membrane protein 1 induces epithelial to mesenchymal transition by inducing V-set Ig domain containing 4 (VSIG4) expression via NF-kB in renal tubular epithelial HK-2 cells

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The epithelial to mesenchymal transition (EMT), a hallmark of chronic kidney disease, is a key event in the conversion from tubular epithelial cells to myofibroblasts in renal fibrosis. Epstein-Barr virus (EBV) is a γ-herpes oncovirus associated with chronic kidney disease. However, the relationship between EBV and the EMT process in renal tubular epithelial cells is not well understood. Among EBV-latent genes, EBV-encoded latent membrane protein 1 (LMP1) induces EMT by regulating a variety of molecules in EBV-induced oncogenic transformation. In this study, we investigated EBV-encoded LMP1 and EMT process markers in human proximal tubule epithelial cell line HK-2. LMP1 overexpression induces cell morphological changes via the epithelial to mesenchymal process in HK-2 cells, and these changes accelerate cell proliferation, cell motility, and invasion. Furthermore, VSIG4 upregulation by EBV-LMP1 induced LMP1-mediated EMT, cell motility, and invasion. VSIG4

upregulation by LMP1 was regulated at the transcriptional level via the NF-kB signaling axis. These results suggest that EBV-encoded LMP1 regulates EMT through the NF-kB-VSIG4 axis in HK-2 cells, and VSIG4 is a potential target in EBV-induced chronic kidney diseases.

Keywords: EBV, LMP1, NF-kB, VSIG4, EMT

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The Roles and Expression of MED30 in Hepatocellular Carcinoma Cells

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Hepatocellular carcinoma (HCC) is the secondleading cause of death in the world. Also, its late diagnosis andchemoresistance increase death rate. Hence, it is necessary to find newdiagnostic and therapeutic targets in HCC. MED30 is one of the Mediator complexsubunits, which connects between the Mediator complex and RNA Polymerase II.However, the expression and functions of MED30 in cancer have been rarelyunderstood. Therefore, we tried to figure out the expression and functions ofMED30 in HCC. The analysis of TCGA database showed MED30 was frequentlyamplified in HCC. Moreover, immunohistochemistry also showed its overexpressionin HCC tissues compared to the surrounding normal liver tissue. To examineroles of MED30, we knock-downed MED30 in several HCC cell lines using siRNA.MED30 Knock-down decreased proliferation and tumorigenicity in soft agar assayin Hep3B, HepG2 and SK-Hep1 cells, and decreased migration rate in SK-Hep1cells. For gain-of-function study, we overexpressed MED30 in SK-Hep1 and HepG2cells using cDNA and its overexpression showed increased proliferation ofSK-Hep1 and migration of HepG2 cells. Also, the overexpression of MED30increased the tumorigenicity in vitro and in vivo. However, MED30overexpression decreased proliferation in HepG2 cells and migration in SK-Hep1cells. These results suggest MED30 is involved in the tumorigenicity in HCCcell lines and further studies need to be done for the discovery of mechanism.

Keywords: Cancer Hepatocellularcarcinoma Liver Mediatorcomplex

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P60

APX-115A, a pan-NADPH oxidase inhibitor, induces caspase-dependent apoptosis by suppressing NOX4-ROS signaling in EBV-infected ARPE-19 cells

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Bacground: Epstein-Barr virus is a g-herpes virus that infects primary B cells and can transform infected cells into immortalized lymphoblastoid cell lines (LCL). The role of EBV in malignancies such as Burkitt's lymphoma and nasopharyngeal carcinoma is well understood, however, its role in EBV-infected retinal cells remains poorly understood. Therefore, we investigated the effect of EBV on the growth of retinal cells.
Methods: Previously, we established and reported a cell line model to address the relationship between EBV infection and retinal cell proliferation that used adult retinal pigment epithelium (ARPE-19) and EBV infection. To determine the effect of EBV on ARPE-19 cells, cell death was measured by propidium iodine/annexin V staining and reactive oxygen species (ROS) were measured by FACS, and protein expression was evaluated using western blot analysis. Also, downregulation of LMP1 and NADPH oxidase 4 (NOX4) expression was accomplished using siRNA technology.
Results: We found that ROS were dramatically increased in EBV-infected ARPE19 cells (APRE19/EBV) relative to the parental cell line. Additionally, the expression level of NOX4, a main source of ROS, was upregulated by EBV infection. Interestingly, downregulation of LMP1, one of the EBV viral onco-proteins, completely decreased EBV-induced ROS accumulation and the upregulation of NOX4. Treatment with APX-115A, a pan-NOX inhibitor, induced apoptotic cell death of only the EBV-infected ARPE19 cells but

not the parental cell line. Pretreatment with z-VAD, a pan-caspase inhibitor, inhibited NOX inhibitor-induced cell death in ARPE19/EBV cells. Furthermore, APX-115A-induced cell death mediated the activation of JNK and ERK.

Conclusion: Taken together, these our results suggest that APX-115A could be a therapeutic agent for treating EBV-infected retinal cells or diseases by inhibiting LMP1-NOX4-ROS signaling.

Keywords: EBV, ROS, LMP1, NOX4, NOX inhibitor

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P61

MED30 Regulates the Proliferation and Motility of Cholangiocarcinoma Cells

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MED30 is component of the Mediator complex, which is a co-activator involved in the regulated transcription of nearly all RNA polymerase II-dependent genes. However, the functional roles of MED30 in cholangiocarcinoma (CCA) have not been determined. We investigated the expression and roles of MED30 during the proliferation, migration, and invasion of CCA cells. MED30 knock-down using specific siRNAs decreased CCA cell proliferation, migration, and invasion, whereas MED30 overexpression promoted all three characteristics. Taken together, these results show MED30 promotes CCA cell proliferation, migration, and invasion, and present MED30 as a potential target for the treatment of CCA.

Keywords: MED30 cholangiocarcinoma

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P62

Intravital imaging set up of lung in mice to directly observe motility and morphology of leukocytes and in real-time manner

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Lung is a critical organ that manages exchanges of oxygen and carbon dioxide in blood stream. Due to lung's direct contact with air, this organ inevitably confronts many pathogens, ranging from dust to virus. Although many respiratory diseases have been consistently studied over the past decade, only a few in vivo imaging studies were conducted because of lung's complex structure and friability. In this research, we designed a unique vacuum chamber for two-photon intravital microscopy with water-dipping lens. The two major obstacles of this project were to maintain mouse alive with open thoracic cavity and to keep appropriate amount of water on the vacuum window while lung was continuously suctioned during entire imaging procedure. With this methodology, inner anatomy of the lung - alveoli, capillaries, and leukocytes - was successfully monitored in real-time manner for more than 1 hour during inflammation. In summary, this technique can be applied for various lung-respiratory related studies to observe the adjustment of leukocytes and change of the pulmonary capillaries in vivo. So I Jeong*a, Sang A Park*a *These authors contributed equally

Keywords: Intravital imaging, Two-photon microscopy, Lung, Neutrophil, Inflammation

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P63

The Transient Intermediate Plexiform Layer, A Plexiform Layer-ike Structure Temporarily Existing in the Inner Nuclear Layer During Retinal Development

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The retina is a highly specialised part of the brain responsible for visual processing. It is well-laminated; three layers containing five different types of neurons are compartmentalised by two synaptic layers. Among the retinal layers, the inner nuclear layer (INL) is composed of horizontal, bipolar, and amacrine cell types. Bipolar cells form one sublayer in the distal half of the IPL, while amacrine cells form another sublayer in the proximal half, without any border-like structure. Here, we report that a plexiform layer-like structure exists temporarily in the border between the bipolar and amacrine sublayers in the INL in the rat retina during retinal development. This transient intermediate plexiform layer (TIPL) appeared at post-natal day (PD) 7 and then disappeared around PD 12. Most apoptotic cells in the INL were found near the TIPL. These results suggest that the TIPL may contribute to the formation of sublayers and the cell number limit in the INL.

Keywords: Apoptosis, Development, Positioning, Retina

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P64

Effects of cilostazol pre-treatment on neuroprotection in kainic acid-induced hippocampal cell death

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Cilostazol is a selective inhibitor of type 3 phosphodiesterase (PDE3) and has been widely used as an antiplatelet agent. Cilostazol mediates this activity through effects on the cyclic adenosine monophosphate (cAMP) signaling cascade. Recently, it has attracted attention as a neuroprotective agent. However, little is known about cilostazol's effect on excitotoxicity induced neuronal cell death. Therefore, this study evaluated the neuroprotective effect of cilostazol treatment against hippocampal neuronal damage in a mouse model of kainic acid (KA)-induced neuronal loss. Cilostazol pre-treatment reduced KA-induced seizure scores and hippocampal neuron death. In addition, cilostazol pre-treatment increased cAMP response element-binding protein (CREB) phosphorylation and decreased neuroinflammation. These observations suggest that cilostazol may have beneficial therapeutic effects on seizure activity and other neurological diseases associated with excitotoxicity.

Keywords: cilostazol; hippocampus; kainic acid; neuronal death; neuroinflammation

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Down-regulation of Cdk5 by Ischemic Preconditioning Attenuates p53-dependent Apoptosis of Hippocampal CA1 Pyramidal Neurons Following a Subsequent Transient Cerebral Ischemia

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Deregulation of cyclin-dependent kinase 5 (Cdk5) is related to pathological conditions. Ischemic preconditioning (IPC) provides neuroprotective effects against subsequent ischemic insults. We examined effects of IPC (2-min transient cerebral ischemia) on expressions of molecules related with Cdk5 in the hippocampus following 5-min subsequent transient cerebral ischemia (TCI) in gerbils grouped into sham-operated, TCI-operated, IPC-treated and

sham-operated, IPC-treated and TCI-operated, roscovitine (inhibitor of Cdks)-treated and sham-operated, and roscovitine-treated and TCI-operated groups. Pyramidal neurons in the hippocampal CA1 area were dead at 5 days post-TCI; however, IPC and roscovitine treatment protected the neurons from TCI. In the TCI-operated group, Cdk5 and phospho (p)-p53 expressions were shown only in nuclei of pyramidal neurons 1 and 2 days after TCI. In addition, expression of p25 increased in the nuclei 1 and 2 days after TCI. However, IPC and/or roscovitine treatment decreased Cdk5, p25 and p-p53 expressions in pyramidal neurons following TCI, in particular, Cdk5 and p-p53 immunoreactivities in their nuclei decreased. Furthermore, TUNEL-positive pyramidal neurons were detected 5 days after TCI with increases of Bax, PUMA and activated caspase-3 expressions, and TUNEL-positive cells and the increased molecules were cut off by IPC and roscovitine treatment. Briefly, IPC protected CA1 pyramidal neurons from TCI through down-regulation of Cdk5, p25 and p-p53, and the down-regulation of Cdk5 by IPC might be a key factor in attenuation ofp53-dependent apoptosis in CA1 pyramidal neurons after TCI. Thus, we suggest that inhibition of Cdk5 translocation into neuronal nuclei is critical in neuroprotection against ischemic insults.

Keywords: Ischemic tolerance, Delayed Neuronal Death, Cyclin-dependent kinase 5, p53, TUNEL

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Effects of TonEBP Haplodeficiency on hippocampal inflammation in diabetic mice

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Neuroinflammation in the adult hippocampus may contribute to major riskfactor of diabetes mellitus. Recent studies have reported that overexpressionof tonicity-responsive enhancer binding protein (TonEBP) is associated withmany inflammatory diseases. However, the exact mechanism in diabeticneuroinflammation is unknown. Here we report that haplodeficiency of TonEBPinhibits hepatic and hippocampal high-mobility group box-1 (HMGB-1) in diabetic-mice. The Male C57BL/6 TonEBP (+/+) and TonEBP heterozygote (+/-) mice fed witha high-fat diet (HFD) for 16 weeks and received 100 mg/kg of streptozotocin(STZ) injected intraperitoneally. After 4 weeks, mice developed hyperglycemiaand hepatic steatosis in HFD/STZ-induced diabetic mice. Diabetic TonEBP(+/-)mice showed decrease in body weight, fat mass, hepatic steatosis, andmacrophage infiltration compared to diabetic TonEBP (+/+) mice. We found thatTonEBP increases adipogenesis and HMGB1 expression in the liver ofHFD/STZ-induced diabetic mice. In the hippocampus, nuclear TonEBP and HMGB1expression in TonEBP (+/-) mice was decreased compared to those in HFD/STZ-treatedTonEBP (+/+) mice. Immunoreactivity of iba-1 in the hippocampus was alsodecreased in HFD/STZ-treated TonEBP (+/-) mice compared to TonEBP (+/+) mice.Our findings suggest that TonEBP is required for the prevention of theprogression of diabetes-associated hepatic steatosis and neuroinflammation.

Keywords: Type 2 diabetes mellitus; TonEBP; HMGB1, Neuroinflammation

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P67

Infliximab regulates the expression of cytokines and inhibits cell death in astrocytes through NF-κB signaling in in vitro inflammatory condition

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Neuroinflammation is a key in the onset and development of neurological diseases such as Alzheimer's disease and Parkinson's disease. In neuroinflammatory process, astrocyte has been considered as an important inflammatory regulator in CNS, in that they could secrete diverse inflammatory factors, and control homeostasis and support neuronal cell survival. The study on astrocyte's role in oxidative stress is necessary to treat neuropathogenesis and to understand the mechanisms in neuroinflammatory diseases. Infliximab as a TNF-α antagonist is commonly used as a medicine in Crohn's disease. Recently, its anti-inflammatory role has been highlighted in CNS, but its specific mechanisms was not fully understood until now. In present study, we investigate whether infliximab control the secretion of cytokines and ER stress response and cell death signaling in C8D1A astrocytes against in vitro inflammatory condition. We performed western blotting, reverse transcription PCR, and immunocytochemistry to check diverse factors. Our protein data and mRNA data showed that infliximab attenuates the expression of pro-inflammatory cytokines and inhibits ER stress induced cell death through NF-κB signaling. Taken together, we suggest that infliximab is a promising medicine for alleviating neuroinflammation by suppressing ER stress and cell death signaling in astrocytes.

Keywords: Infliximab, Astrocytes, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), Endoplasmic reticulum (ER) stress

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Effects of myeloid SIRT1 deficiency on neuroinflammation in chronic high-fat diet-fed mice

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Obesity-induced peripheral inflammation is associated with hippocampal inflammation. Sirtuin 1 (SIRT1) regulates cellular metabolism and inflammatory response. Nuclear factor kappa B (NF-κB)-mediated inflammation contributes to the development of insulin resistance and diabetes, however, the myeloid-specific SIRT1 function in the context of neuroinflammation is largely unknown. Myeloid-specific SIRT1 knockout (KO) mice were fed a high-fat diet (HFD) or normal diet (ND) for 40 weeks. HFD-fed SIRT1 KO mice had an increase in hepatic inflammation and macrophage infiltration of adipocytes compared to HFD-fed wild type (WT) mice. Hippocampal expression levels of acetylated NF-κB were increased in KO mice compared to WT mice. In particular, HFD-induced lipocalin-2 was increased in liver, adipose tissue, and hippocampus of WT mice. However, their expressions were decreased in HFD-fed KO mice compared to HFD-fed WT mice. SIRT1 deletion increased hippocampal iba1 and amyloid precursor protein expression in HFD-fed mice. These results suggest that myeloid-specific SIRT1 deletion may contribute to the reduced secretion or production of lipocalin-2 and lead to suppression of anti-inflammatory responses against HFD-induced obesity.

Keywords: obesity; SIRT1; lipocalin-2; hippocampus; inflammation

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Long-term Treadmill Exercise Improves Memory Impairment through Restoration of Decreased SynapticAdhesion Molecule 1/2/3 Induced by Transient Cerebral Ischemia in the Aged Gerbil Hippocampus

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Exercise improves cognitive impairments induced by transient cerebral ischemia and modulates synaptic adhesion molecules. In this study, we investigated effects of long-term treadmill exercise on cognitive impairments and its relation to changes of synaptic cell adhesion molecule (SynCAM) 1/2/3 in the hippocampus after 5 min of transient cerebral ischemia in aged gerbils. Animals were assigned to sedentary and exercised groups, given treadmill exercise for 4 consecutive weeks from 5 days after transient ischemia and evaluated cognitive function through passive avoidance test and Morris water maze test. SynCAM 2 protein levels were determined in the hippocampus by western blot. In addition, neuronal and synaptic changes were examined by NeuN immunohistochemistry, and SynCAM 1/2/3 and MAP2 double immunofluorescence, respectively. We found that transient cerebral ischemia led to neuronal death in the CA1 area and dentate gyrus, and impaired conflictive function; however, treadmill exercise improved ischemia-induced memory impairment. In addition, SynCAM 1/2/3 expression in the hippocampus was significantly decreased in the sedentary group after transient cerebral ischemia; however, SynCAM 2 protein level was significantly increased in the ischemic group with exercise. These results suggest that long-term treadmill exercise improves memory impairment through the restoration of decreased SynCAM 1/2/3 expression in the hippocampus induced by transient cerebral ischemia in the aged gerbil.

Keywords: Cerebral ischemia; Learning and memory; Rehabilitation; Synaptic adhesion molecules; Treadmill exercise

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Reexamination of Dopaminergic Amacrine Cells in the Rabbit Retina: Confocal Analysis with Double- and Triple-Labeling Immunohistochemistry

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Dopaminergic amacrine cells (DACs) are among the most well-characterized neurons in the mammalian retina, and their connections to AII amacrine cells have been described in detail. However, the stratification of DAC dendrites differs based on their location in the inner plexiform layer (IPL), raising the question of whether all AII lobules are modulated by dopamine release from DACs. The present study aimed to clarify the relationship between DACs and AII amacrine cells, and to further elucidate the role of dopamine at synapses with AII amacrine cell. Whole-mount preparations of rabbit retinas were double- and triple-labeled with antibodies against tyrosine hydroxylase (a DAC marker), calretinin (an AII amacrine cell marker), and vesicular glutamate transporter 1 (a bipolar axon terminal marker). DAC dendrites were observed in strata 1, 3, and 5 of the IPL. In stratum 1, most DAC dendritic varicosities—the presumed sites of neurotransmitter release—made contact with the somata and lobular appendages of AII amacrine cells. In addition, some varicosities in strata 3 and 5 contacted the arboreal dendrites of AII amacrine cells. However, most lobular appendages of AII amacrine cells localized within stratum 2 of the IPL exhibited little contact with DAC varicosities. In addition, double- or triple-labeling experiments revealed that DACs did not express the GABAergic neuronal markers anti-GABA, vesicular GABA transporter, or glutamic acid decarboxylase. These findings suggest that the lobular appendages of AII amacrine cells are involved in at least two different circuits. We speculate that the circuit associated with stratum 1 of the IPL is modulated by DACs, while that associated with stratum 2 is modulated by unknown amacrine cells expressing a different neuroactive substance. Our findings further indicate that DACs in the rabbit retina do not use GABA as a neurotransmitter, in contrast to those in other mammals.

Keywords: Dopamine, AII amacrine cell, Scotopic pathway, GABA, Retinal circuit

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Evaluation of the Protective Effect of Shuanghe-tang Based on Dongeuibogam Analysis using Ischemic Stroke Mice Model

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Ethnopharmacological relevance: Stroke is one of major causes of death and long-term disability, but stroke is not completely treated. In Dongeuibogam, an ancient literature on Korean medicine, many medicinal herbs and formulas were used to treat the symptoms related with stroke.

Aim of study: In this study, we screened out candidate medicinal herbs from Pung chapter in Dongeuibogam through text-mining. We evaluated the protective effect of candidate herbs on ischemic stroke using cerebral ischemic mouse model.

Materials and Methods: Focal cerebral ischemia was induced by photothrombotic cortical ischemia. Twenty nine herbs were chosen from Dongeuibogam through text-mining analysis for treatment of stroke. Mice (C57BL/6 male, 6w) were orally administered each herb extracts for 3 days before ischemic injury. Extracts of Shuanghe-tang or Zengsunsiwu-tang were orally offered once a day for 5 days. Infarct volume, brain edema, neurological deficits, rota-rod, wire-grip and Evans blue leakage were evaluated at 24 h after ischemic injury. Immunofluorescence staining for tight junction proteins was performed in brain tissues after ischemic injury.

Results: We chose 5 candidate herbs among 29 herbs, which reduced the infarct and edema volume and improved the rota-rod performance after ischemic brain injury. We selected two prescriptions, Shuanghe-tang and Zengsunsiwu-tang, which consist of more than 60 % of 5 candidate herbs as main components. Pretreatment of Shuanghe-tang significantly reduced infarct volume and edema and improved neurological and motor functions, but Zengsunsiwu-tang did not. In addition, Shuanghe-tang dose-dependently (30, 100, and 300 mg/kg) decreased brain infarct and edema, and recovered neurological deficit. Shuanghe-tang pretreatment significantly decreased blood-brain barrier (BBB) breakdown as measured by Evans blue leakage even after focal cerebral ischemia. Immunohistochemical analysis reveals that ZO-1 and occludin expression in ipsilateral site were significantly increased in Shuanghe-tang pretreated mice. Ischemia-induced aquaporin (AQP)-4, a water channel protein, was down-regulated, whereas pretreated mice were improved AQP-4 expression.

Conclusions: These results indicate that Shuanghe-tang identified by text-mining technique has the protective effects on ischemic brain injury, and suggest the possible application for potential stroke patients especially in elder person. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (2014R1A5A2009936).

Keywords: Stroke, Dongeuibogam, Text-mining, Medicinal herb

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Assessment of High-fat Diet-induced Alzheimer's Disease in Outbred Mice Using Touchscreen Operant Platform

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Studies show that beta amyloid aggregation at any stage is insufficient to develop a sporadic Alzheimer's disease (AD) which accounts for more than 85% of all type of AD. Recent studies also show that sporadic AD arises from dysregulation of brain glucose metabolism that the amyloid hypothesis does not explain and that it occurs before amyloid plaques accumulates in the brain. In our previous results, mice were fed on 60% high-fat diet (HFD) for 24 weeks and subjected to dynamic nuclear polarization-enhanced hyperpolarized 13C magnetic resonance spectroscopic imaging (DNP-MRSI). Abnormal pyruvate-lactate conversion was observed in the medial

temporal lobe of high-fat diet-fed mice. Accumulation of beta amyloid was confirmed in CA1 and DG through immunohistochemistry . These results demonstrate that HFD-induced metabolic stress plays pivotal role of AD-like pathogenesis. Although many pathological states are now detectable through imaging and biochemical analyses, neuropsychological tests are still widely used to confirm the diagnosis, especially for AD and schizophrenia. The touchscreen-based automated battery system, which is more accurate and less invasive than conventional behavior test tools, is used to assess cognition of the mouse with dysregulated metabolism. This system was introduced in humans to evaluate cognitive function and recently back-translated in monkeys and rodents. We used outbred ICR mice fed on HFD and conducted the paired associates learning (PAL) test to detect their visual memory and new learning ability loss and to diagnose metabolic Alzheimer's disease. Also, the Fixed Ratio (FR) test was conducted before PAL to examine mice's motivation towards the task. We found how dysregulation of metabolism by consuming excessive fats affects the mice's motivation, learning ability and visual memory function. This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HI14C2173)

Keywords: Touchscreen, Animal Behavior, Learning and Memory, Alzheimer's Disease, Brain Metabolism

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Osteopontin Peptide Icosamer Containing RGD and SLAYGLR Motifs Enhances The Mmotility and Phagocytic Activity of Microglia

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Osteopontin (OPN) is a secreted glycoprotein that is expressed in various tissues, including brain, and mediates a wide range of cellular activities. In a previous study, theauthors observed the robust neuroprotective effects of recombinant OPN and of RGD and SLAYGLR-containing OPN-peptide icosamer (OPNpt20) in an animal model oftransient focal ischemia, and demonstrated anti-inflammatory and pro-angiogenic effects of OPNpt20 in the postischemic brain. In the present study, we investigated the effects of OPNpt20 on the motility and phagocytic activity of BV2 cells (a microglia cell line). F-actin polymerization and cell motility were significantly enhanced in OPNpt20-treated BV2 cells, and numbers of filopodia-like processes increased and lamellipodia-like structures enlarged and thickened. In addition, treatment of cells with either of three mutant OPN icosamers containing mutation within RGD, SLAY, or RGDSLAY showed that the RGD and SLAY motifs of OPNpt20 play critical roles in the enhancement of cell motility, and the interaction between exogenous OPNpt20 and endogenous αv and α4 integrin and the activations of FAK, Erk, and Akt signaling pathways were found to be involved in the OPNpt20-mediated induction of cell motility. Furthermore, phagocytic activity of microglia was also significantly enhanced by OPNpt20 in a RGD and SLAY dependent manner. These results indicate OPNpt20 containing RGD and SLAY motifs triggers microglial motility and phagocytic activity and OPNpt20-integrin mediated signaling plays a critical role in these activities.

Keywords: Osteopontin Cell motility RGD and SLAY motif OPNpt20

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Tat-protein Disulfide-isomerase A3: A Possible Candidate for Preventing Ischemic Damage in the Spinal Cord

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In the present study, we searched for possible candidates that can prevent ischemic damage in the rabbit spinal cord. For this study, we used two-dimensional gel electrophoresis followed by matrix-

assisted laser desorption/ionization time-of-flight mass spectrometry, in sham- and ischemia-operated animals. Since the level of protein disulfide-isomerase A3 (PDIA3) significantly decreased 3 h after ischemia/reperfusion, we further investigated its possible role against ischemic damage using an in vitro spinal cord cell line and in vivo spinal cord ischemic model. The administration of Tat-PDIA3 significantly reduced the hydrogen peroxide-induced formation of reactive oxygen species and cell death, based on terminal deoxynucleotidyl transferase-mediated biotinylated dUTP nick end labelling and a colorimetric WST-1 assay. Further, Tat-PDIA3 significantly ameliorated the ischemia-induced deficits in motor function, based on Tarlov's criteria, 24–72 h after ischemia/reperfusion, as well as the degeneration of motor neurons in the ventral horn 72 h after ischemia/reperfusion. Tat-PDIA3 administration also reduced the ischemia-induced activation of microglia and lipid peroxidation in the motor neurons 72 h after ischemia/reperfusion. PDIA3 also potentially ameliorated the ischemia-induced increase in oxidative markers in serum and decreased the activity of Cu,Zn-superoxide dismutase, Mn-superoxide dismutase, and glutathione peroxidase in spinal cord homogenates, 24 h and 72 h after ischemia/reperfusion. These results suggest that Tat-PDIA3 could be used to protect spinal cord neurons from ischemic damage, due to its modulatory action on the oxidative/anti-oxidative balance. Tat-PDIA3 could be applicable to protects neurons from the ischemic damage induced by thoracoabdominal aorta obstruction.

Keywords: Protein Disulfide-isomerase A3; Spinal Cord Ischemia; Oxidative Stress; Tat Peptide; Antioxidants

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Role of phosphatidylethanolamine-binding protein 1 in the hippocampus after transient forebrain ischemia in Mongolian gerbil: its potential roles for neuroprotective agents for ischemic brain damage

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In the present study, we investigated the temporal and spatial changes of phosphatidylethanolamine-binding protein 1 (PEBP1) in the hippocampus after 5 min of transient forebrain ischemia in gerbils. In addition, we also observed the effects of PEBP1 against H2O2 damage in the HT22 hippocampal cell lines and ischemic damage in the Mongolian gerbils. In the sham-operated animals, weak PEBP1 immunoreactivity was found in the hippocampal CA3 region, not in the CA1 region and dentate gyrus. PEBP1 immunoreactivity was significantly and transiently increased in the hippocampal CA1 region at 1 day after ischemia compared to that in the sham-operated group. PEBP1 immunoreactivity was decreased 2 days after ischemia. Western blot analysis showed that PEBP1 significantly increased in the hippocampal homogenates at 1 day after ischemia. To elucidate the effects of PEBP1, we made a PEP1-PEBP1 fusion protein, which facilitates the transducing PEBP1 into cells. We observed significant ameliorative effects of PEP1-PEBP1 against H2O2-induced neuronal damage and reactive oxygen species formation in the HT22 hippocampal cells. In addition, administration of PEP1-PEBP1 fusion protein significantly reduced the ischemia-induced hyperactivity of locomotion 1 day after ischemia and PEP1-PEBP1 reduced neuronal damage and reactive gliosis (astrocytosis and microgliosis) in the gerbil hippocampal CA1 region 4 days after ischemia. Administration of PEP1-PEBP1 fusion protein significantly reduced the ischemia-induced increases in pro-inflammatory cytokines such as interleukin-1β and tumor necrosis factor-α, and ameliorated the ischemia-induced increases of phosphorylation of extracellular signal-regulated kinases (ERK1/2) and c-jun N-terminal kinases (JNK1/2) in ischemic hippocampus at 1 and 4 days after ischemia. These results suggest that the reduction of PEBP1 and increase of PEBP1 phosphorylation causes neuronal damage in the hippocampus and the treatment with PEP1-PEBP1 fusion protein affords neuroprotection from ischemic damage decreasing phosphorylation of ERK1/2 and JNK1/2 as well as the decreasing the inflammatory responses induced by transient forebrain ischemia in the gerbil hippocampus.

Keywords: Phosphatidylethanolamine-binding protein 1; Hippocampus; Gerbil; Oxidative stress; MAPK

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Postnatal Changes Of Constitutively Expressed Cyclooxygenase-2 In The Hippocampus And Its Function To Synaptic Plasticity

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Cyclooxygenase-2 (COX-2) expression is closely correlated with inflammation in the brain. However, COX-2 is constitutively expressed in the brain and its expression is regulated by synaptic activity. In the present study, we investigated the postnatal expression of COX-2 in the hippocampus at postnatal days (P) 1, 7, 14, 28, and 56. In addition, we also observed the effects of COX-2 on the synaptic plasticity with Arc immunohistochemistry using COX-2 knockout and its wild-type mice. Very weak COX-2 immunoreactivity was detectable in hippocampal CA1-3 as well as the dentate gyrus at P1. At P7, COX-2 immunoreactivity was detected in the stratum pyramidale of the CA1-3 regions and the outer granule cell layer of the dentate gyrus. At P14, peak COX-2 immunoreactivity was observed in all hippocampal subregions including the dentate gyrus. At P28, COX-2 immunoreactivity was significantly decreased in these regions. At P56, the COX-2 immunoreactivity and distribution pattern were similar in hippocampal CA1-3 to those observed at P28. However, in the dentate gyrus, COX-2 immunoreactivity was found in the inner half of the granule cell layer. Western blot analysis showed that COX-2 protein levels peaked at P14 and decreased by P28 and P56. Arc immunoreactivity was found in the granule cell layer of dentate gyrus, but Arc immunoreactivity was significantly decreased in the dentate gyrus of COX-2 knockout mice compared to that in the wild-type mice. These results suggest that COX-2 plays an important role in synaptic plasticity in the hippocampus and changes in the levels of constitutively expressed COX-2 may be associated with postnatal development of the hippocampus.

Keywords: Cyclooxygenase-2; Postnatal development; Synaptic plasticity; Hippocampus; Mice

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Light-Emitting Diode Treatment Ameliorates Amyloid Pathology in the 5XFAD Mouse Model of Alzheimer's Disease

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Backgroud: Low-level light emitting diode therapy (LED-T) can be rapidly applied in a safe and non-invasive way, acting on various pathways. This treatment is effective for chronic disease because it has fewer side effects than drugs. In this study, we aimed to investigate the effects of LED-T on activating cognitive neural network and inhibiting neuronal cell death to prevent cognitive impairment and dementia, and optimal timing of LED-T initiation for functional recovery.
Method: LLLT was applied by placing the skin-adhesive light-emitting probes onto the skin at two locations on the head (the right midpoint of the parietal bone and the posterior midline of the seventh cervical vertebra). Experimental groups receiving treatment are divided into early-treat group and late-treat group according to the time of starting LED-T [3 month (early group) or 6 month (late group)], and the mice of each groups received LED-T 3 times a week for 14 weeks, 20 minutes per session. Morris Water Maze, passive avoidance test, and elevated plus maze were evaluated at 10 month of age.
Result: Early-treat group but not late-treat group showed improved learning and memory, and reduced anxiety compared to the light-untreated group. Consistent with the behavioral results, amyloid

plaque load was significantly decreased in the cortex, hippocampus and corpus callosum of early LED-T group, but not late LED-T group.

Conclusion: LED-T reduced the amyloid plaque in the 5XFAD mouse and alleviated the behavioral characteristics of Alzheimer's disease. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2016R1A2B2007862).

Keywords: Light-Emitting Diode Treatment LLLT Alzheimer's Disease Amyloid Beta Plaque

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P78

Indoleamine 2,3-dioxygenase-dependent Kynurenic Metabolites Induces Depressive-like Behavior in Mouse Model of Post-Stroke Depression

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Background: The development of depression after stroke is clinically important because post-stroke depression is associated with increased mortality, slows recovery and leads worse functional outcomes. In addition, the underlying pathophysiological mechanisms remain inadequately understood. Here, we investigated the neurobiology of post-stroke depression (PSD) and the beneficial effects of an atypical antipsychotic drug, Aripiprazole (APZ) using a mouse model of PSD.

Methods: PSD was induced a combination of the middle cerebral artery occlusion (MCAO) and restraint stress. Behavioral tests to measure the degree of PSD-like behavior such as sucrose preference test, forced-swim test and Morris water maze test were performed at 8, 10 and 12 weeks after modeling.

Results: PSD mice showed significant depressive behaviors in sucrose preference test, forced-swim test and Morris water maze test. In immunohistochemistry analysis, significant increases in the expression of indoleamine 2,3-dioxygenase (IDO) were observed in the nucleus accumbus, hippocampus and hypothalamus of PSD mice, which were not seen in the striatum. In addition, these increased IDO expressions were colocalized with Iba(+) cells but not NeuN(+) and GFAP(+) cells, suggesting that IDO production by microglia was prominent in PSD mice brain. Moreover, 3-hydroxyanthranilate 3,4-dioxygenase (HAAO) and quinolinic acid (QA), which are kynurenine metabolites, were significantly increased in the nucleus accumbus, hippocampus and hypothalamus of PSD mice. Finally, treatment of APZ (1 mg/kg, po) initiated 1 day after MCAO for 2 weeks reversed the behavioral phenotype, IDO expression, IDO(+)/Iba-1(+) cells and kynurenic metabolites.

Conclusion: Our results suggests the importance of IDO-dependent neurotoxic kynurenic metabolism by microglia as a pathogenic mechanism of PSD. The beneficial effect of APZ on PSD-like behavior may be involved via inhibition of IDO-dependent kynurenic metabolites.

Keywords: Chronic Restrainment Stress, Post-Stroke Depression, Aripiprazole, Indole 2,3-dioxygenase, Kynurenic Pathway

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Ultrastructural Quantitative Analysis Of Axons Expressing Parvalbumin, Calbindin, Calretinin, Stage-Specific Embryonic Antigen-4 and RT97 In The Sensory Root Of The Rat Trigeminal Ganglion

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Parvalbumin (PV), calbindin (CB), calretinin (CR), stage-specific embryonic antigen-4 (SSEA-4) and RT 97 (phosphorylated NF200)

are commonly used as markers for neurons with A myelinated fibers or with large myelinated Aβ fibers. To study the selectivity of these markers for A myelinated neurons, we analyzed their expression in neurons and axons in the rat trigeminal ganglion by light- and electron-microscopic immunohistochemistry and quantitative analysis. Most (98.1%) of the RT97-immunopositive (+) fibers and all (100%) of the CB+, CR+ and SSEA-4+ fibers were myelinated: Each half of the PV-immunopositive (+) was small myelinated Aδ (<20 μm2 in cross-sectional area, equivalent to <5 μm in diameter) and large myelinated Aβ fibers (>20 μm2 in cross-sectional area, equivalent to <5 μm in diameter), respectively. Whereas majority of CB+ (86%) and SSEA-4+ (64%) fibers were small myelinated Aδ fibers, majority of CR+ fibers (86%) were large myelinated Aβ fibers. Majority (62%) of RT97+ fibers were myelinated, but large fraction (38%) were unmyelinated. These findings suggest that PV, CB, CR and SSEA-4 can be used as reliable markers for neurons with myelinated fibers, but not for neurons with large myelinated Aβ fibers, and question the suitability of RT97 as a marker for neurons with myelinated fibers.

Keywords: Neuronal Marker, Myelinated Fiber, Fiber Type, Ultrastructure, Trigeminal Ganglion

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P80

Blocking the phosphatidylinositol 3-kinase pathway inhibits neuregulin-1-mediated rescue of neurotoxicity induced by Aβ1–42

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Neuregulin-1 (NRG1) has an important role in both the development and the plasticity of the brain as well as neuroprotective properties. In this study, we investigated the downstream pathways of NRG1 signalling and their role in the prevention of Aβ1–42-induced neurotoxicity. Lactate dehydrogenase (LDH) release, reactive oxygen species (ROS) generation, superoxide dismutase (SOD) activity and TUNEL staining were assayed to examine the neuroprotective properties in primary rat cortical neurons. Key findings The inhibition of PI3K/Akt activation abolished the ability of NRG1 to prevent Aβ1–42-induced LDH release and increased TUNEL-positive cell count and reactive oxygen species accumulation in primary cortical neurons. Our results demonstrate that NRG1 signalling exerts a neuroprotective effect against Aβ1–42-induced neurotoxicity via activation of the PI3K/Akt pathway. Furthermore, this suggests that NRG1 has neuroprotective potential for the treatment of AD.

Keywords: Alzheimer's disease; amyloid beta-peptide; neuregulin 1; neurotoxicity; PI3K/Akt

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P81

Neuregulin 1 Regulates Amyloid Precursor Protein Expression and Non-amyloidogenic Processing on the Cell Surface

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The amyloid precursor protein (APP) is a key molecule in Alzheimer disease. The prevailing view is that APP is initially transported to the plasma membrane as full-length protein. Its localization at the cell surface can trigger downstream signaling and APP cleavages. Our previous work has shown that Neuregulin 1 (NRG1) has neuroprotective effects on Alzheimer's disease model. In the present study, we examine whether NRG1 signaling involved APP expression and non-amyloidogenic processing in neuronal cells. Here, we show that NRG1 increase cell surface expression of APP without changing the total amount of APP protein and mRNA in SH-SY5Y cells and rat primary cortical neurons. Furthermore, NRG1 significantly increased the levels of the secreted form of sAPPa in the conditioned media. In addition, the ablation of ErbB4 in parvalbumin (PV)-positive interneurons in PV-Cre; ErbB4-/- mice suppressed APP expression, indicating a critical role for ErbB4 in regulating APP expression

in PV-positive interneurons. Our results demonstrate that NRG1 increase Amyloid Precursor Protein expression on the Cell Surface and sAPPa secretion in neuronal cells. Taken together, these results suggest a role for NRG1 in the non-amyloidogenic processing.

Keywords: Amyloid Precursor Protein (APP), Alzheimer's Disease(AD), Neuregulin 1 (NRG1), ErbB4, sAPPa

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P82

Overall expression pattern of vaspin in the hypothalamus and brainstem of mice

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Objective: Visceral adipose tissue-derived serine protease inhibitor (vaspin) is an adipokine with insulin-sensitizing effects and is secreted from the visceral white adipose tissue of the Otsuka Long-Evans Tokushima fatty (OLETF) rats. In the brain, the hypothalamus plays a critical role in the regulation of energy homeostasis, food intake, and body weight. Other brain sites are also involved in the regulation of food intake, such as the cerebellum and brainstem. It was reported recently that vaspin was expressed in the hypothalamus of C57BL/6 and db/db mice using western blot analysis. Therefore, the present study examined the expression pattern of vaspin in the mouse hypothalamus, cerebellum, and brainstem using immunohistochemical staining.

Methods: We performed immunohistochemistry to examine vaspin expression patterns in the hypothalamus, cerebellum, and brainstem of mice. Considering the anorexic effect of vaspin, we performed double immunostaining of vaspin and β-endorphin, which is derived from proopiomelanocortin (POMC), in the hypothalamus.

Results: Vaspin was expressed in the neurons of the arcuate, paraventricular, and periventricular nuclei of the hypothalamus, and locus ceruleus and mesencephalic trigeminal nucleus of the brainstem, whereas not expressed in the neurons of the cerebellar nuclei. Using immunofluorescence in the hypothalamus, vaspin was found to be co-expressed with β-endorphin in some of the neurons of the arcuate nucleus of the hypothalamus, especially in the rostral part. In the paraventricular nucleus, vaspin was not co-expressed with β-endorphin in the neurons, whereas β-endorphin was expressed in the nerve fibers of the paraventricular nucleus, suggesting that synapse could form between vaspin cell bodies and POMC nerve fibers in the paraventricular nucleus.

Conclusions: These findings suggest that vaspin was found in regions of the hypothalamus that are implicated in the neural control of feeding behavior and that vaspin expression in the hypothalamus could be related to anorexic and weight-reducing effects. Our data provide anatomical evidence for the expression of vaspin in the hypothalamus.

Keywords: Vaspin, Hypothalamus, Brainstem, Immunohistochemistry

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P83

GlcNAc Kinase Regulates Dynein-NudC Complex in Cell Migration

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Recently, we showed that N-acetylglucosamine kinase (GlcNAc kinase or NAGK), an enzyme of amino sugar metabolism, interacts with dynein motor and plays an essential structural role in axodendritic growth. Here we report that NAGK interacts with nuclear distribution protein C (NudC) and lissencephaly 1 (Lis1) in dynein complex. Combination of immunocytochemistry and proximity ligation assay (PLA) revealed NAGK-NudC-Lis1-dynein complex around nuclei and at the leading pole of migrating HEK293T cells and the tip of migratory processes of cultured rat neuroprogenitor cells. Exogenous expression of RFP-tagged NAGK accelerated migration of HEK293T cells in in vitro wound healing assay, neurons in neurosphere migration assay in E-14 neuronal projenitor cell culture and migrating neurons in developing mouse cerebral cortex in in utero electroporation assay, whereas NAGK knockdown by shRNA retarded migration. These data indicate a functional interac-

tion of NAGK with dynein-NudC-Lis1 complex at nuclear envelope and leading process in regulating cell migration.

Keywords: dynein, Lis1, NAGK, neuronal migration, NudC

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P84

Transcriptome Analysis of the Effects of Stigmasterol on Neuronal Development In Vitro

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Stigmasterol (ST), a naturally occurring phytosterol, exerts diverse physiological function including neuromodulation. However, molecular mechanism regarding neuromodulation of ST remained unknown. We therefore, in the present study explored the ST mediated changes of gene expression profile in the primary hippocampal neurons using RNA-sequencing (RNA-seq). We found that ST induces genes (p-value < 0.05) of various GO groups regarding different biological process and signaling pathways. Among them larger part of this upregulated genes related to central nervous system development, positive regulation of synaptic transmission on the contrary downregulates genes representing potassium ion transport and cyclic nucleotide metabolic process. Moreover, gene co-expression network analysis revealed that Ntrk2, Reln, Egr1 and Slc24a2 are the highly interconnected hubs genes in this upregulated groups and plays important role in neuronal differentiation and function. Furthermore, at FDR cut-off of less than 0.05, ST induces many immediate early genes (IEGs) such as Egr1, Fos, Npas4 and Nr4a1. Sequencing data were confirmed by immunocytochemistry of Reln, Map2, Dcx, Nr4A1, Egr-1and Arc genes at protein level on DIV 12 hippocampal neurons. In addition, at older culture (DIV 14), double-staining with antibodies against synaptic vesicle protein 2 (SV2, a marker of axon terminals) and postsynaptic density-95 (PSD-95, a postsynaptic marker) showed that ST increased the densities of both pre- and postsynaptic markers. Taken together, these results indicate that stigmasterol has neuritogenic and synaptogenic effects, and suggest that it be considered a potential therapeutic for the treatment of brain disorders.

Keywords: cytoarchitecture, hippocampal neuron, total mRNA-seq, stigmasterol, transcriptomics, immediate early genes

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Neutrophin-Mimetic Effects of Stigmasterol in the Development of Cytoarchitecture of Cultured Rat Hippocampal Neurons

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Disruptions in synaptic vesicle reserve pool, synaptic dysfunction, changes in dendritic spine shape, size or number accompany a large number of brain disorders like Alzheimer's disease (AD) and Parkinson's disease (PD). A naturally occurring phytosterol stigmasterol (ST) found in diverse food can modulates neuronal functions. In the present study, we investigated the potential role of ST in pre synaptic function, synapse formation and transcription related nuclear signaling leading to spinogenesis. We found that ST at 75 μM concentration ST increased the size of synaptic vesicle pool in the presynaptic terminals revealed by FM1-43 staining. Postsynaptically, ST increased the expression of GluN2A and GluN2B subunits of N-acetyl-D-glutamate (NMDA) receptors (NMDARs) and their synapses as well as activated the extracellular signal-regulated kinase 1/2 (Erk1/2) and cAMP response element-binding protein (CREB) which activate multiple cellular cascades. Subsequently through live stain of neuron with lipophilic dye DiO on DIV 13 and 17 reveals that ST induces dendritic filopodial growth and spine formation. Furthermore, expression of downstream signaling molecules of ERK and CREB involves in spine formation and maturation like Cell division cycle (CDC-42), postsynaptic density-95 (PSD-95), Actin related protein 2 (ARP-2) were confirmed by immunocytochemisty and western blot experiment which was also increased. Taken together these results indicate ST promotes both pre-and post synaptic plasticity therefore, it could help in the formation and stor-

age of memory resides in activity-driven modifications of synaptic strength and structural remodeling of synapses thus could be a potential preventative for age related neurological disorder.

Keywords: cCc42, Erk1/2, FM1-43, NMDAR, Spinogenesis, Stigmasterol, Synaptogenesis.

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P86

Unpredictable foot shock-induced learned helplessness and depression-like behaviors

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The unpredictable and inescapable electric shock-induced "learned helplessness" paradigm has long been used to produce an animal model of depression to identify the molecules associated with depressive symptoms or to assess the efficacy of pharmacological treatments for depression. After exposure to unpredictable and inescapable shocks (uncontrollable stress), most of mice showed defect in escape behavior in active avoidance test (learned helplessness, LH), while others did not (non-learned helplessness, NLH). Here, we investigated whether mice with LH or NLH exhibited depressive symptoms, including anhedonia, anxiety, and despair. We found that compared with control naïve mice, both uncontrollable shocks-induced LH and NLH mice showed increased anhedonia- and anxiety- but not despair-like behaviors. Notably, mice subjected to uncontrollable shocks showed similar behaviors, irrespective of whether they also showed LH or NLH. Furthermore, since both LH and NLH mice showed only anhedonia- and anxiety- but not despair-like behaviors, this model may be generally inadequate for classic depression-like behavior assessment. In conclusion, uncontrollable electric shock induces depression-like behavior, irrespective of the state of helplessness.

Keywords: Learned helplessness, Depression, Active avoidance test, Anhedonia

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The Neuronal Excitatory Amino Acid Carrier 1 (EAAC1) Expression was changed in Neonatal Maternal Separation (NMS) Rat.

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Early adverse life events(EALs) are relevant to neuropsychiatric disorder in adulthood. Neonatal Maternal separation(NMS), as one of the EALs, serves as a risk factor for developing emotional disorders. Glutamate transporters play a crucial role in physiological glutamate homeostasis, neuronal development and plasticity. We investigated whether NMS would changes the expression level of the neuronal glutamate transporters in different age stages. We compared with normal control group, NMS rats changed the neuronal excitatory amino acid carrier1(EAAC1) expression in different age stages (P7, P14, P21).

Keywords: Maternal Separation, EAAC1, Development

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A Role of Polyphenol for Delaying Wallerian Degeneration in the Peripheral Nerve

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Polyphenol is organic chemicals consisting of large multiple of phenol structural units, which are largely naturally extracted or, some-

times, synthesized. Even though physical and chemical characteristics of polyphenols are distinct each other, it has been well known as its anti-oxidant and anti-inflammatory effect, however, effect of the drug on peripheral nervous system (PNS) needs to be understood more. Thus, we have tried to reveal its effect on Wallerian degeneration (WD) through 3 days in vitro (3DIV) sciatic nerve explant culture. Firstly, we have found that 3DIV cultured nerves on complete DMEM with the drug keeps its unaltered morphology compared to 3DIV cultured nerve without the drug. In addition, the fibers showed striking inhibition of ovoid-shaped structure formation compared to control. Also, we scrutinized the effects of polyphenol on triggering both Schwann cell de-differentiation and proliferation, using diverse markers. From that, we have confirmed that polyphenol successfully helps drop all of the level of proteins, which means polyphenol really acts on WD inhibition on molecular scale and could be a candidate for relieving PNS related diseases like diabetic neuropathy, Charcot-Marie-Tooth disease and so on. In conclusion, polyphenol could be a potential drug for delaying onset of WD.

Keywords: Polyphenol, Schwann Cells, Wallerian Degeneration, De-differentiation, Proliferation

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The Effect of Transient Receptor Potential (TRP) on Delaying Wallerian Degeneration

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Ion channel molecules are well known as its critical roles in cell signaling pathway. Among them, transient receptor potential (TRP) has shown in the previous studies that its level is increased by peripheral nerve injury to proximal part, however, its role in the degeneration is still unclear. Here, we activated transient receptor potential V3 (TRPV3) and A1 (TRPA1) for checking its role in Wallerian degeneration (WD) in 3 days in vitro (3DIV) sciatic nerve explant culture model. At first, we found that TRP activation strikingly helps keep stripes on the nerve compared to 3DIV cultured the nerve without the drug. In addition, the fibers showed inhibition of forming ovoid-shaped structure formation compared to control. Also, we discovered the effects of TRP activator on triggering both Schwann cell de-differentiation and proliferation, using diverse markers. Thus, we confirmed that TRP activator successfully drop the level of proteins, which means TRP acts on WD inhibition on molecular scale and could be a candidate for relieving peripheral nervous system related hereditary diseases like diabetic neuropathy, Charcot-Marie-Tooth disease and so on. In conclusion, TRP activator could be a potential drug on delaying onset of WD.

Keywords: Transient Receptor Potential, Schwann Cells, Wallerian Degeneration, De-differentiation, Proliferation

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P90

A Role of Aminoacyl-tRNA Synthetase-Interacting Multifunctional Proteins (AIMPs) in Peripheral Nerve Degeneration and Regeneration

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Aminoacyl-tRNA synthetase-interacting multifunctional proteins (AIMPs) are co-factor of aminoacyl-tRNA synthetases (ARSs) in protein synthesis. In addition to its basic role, current studies have shown that dysfunction of AIMPs in the central nervous system causes several diseases like Parkinson's disease, Pelizaeus-Merzbacher, chronic myeloid leukemia and so on. However, non-canonical functions of AIMPs in peripheral nervous system (PNS) have yet been discovered well. According to our research, both mRNA and protein expression of AIMPs are increased as peripheral nerve injury is applied. In addition, their expressions are mainly detected in Schwann cells, not in axons. Co-localization and expression patterns of AIMPs with several markers indicate their relationships with Schwann cell de-differentiation. Thus, AIMPs could play a key role

in PNS degeneration as well as regeneration.

Keywords: AIMPs, Schwann Cells, Wallerian Degeneration, Peripheral Regeneration, De-differentiation

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Transcriptome Analysis of the Effects of Stigmasterol on Neuronal Development In Vitro

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Stigmasterol (ST), a naturally occurring phytosterol, exerts diverse physiological function including neuromodulation. However, molecular mechanism regarding neuromodulation of ST remained unknown. We therefore, in the present study explored the ST mediated changes of gene expression profile in the primary hippocampal neurons using RNA-sequencing (RNA-seq). We found that ST induces genes (p-value < 0.05) of various GO groups regarding different biological process and signaling pathways. Among them larger part of this upregulated genes related to central nervous system development, positive regulation of synaptic transmission on the contrary downregulates genes representing potassium ion transport and cyclic nucleotide metabolic process. Moreover, gene co-expression network analysis revealed that Ntrk2, Reln, Egr1 and Slc24a2 are the highly interconnected hubs genes in this upregulated groups and plays important role in neuronal differentiation and function. Furthermore, at FDR cut-off of less than 0.05, ST induces many immediate early genes (IEGs) such as Egr1, Fos, Npas4 and Nr4a1. Sequencing data were confirmed by immunocytochemistry of Reln, Map2, Dcx, Nr4A1, Egr-1and Arc genes at protein level on DIV 12 hippocampal neurons. In addition, at older culture (DIV 14), double-staining with antibodies against synaptic vesicle protein 2 (SV2, a marker of axon terminals) and postsynaptic density-95 (PSD-95, a postsynaptic marker) showed that ST increased the densities of both pre- and postsynaptic markers. Taken together, these results indicate that stigmasterol has neuritogenic and synaptogenic effects, and suggest that it be considered a potential therapeutic for the treatment of brain disorders.

Keywords: cytoarchitecture, hippocampal neuron, total mRNA-seq, stigmasterol, transcriptomics, immediate early genes

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Spinal nerve ligation-induced neuropathic pain is reduced by intrathecal injection of Evans blue, a vesicular nucleotide transporter antagonist

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Background Neuropathic pain generated by spinal or peripheral nerve injury is highly resistant to common pain killers, nerve block, and other pain management approaches. Therefore, new therapeutic candidates are being developed and tested in order to manage the neuropathic pain. In this study, we investigated whether Evans blue (EB), a vesicular nucleotide transporter (VNUT) competitor, could reduce neuropathic pain in L5 spinal nerve ligation (SNL) model and studied the mechanism of EB. Results When EB was intrathecally administrated into SNL-operated rats, it co-localized with VNUT in primary afferent neurons. The amount of ATP in CSF from spinal cord in EB-treated animals was reduced compared to saline-treated ones. Likewise, microglial activation in the laminar layer I-III of ipsilateral dorsal horn was also decreased by EB injection. Besides, ROS production and proinflammatory gene expression such as TNF-a and IL-1b were weakened in a EB-delivered group. In addition, the level of autophagy and ER stress in GABAergic neurons were lessened following EB introduction. Furthermore, EB alleviated efficiently the pain behavior (allodynia) evaluated with von Frey filament in a dose-dependent manner for 5 days. Conclusions We demonstrated that Evans blue may have an analgesic effect

in neuropathic pain of the SNL animal model, and would be a new potential therapeutic for the treatment of chronic pain.

Keywords: neuropathic pain, Evans Blue, vesicular nucleotide transporter , ATP

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Increased p-Tau in chronic traumatic encephalopathy by uncoupled eNOS

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Chronic traumatic encephalopathy (CTE) is a progressive neurodegenerative disease thought to be caused by repetitive traumatic brain injury (TBI) and sub-concussive injuries. Neuropathological changes that occur with CTE include the hyperphosphorylation of tau (p-Tau), which is attributed to astrocytic tangles (ATs) and neurofibrillary tangles. While these molecular mechanisms are likely involved in CTE, there are limited neuropathological or molecular data. By utilizing repetitive mild TBI (rmTBI) mouse models, we examined the pathological changes of CTE-associated structures, specifically the ATs. The rmTBI model mice displayed symptoms of depressive behavior, alongside an increased p-Tau expression in their neurons and astrocytes in both the hippocampus and cortex. Furthermore, there was an increase of nitric oxide (NO) and lipid peroxidation, but not reactive oxygen species, with a concomitant increase of the proinflammatory cytokines in the hippocampus of rmTBI mice and an increase of the uncoupled endothelial nitric oxide synthase. In addition, hypoxia induced an accumulation of cytoplasmic p-Tau, increased activation of NFkB, and increased expression of iNOS and HIF1a in primary astrocytes. Taken together, our results suggest that hypoxia-mediated NO production may play an important role in the formation of ATs and may be associated with some of the pathophysiological aspects of human CTE.

Keywords: chronic traumatic encephalopathy (CTE); repetitive mild traumatic brain injury (rmTBI); inducible nitric oxide synthase (iNOS); hypoxia; astrocytic tangles

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Neuroprotective Effect of Combined with Constraint Induced Movement Therapy and Electroacupuncture in Neonatal Hypoxic-ischemic Brain

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Backgroud: Neonatal hypoxic-ischemic (HI) injury, such as cerebral palsy (CP), is one of the most serious injuries in children. However, there is no definite treatment for CP, therefore different therapeutic strategies have continuously been investigated to improved therapeutic outcomes. In the previous study, we tested the efficacy of constraint induced movement therapy (CIMT), which forced intensive use of the hemiplegic arm through immobilization of the unaffected arm, on promoting functional recovery in HI rat model and CIMT yielded a modest recovery of motor and cognitive function. In this study, we investigated the efficacy of CIMT plus electroacupuncture (EA) for the rehabilitation in rat neonatal HI brain injury.
Method: The rat neonatal HI brain injury model was induced by

ligation of the left common carotid artery at postnatal day 7, and exposure to hypoxia chamber containing oxygen of 8% for 2 hours. CIMT was implemented at 3 weeks, post HI injury, using a pouch to constrain the unimpaired forelimb and forcing use of the affected forelimb using a motorized treadmill. EA, which was delivered by electrical stimulation (2 Hz, 1 mA) at Baihui (GV 20) and Zusanli (ST 36), was performed concurrently with CIMT after 3 weeks of HI.

Result: In the behavioral examination, markedly improved performances in the cylinder test were observed in the rats that underwent CIMT and EA compared to the untreated rats subjected to HI. However, CIMT and EA did not reduce the size of the HI lesion or post-HI volumetric decreases in the brain tissue. In addition, the combination treatment of CIMT and EA increases neurons and reduces astrocytes in the cerebral cortex area. Furthermore, the expression of cleaved caspase-3 was decreased in the cortical area.

Conclusion: Combined treatment with CIMT and EA may improve motor function following HI via neuronal cell survival. Thus, the combination treatment of CIMT and EA offers another treatment option to promote functional recovery in cerebral palsy.

Keywords: Neonatal hypoxic-ischemic injury, Constraint induced movement therapy, Electroacupuncture, Rehabilitation, Cerebral palsy

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Significant Treatment Effects of Adult Human Multipotent Neural Cells on Spinal Cord Injury are Mediated by Proangiogenic Paracrine Activites

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Neural stem cells are emerging as a regenerative therapy for spinal cord injury (SCI), sincethey differentiate into functional neural cells and secrete beneficial paracrine factors into thedamaged microenvironment. Previously, we successfully isolated and cultured adult humanmultipotent neural cells (ahMNCs) from the temporal lobes of epileptic patients. In this study,we investigated the therapeutic efficacy and treatment mechanism of ahMNCs for SCI usingrodent models. When 1 × 106 ahMNCs at in vitro passage 9 were transplanted into injuredspinal cords at 7 day after contusion, the injection group showed significantly betterfunctional recovery than the control group (media injection after contusion), which wasdetermined by Basso, Beattie and Bresnahan (BBB) score. Although transplanted ahMNCsdisappeared continuously and expressed few differentiated neural cell markers in the injuredspinal cords, the number of CD31-positive microvessels significantly increased in theinjection group than that of the control group. The paracrine pro-angiogenic activities ofahMNCs were confirmed by in vitro tube formation assay and in vivo Matrigel plug assay.Moreover, we identified CCL2/MCP-1 and CXCL1/GROα in the conditioned media ofahMNCs that independently mediated the pro-angiogenic effects of ahMNCs. Together, theresults indicate that ahMNCs have significant therapeutic efficacy in SCI via paracrine proangiogenic effects on the microenvironment of SCI.

Keywords: Spinal cord injury, Adult stem cells, Neural stem cells (NSCs), Microvasculature, Chemokine

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Primary Cilia Modulate TLR4-mediated Inflammatory Responses In Hippocampal Neurons

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Background: The primary cilium is an organelle that can act as a master regulator of cellular signaling. Despite the presence of primary cilia in hippocampal neurons, their function is not fully understood. Recent studies have demonstrated that the primary cilium influences interleukin (IL)-1b-induced NF-kB signaling, ultimately mediating the inflammatory response. We, therefore, investigated ciliary function and NF-kB signaling in lipopolysaccharide (LPS)-induced neuroinflammation in conjunction with ciliary length analysis.

Methods: Since TLR4/NF-kB signaling is a well-known inflammatory pathway, we measured ciliary length and inflammatory mediators in wild type (WT) and TLR4-/- mice injected with LPS. Next, to exclude the effects of microglial TLR4, we examined the ciliary length, ciliary components, inflammatory cytokine and mediators in HT22 hippocampal neuronal cells.

Results: Primary ciliary length decreased in hippocampal pyramidal neurons after intracerebroventricular injection of LPS in WT mice, whereas it increased in TLR4-/- mice. LPS treatment decreased primary ciliary length, activated NF-kB signaling, and increased Cox2 and iNOS levels in HT22 hippocampal neurons. In contrast, silencing Kif3a, a key protein component of cilia, increased ARL13B ciliary protein levels and suppressed NF-kB signaling and expression of inflammatory mediators.

Conclusions: These data suggest that LPS-induced NF-kB signaling and inflammatory mediator expression are modulated by cilia, and that the blockade of primary cilium formation by Kif3a siRNA regulates TLR4-induced NF-kB signaling. We propose that primary cilia are critical for regulating NF-kB signaling events in neuroinflammation and in the innate immune response.

Keywords: Primary cilia, hippocampus, NFκB, TLR4, neuroinflammation

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Immunoreactivity Of Neurogenic Factors And ERK/pERK In A Rat Model Of Intrauterine Growth Retardation Induced By Uterine Artery Ligation

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Intrauterine growth retardation (IUGR) is associated with neurogenesis, which is a process that encompasses the proliferation, growth, migration, and survival of neuronal cells. In our previous study, cell survival and expression of brain-derived neurotrophic factor (BDNF) were reduced in the cerebral cortex and dentate gyrus of fetuses with chronic placental insufficiency. BDNF protected cortical neurons against hypoxic injury via activation of the extracellular signal-related kinase (ERK) pathway. The aim of the current study was to observe the immunoreactivity of ERK and phosphate-ERK (pERK) in mature neurons and proliferating cells. Uterine artery ligation was performed at 17 days of gestation (dg), and Sprague-Dawley rat fetuses were obtained at 21 dg using cesarean section. Fetuses were designated either to the growth retardation (GR) group (n=45) when removed from the horn with uterine artery ligation, or to the control group (n=47) when removed from the other horn with the untied artery. Immunohistochemistry was performed with primary antibodies on paraffin-embedded forebrain sections The density and proportion of cells expressing PCNA, ERK, and phosphate ERK in the subventricular zone (SVZ) was not different between the control and GR group. The density and proportion of NeuN- and phosphate ERK-IR cells in the cerebral parietal cortex was lower in the GR group, compared to the control group. Although IUGR had no effect on the proliferation of cells in the SVZ, it reduced neuronal survival in the cerebral parietal cortex, which was associated with the decrease of pERK-IR cell density and proportion in the cerebral cortex.

Keywords: Hypoxia, ERK, Phosphate-ERK, Cortex, SVZ

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Agmatine Modulates The Phenotype Of Macrophage Acute Phase After Spinal Cord Injury In Rats

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Agmatine is a decarboxylated arginine by arginine decarboxylase. Agmatine is known to be a neuroprotective agent. It has been reported that agmatine works as a NMDA receptor blocker or a competitive nitric oxide synthase inhibitor in CNS injuries. In spinal cord injury, agmatine showed reduction of neuropathic pain, improvement of locomotor function, and neuroprotection. Macrophage is a key cellular component in neuroinflammation, a major cause of impairment after spinal cord injury. Macrophage has subtypes, M1 and M2 macrophages. M1 macrophage induces a pro-inflammatory response, but M2 inspires an anti-inflammatory response. In this study, it was clarified whether the neuroprotective effect of agmatine is related with the modulation of macrophage subdivision after spinal cord injury. Spinal cord injury was induced in rats with contusion using MASCIS. Animals received agmatine (100mg/kg, IP) daily for 6 days beginning the day after spinal cord injury. The proportion of M1 and M2 macrophages are confirmed with immunohistochemistry and FACS. CD206+ & ED1+ cells were counted as M2 macrophages. The systemic treatment of agmatine increased M2 macrophages caudal side to epicenter 1 week after spinal cord injury in immunohistochemistry. M2 macrophage related markers, Arginase-1 and CD206 mRNA, were increased in the agmatine treatment group and M2 macrophage expressing and stimulated cytokine, IL-10 mRNA, also was significantly overexpressed by agmatine injection. Among BMPs, BMP2/4/7, agmatine significantly increased only the expression of BMP2 known to reduce M1 macrophage under inflammatory status. These results suggest that agmatine reduces impairment after spinal cord injury through modulating the macrophage phenotype.

Keywords: Agmatine, Spinal cord injury, Macrophage, M2 polarization, Neuroinflammation

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Temporally characteristic phenotypes of microglia and blood-derived macrophage on neuroinflammatory responses in cerebral ischemia model using CX3CR1::EGFP transgenic mice

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Ischemic stroke is a devastating disease, second only to cardiac ischemia as a cause of death worldwide and a common type of strokes caused by blood clots that stop the flow of the blood to an area of the brain. As the blood supply is insufficient to the brain tissue followed by occlusion of the cerebral artery, molecular cues generated by cerebral ischemia activate the components of innate immunity, promote inflammatory signaling and contribute to tissue damage. Microglia known as an immune cell in the central nervous system (CNS) has functions similar to those of macrophages in the periphery. At the functional point of view, resident microglia (M0) can be polarized by molecular cues: M1 phase microglia and M2 phase microglia – former is related to pro-inflammatory responses and the latter is associated with anti-inflammatory responses. Moreover, blood-brain barrier (BBB) causes the extravasation of blood-derived macrophage. However, the interaction between the microglia and blood-derived macrophage is still unknown. We used CX3CR1::EGFP transgenic mice to visualize the microglia and blood-derived monocytes dynamics on neuroinflammatory responses. CX3CL1, a cell surface–bound chemokine constitutively expressed by neurons, suppresses microglial activation through its microglial receptor CX3CR1. In this study our goal is to observe the activation of microglia and the migration of activated microglia and infiltrated macrophage to the injured area using transgenic mice and two-photon microscope technique on neuroinflammatory responses by transient middle cerebral artery occlusion (tMCAO) intravial system, time-dependently. Our preliminary data showed that it is morphologically possible to distinguish activated microglia

and infiltrated monocytes from the resident microglia specifically. In addition, infiltrated blood-derived monocytes and resident microglia showed different polarization patterns by specific markers (Iba1, CD86, CD206, and CD45) in time-dependent manners (n=3 / 6h, 1, 3, 5, 7 days) after tMCAO. Furthermore, we performed the cytokine/chemokine array to evaluate the level of specific cytokine/chemokine on ischemic stroke using the serum and brain tissue. In results, the levels of serum and brain tissue of specific cytokine/chemokine showed different levels in all experimental time courses. Taken together, the overall data demonstrated that dynamics of microglia and blood-derived macrophage using specific type of transgenic mice could be a novel strategy for regulating the M2 anti-inflammatory microglia phenotype rather than M1 pro-inflammatory microglia and finding the optimal time point of drug treatment attenuating ischemic stroke."This research was supported by the Brain Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning(NRF-2016M3C7A1905098)"

Keywords: macrophage, microglia, ischemic stroke, neuroinflammation, CX3CR1

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사람 뇌 연속 관상 절편(3 mm) 영구표본 제작

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사람 뇌의 육안적 구조분석은 뇌 구조를 이해하고 기능을 밝히는 기초가 되며, 의학 관련 여러 분야에 적용될 수 있다. 그러므로 사람 뇌 연속 절편을 일정한 두께로 절단하고 영구보존할 수 있는 기술의 개발은 관련 분야에 다양하게 적용될 수 있다. 본 연구에서는 사람 뇌를 3 mm 두께의 일정간격으로 관상 절단하고, 생성된 절편을 자외선 경화형 수지(UV resin)를 이용해 영구조직표본으로 제작하였다. 사람 뇌의 연속절편 생성을 위해 3D printer를 이용하여 Human Brain Cutting Mold (HBCM)를 제작하였다. 2% 한천 용액으로 사람 뇌를 HBCM에 포매하였으며, brain knife를 이용하여 3 mm 간격의 연속 관상 절편을 제작하였다. 제작된 모든 절편의 단면을 촬영하여 이미지화 하였으며, 생성된 각각의 뇌 절편은 특수 제작한 brain slice cassette와 자외선 경화형 수지를 이용하여 영구표본으로 만들었다. 이 연구를 통해, 연구자는 사람 뇌 연속 관상 절편을 3 mm 간격으로 일정하게 제작 할 수 있는 새로운 방법을 제시하였으며, brain slice cassette와 자외선 경화형 수지를 이용하여 사람 뇌 관상 절편의 영구표본 제작에 성공하였다. 이 연구 결과는 사람 뇌 구조의 육안적 연구 및 관련 교육 분야에 널리 적용될 수 있을 것으로 생각된다. This work was partly supported by institute for information & communications Technology Promotion (iiTP) grant funded by the Korea government (MSiP) (no. B0132151001000303.

Keywords: Human Brain Cutting Mold, Brain Slice Cassette, 자외선 경화형 수지(UV resin)

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Neural stem/progenitor cells over-expressing arginine decarboxylase promotes PH resistance after acidic stress

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Neural stem/progenitor cell (NSPC) replacement therapy has the therapeutic potential to treat various neurological diseases and injuries. However, transplanted NSPCs were less efficient in ischemic lesions comprised of extracellular stimuli, such as glutamate toxicity, inflammatory cytokines, excessive extracellular calcium influx, and extracellular acidosis. In this study, we suggest that the third acidic stress resistance (AR) system, the arginine decarboxylase (ADC) which has been reported to protect low pH levels in bacteria and plants but poorly understood in the roles of CNS diseases. To determine the role of ADC in acidic stress after NSPCs replacement

therapy, highly expressed ADC-NSPCs were exposed in various pH gradients. Cells were significantly reduced the number of PI-positive cells and ROS generation under the low pH value. To confirm the changes of mitochondrial membrane potential after acidic stress, we performed XF24 extracellular flux analyzer. The results suggest that ADC has resisted mitochondrial membrane potential ($\Delta\Psi m$) collapse against severe pH gradient in NSPCs. Moreover, the mitochondrial length of ADC-NSPCs was significantly elongated under the low pH value. Following these results suggest that ADC gene has relevant cell therapeutics for the pH resistance following various CNS diseases.

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Keywords: Human Arginine decarboxylase (ADC), Neural Stem/Progenitor Cells (NSPCs), PH resistance, Mitochondrial Membrane Potential

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Neuropeptide Y (NPY) or cocaine- and amphetamine-regulated transcript (CART) fiber innervation on amygdaloid neurons that project to the locus coeruleus and dorsal raphe in the rat

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Neuropeptide Y (NPY) or cocaine- and amphetamine-regulated transcript (CART) fiber innervation on amygdaloid neurons that project to the locus coeruleus and dorsal raphe in the rat Young G. Hwang, Hyun S. Lee Department of Anatomy, School of Medicine, Konkuk University, 05029, Seoul, Korea The amygdaloid nuclear complex has been linked to the regulation of emotional behavior and food intake in that emotional stress might cause either cessation or enhancement of eating. We observed that central (CeA) as well as medial amygdaloid nucleus exhibited dense NPY (or CART)-immunoreactive (ir) fibers as well as a substantial number of labeled somata. When we examined hypothalamic neuronal origins of NPY (or CART) fibers projecting to the amygdala, medial and lateral arcuate nuclei were origins of NPY and CART neurons, respectively. On the other hand, melanin-concentrating hormone (MCH)-cocontaining CART cells projecting to the amygdala were located in the lateral hypothalamus (LH), zona incerta (ZI), and dorsal hypothalamic area (DA). In the amygdala, we also observed that NPY (or CART)-ir varicosities formed close appositions to amygdaloid neurons which projected to the locus coeruleus (LC) or dorsal raphe. Based on the observation that MCH neurons project to the CeA which densely innervates the LC, we examined the existence of MCH axon collaterals to the two targets. The present anatomical study revealed that MCH neurons in the LH, ZI, and DA provided divergent axon collaterals to the CeA and LC. Although MCH has been recently accepted as a powerful hypnogenic factor, the possible involvement of these dual-projecting MCH neurons in the regulation of cataplexy (as well as REM sleep) remains to be determined.

Keywords: Amygdala, LC, CART, NPY, MCH

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Suppression of microRNA let-7a expression promotes neurogenesis in arginine decarboxylase-neural stem cells after ischemia

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Neural stem cells (NSCs) have been studied to treat the central nervous system (CNS) disorders due to the potential of differentiation into neuron. To increase therapeutic efficiency of NSCs, recent researchers have focused on the study of the role of microRNA in CNS. MicroRNA let-7a (let-7a), a regulator of cell differentiation, also regulates genes associated with CNS neurogenesis. Agmatine, an endogenous primary amine produced by decarboxylation of L-arginine by arginine decarboxylase

(ADC), has neuroprotective effects and contributes to cellular proliferation and differentiation. Moreover, human ADC gene delivery into the NSCs using retroviral vector (vhADC) prevents the cell death and improves cell survivability against oxidative insult in vitro. The purpose of this study is to investigate the role of arginine metabolic enzyme which regulated let-7a in neural stem cell differentiation. In vitro study suggested that high levels of let-7a promoted the expression of TLX and c-Myc, as well as repressed DCX and ERK expression. In addition, agmatine attenuated the expression of TLX and increased the expression of ERK by negatively regulating let-7a. To confirm the effects of arginine metabolic enzyme and let-7a in vivo, mice were subjected to distal middle cerebral artery occlusion (dMCAO). Following dMCAO, mice were treated agmatine by intraperitoneal injection, let-7a mimic by osmotic pump and vhADC-NSCs via intracranial injection at the corpus callosum. We found that vhADC-NSC and let-7a co-treatment group reduced the infarct volume, increased the expression of DCX, Neurogenin2, Olig2, and attenuated the expression of GFAP. Therefore, our study suggests that the therapeutic efficiency of the vhADC-NSC on neural stem cell differentiation through suppression of let-7a in ischemic disorders. "This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MEST) (NRF-2014R1A2A2A01006556 and NRF-2017R1A2B2005350)."

Keywords: Neural stem cells(NSCs), MicroRNA let-7a(let-7a), Agmatine, Human arginine decarboxylase genes delivery into neural stem cells using by retroviral vector(vhADC), Ischemic condition

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The beneficial value of the stems of Schisandra chinensis (SSC) in neurological diseases is unclear. We examined whether SSC aqueous extract (SSCE) alleviates striatal toxicity in a 3-nitropropionic acid (3-NPA)-induced mouse model of Huntington's disease (HD). SSCE (75, 150, or 300 mg/kg/day, p.o.) was given daily before or after 3-NPA treatment. Pre- and onset-treatment with SSCE displayed a significant protective effect and pretreatment was more effective as assessed by neurological scores and survival rate. These effects were related to reductions in mean lesion area, cell death, succinate dehydrogenase activity, microglial activation, and protein expression of inflammatory factors including interleukin (IL)-1β, IL-6, tumor necrosis factor-alpha, inducible nitric oxide synthase, and cyclooxygenase-2 in the striatum after 3-NPA treatment. Pretreatment with SSCE stimulated the nuclear factor erythroid 2-related factor 2 pathway and inhibited phosphorylation of the mitogen-activated protein kinase and nuclear factor-kappa B signaling pathways in the striatum after 3-NPA treatment. The gomisin A and schizandrin components of SSCE significantly reduced the neurological impairment and lethality induced by 3-NPA treatment. These results indicate for the first time that SSCE may effectively prevent 3-NPA-induced striatal toxicity during a wide therapeutic time window through anti-oxidative and anti-inflammatory activities. SSCE has potential value in preventive and therapeutic strategies for HD-like symptoms.

Keywords: Stems of Schisandra chinensis, 3-nitropropionic acid, Nuclear Factor Erythroid 2-related Factor 2, Mitogen-Activated Protein Kinases, Nuclear Factor-kappa B

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Schisandra chinensis Stem Ameliorates 3-nitropropionic acid-induced Striatal Toxicity via Activation of the Nrf2 Pathway and Inhibition of the MAPK and NF-κB pathways

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P106

Multitarget effects of Korean Red Ginseng in Animal Model of Parkinson's Disease: Anti-apoptosis, Anti-oxidant, Anti-inflammation, and Maintenance of Blood-brain Barrier Integrity

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Ginsenosides are the main ingredients of Korean red ginseng (KRG). They have extensively been studied for their beneficial value in neurodegenerative diseases like Parkinson's disease (PD). However, the multitarget effects of KRG extract (KRGE) with various components are unclear. We investigated the multitarget activities of KRGE on neurological dysfunction and neurotoxicity in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced mouse model of PD. KRGE (37.5, 75, or 150 mg/kg/day, p.o.) was given daily before or after MPTP intoxication. Pretreatment with 150 mg/kg/day KRGE produced the greatest protective effect in motor dysfunction as assessed using rotarod, pole, and nesting tests, and on the survival rate. KRGE displayed a wide therapeutic time window. These effects were related to reductions in the loss of tyrosine hydroxylase-immunoreactive dopaminergic neurons, apoptosis, microglial activation, and activation of inflammatory factors in the substantia nigra pars compacta and/or striatum after MPTP intoxication. Also, pretreatment with KRGE activated the nuclear factor erythroid 2-related factor 2 pathways and inhibited phosphorylation of the mitogen-activated protein kinases and nuclear factor-kappa B signaling pathways, as well as blocking the alteration of blood-brain barrier (BBB) integrity. These results suggest that KRGE may effectively reduce MPTP-induced neurotoxicity with a wide therapeutic time window through multitarget effects including anti-apoptosis, anti-inflammation, antioxidant, and maintenance of BBB integrity. KRGE has potential as a multitarget drug or functional food for safe preventive and therapeutic strategies for PD.

Keywords: Korean Red Ginseng Extract, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, Multitarget effect

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Panax ginseng Exerts Antidepressant-like Effects by Suppressing Neuroinflammatory Response and Upregulating Nuclear Factor Erythroid 2 related Factor 2 Signaling in the Amygdala

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Background: Depression is one of the most commonly diagnosed neuropsychiatric diseases, but the underlying mechanism and medicine are not well-known. Although Panax ginseng has been reported to exert protective effects in various neurological studies, little information is available regarding its antidepressant effects.

Methods: Here, we examined the antidepressant effect and underlying mechanism of P. ginseng extract (PGE) in a chronic restraint stress (CRS)-induced depression model in mice.

Results: Oral administration of PGE for 14 d decreased immobility (depression-like behaviors) time in forced swim and tail suspended tests after CRS induction, which corresponded with attenuation of the levels of serum adrenocorticotropic hormone and corticosterone, as well as attenuated c-Fos expression in the amygdala. PGE enhanced messenger RNA expression level of brain-derived neurotrophic factor but ameliorated microglial activation and neuroinflammation (the level of messenger RNA and proteinexpression of cyclooxygenase-2 and inducible nitric oxide synthase) in the amygdala of mice after CRS induction. Interestingly, 14-d treatment with celecoxib, a selective cyclooxygenase-2 inhibitor, and Nunitro-L-arginine methyl ester hydrochloride, a selective inducible nitric oxide synthase inhibitor, attenuated depression-like behaviors after CRS induction. Additionally, PGE inhibited the upregulation of the nuclear factor erythroid 2 related factor 2 and heme oxygenase-1 pathways.

Conclusion: Taken together, our findings suggest that PGE exerts antidepressant-like effect of CRSinduced depression by antineuroinflammatory and antioxidant (nuclear factor erythroid 2 related factor 2/heme oxygenase-1 activation) activities by inhibiting the hypothalamo-pituitary-adrenal axis mechanism. Further studies are

needed to evaluate the potential of components of P. ginseng as an alternative treatment of depression, including clinical trial evaluation.

Keywords: Antineuroinflammation, Chronic Restraint Stress, Depression, Nuclear Factor Erythroid 2 related Factor 2, Panax Ginseng

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P108

6-OHDA toxicity induced the expression of Galectin-3 and Activating Transcription Factor 3 in Degenerating Nigral Dopaminergic Neurons

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Parkinson's disease (PD) is a common age-related neurological motor disorder, marked by the relatively selective and progressive neuronal degeneration of dopaminergic (DA) neurons in the substantia nigra (SN). 6-Hydroxydopamine (6-OHDA) is able to induce retrograde degeneration of the nigrostriatal DA neurons and has been the most widely used tool to mimic PD pathology. Galectin 3, a member of the Galectin family of β-galactoside binding lectins, plays an important role in the cell adhesion, immune responses, and signal cascades. Activating transcription factor 3 (ATF3), a member of CREB/ATF family, is induced in wide spectrum of tissues by various types of insults and suggested to be an important immediate early gene to initiate the signal cascades related in cell death or survival. To elucidate the neurobiological role of these molecules in DA neuronal degeneration, we investigated temporal and spatial profiles of Galectin-3 and ATF3 expression in 6-OHDA PD animal model. The 6-OHDA cytotoxicity in the striatum induced the retrograde DA neuronal cell death in SN in time point dependent manner. Both ATF3 and Galectin-3 were expressed in the tyrosine hydroxylase immunoreactive (TH-ir) neurons in the ipsilateral SN, but not in those of the contralateral SN. In the ipsilateral SN, the number of ATF3 and Galectin-3 positive neurons was increased by 5-7 days post-lesion, and then progressively decreased probably due to the loss of neurons. Concomitant co-localization of ATF3 and Galectin-3 in the same TH-ir neurons was also demonstrated by triple immunofluorescence labeling. To verify the specific expression of Galectin-3 and ATF3, nigral cells were retrogradely labeled at the site of subsequent striatal toxin injection with the fluorescent retrograde tracer fluorogold. These results suggest that Galectin-3 and ATF3 may be closely participating in 6-OHDA induced neurodegeneration.

Keywords: Parkinson's disease Galectin-3 ATF-3 Fluorogold substantia nigra

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Korean Red Ginseng Mitigates Spinal Demyelination in a Model of Acute Multiple Sclerosis by Downregulating p38 Mitogen-activated Protein Kinase and Nuclear Factor-κB Signaling Pathways

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Background: The potential therapeutic values of Korean Red Ginseng extract (KRGE) in autoimmune disorders of nervous system have not been fully investigated.
Methods: We used an acute experimental autoimmune encephalomyelitis animal model of multiple sclerosis and determined the effects and mechanism of KRGE on spinal myelination.
Results: Pretreatment with KRGE (100 mg/kg, orally) for 10 days before immunization with myelin basic protein (MBP)68-82 peptide exerted a protective effect against demyelination in the spinal cord, with inhibited recruitment and activation of immune cells including microglia, decreased mRNA expression of detrimental inflammatory mediators (interleukin-6, interferon-γ, and cyclooxy-

genase-2), but increased mRNA expression of protective inflammatory mediators (insulin-like growth factor β1, transforming growth factor β, and vascular endothelial growth factor-1). These results were associated with significant downregulation of p38 mitogen-activated protein kinase and nuclear factor-κB signaling pathways in microglia/macrophages, T cells, and astrocytes.

Conclusion: Our findings suggest that KRGE alleviates spinal demyelination in acute experimental autoimmune encephalomyelitis through inhibiting the activation of the p38 mitogen-activated protein kinase/nuclear factor-κB signaling pathway. Therefore, KRGE might be used as a new therapeutic for autoimmune disorders such as multiple sclerosis, although further investigation is needed.

Keywords: Korean Red Ginseng Extract, Experimental Autoimmune Encephalomyelitis, Nuclear Factor-κB, p38 Mitogen-activated Protein Kinase, Multiple Sclerosis

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Effects of Long-Term in vitro Expansion on Genetic Stability and Tumor Formation Capacity of Stem Cells

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Stem cell therapeutics are emerging as novel alternative treatments for various neurodegenerative diseases based on their regenerative potentials. However, stem cell transplantation might have side effects such as tumor formation that limit their clinical applications. Especially, in vitro expansion of stem cells might provoke genetic instability and tumorigenic potential. To address this issue, we analyzed genomic alterations of adult human multipotent stem cells (ahMNCs) after a long-term in vitro culture process (passage 9) using sensitive analysis techniques including karyotyping, array comparative genomic hybridization (aCGH), and whole exome sequencing (WES). Genomic changes detected by these techniques were associated with functional in vivo tumorigenic potential in brains of immune-deficient NSG mice. Although karyotyping did not find any major abnormalities in chromosomal number or structure, diverse copy number variations (CNVs) and genetic mutations were detected by aCGH and WES in three independent ahMNCs. CNVs and genetic mutations were increased as in vitro culture progressed. Observed CNVs and genetic mutations were not shared by all three ahMNCs. However, CNVs of CCDC15, DSPP, FN1, MUC17, QRICH2, and ZNF778 were found in two out of three long-term cultured ahMNC lines. The increased genetic instability did not confer in vivo tumorigenic potential to ahMNCs. Collectively, these results indicate that, although genetic instability can be induced by long-term in vitro expansion of stem cells, it is not sufficient to fully exert tumor formation capacity of stem cells. Other functional effects of such genetic instability need to be further elucidated.

Keywords: stem cell, long-term in vitro culture, whole exome sequencing, aCGH, genetic instability, tumorigenic potential

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Roles of Endothelial Cells In Radiation-induced Dementia

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Cognitive impairment including dementia is a common side effect found in patients who receive brain radiation therapy. Endothelial

cells represent an important component of the neurogenic niche and may regulate self-renewal and differentiation of neural progenitor cells (NPCs). Our earlier study demonstrated that transplanted exogenous neural stem cells differentiate into brain endothelial cells in irradiated brains, which was accompanied by the restoration of the brain functions. Based on the previous studies, radiation-induced dementia model with conditional knock-out mice, Ve-Cre;P53(fl/fl) which P53 were knock-out in endothelial cells, and Ve-Cre;P53(fl/+), as control. 8 weeks after fractioned radiation for 5 days (4Gy/day), radiation-induced dementia mice model were performed Memory function tests (Novel object recognition, Morris water maze), Emotional learning (Fear conditioning) and Motor function test (Rota rod). All mice which received radiation, especially Ve-Cre;P53(fl/+) mice, show poor learning ability during Novel object recognition, Morris water maze and Fear conditioning, but no differences were found in Rota rod. Those results indicate that exposure of radiation were relative with P53 apoptosis and critical to cognitive or memory function not to motor function. These findings provide evidence that p53-dependent apoptosis of endothelial cells may regulate NPCs to restoration of the brain functions after genotoxic stress.

Keywords: Radiation-induced Dementia Endothelial Cell, P53-dependent Apoptosis Conditional Knock-out Mice

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Morphological Characterization Of NG2 Glia And Their Association With Neuroglial Cells In The Striatum Of Rats Administered The Mitochondrial Toxin 3-Nitropropionic Acid

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NG2 glia, which are characterized by chondroitin sulfate proteoglycan expression, comprise a distinct class of glial cells in the mammalian central nervous system. In this study, we examined the spatiotemporal expression profiles and morphological characteristics of NG2 glia and their associations with neuroglial cells in the striatum of rats treated with the mitochondrial toxin 3-nitropropionic acid (3-NP). In control striatum, weak NG2 immunoreactivity was restricted to resting NG2 glia with thin processes, but prominent NG2 expression was also noted on vasculature-associated cells, including pericytes and smooth muscle cells, activated microglia/macrophages, and reactive NG2 glia in the lesion core after 3-NP injection. Activation of NG2 glia, including enhanced proliferation and morphological changes, had a close spatiotemporal relationship with infiltration of activated microglia into the lesion core. Thick and highly branched processes of reactive NG2 glia formed a cellular network in the astrocyte-free lesion core and primarily surrounded developing cavities 2-4 weeks post-lesion. NG2 glia became associated with astrocytes in the lesion core and the border of cavities over the chronic interval of 4-8 weeks. Immunoelectron microscopy indicated that reactive NG2 glia had large euchromatic nuclei with prominent nucleoli and well-developed Golgi complexes, as well as thick and branched processes that ramified distally. Thus, our results further support the link between the activation of NG2 glia and microglial activation/recruitment in response to brain insult. Our findings also suggest that NG2 glia may be involved in fibrotic scar formation in the lesion core, and later in glial scar formation in association with astrocytes. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2017R1A2B4002922).

Keywords: NG2 glia, Microglia, Macrophages, Astrocytes, Fibrotic scar

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Time Course And Cellular Distribution Of GRP78 Expression Following Transient Focal Cerebral Ischemia In Rats

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The 78-kDa glucose-regulated protein (GRP78) is an endoplasmic reticulum (ER) lumen-localized chaperone that binds to hydrophobic stretches in newly synthesized proteins to assist in their proper folding, and that plays a central role in signaling the unfolded protein response. Stressful conditions such as ischemia lead to ER stress due to the accumulation of unfolded proteins, ultimately leading to cell death. Several studies have shown that GRP78 is upregulated in the ischemic brain, suggesting its role as a key molecule in the pathophysiology of ischemic insults. However, the temporal regulation and identification of the precise cell phenotype expressing GRP78 in the ischemic brain remains to be established. Thus, in this study, we investigate the spatiotemporal expression profiles and cellular localization of GRP78 in a rat transient focal ischemia model induced by middle cerebral artery occlusion (MCAO). GRP78 expression revealed spatial differences between the infarct core and the peri-infarct penumbra region during 28 days of post-ischemia period. Western Blot analysis revealed similar expression levels in GRP78 protein extracted from contralateral and ipsilateral striatum of sham-operated controls and MCAO rats at all time points. Double and triple immunofluorescence were undertaken to identify the exact identities of cells expressing GRP78. In sham-operated rat striatum, GRP78 was almost exclusively expressed in neurons, whereas it was rarely expressed in GFAP-positive astrocytes and Iba1-positive microglia. On day 1 after the induction of stroke, dying or dead neurons, despite the NeuN-positive neuronal marker still being present, were devoid of GRP78 expression in the core region of ischemic injury. At this time point, however, choline acetyltransferase-positive interneurons, which were not positive for TUNEL yet, showed a rather intense GRP78 expression. In addition, GRP78 expression was induced in large, round brain macrophage; these cells were predominantly localized in the ischemic core on day 3 after reperfusion, which was followed by infiltration of activated stellate microglial cells by day 7. These activated microglia/macrophages in the ischemic core expressed GRP78 up to day 28 after reperfusion. In contrast, GRP78 expression in the peri-infarct region was prominent in reactive astrocytes by day 3 after reperfusion, and thereafter increased progressively throughout the 28-day experimental period. This observation was confirmed by quantification of the mean fluorescence intensity of GRP78 expression in reactive astrocytes, which showed that intensity of astroglial GRP78 expression after ischemia was 4-5 fold higher than that of control. Our results indicate a phenotypic heterogeneity of GRP78-positive cells, suggesting a multifunctional role of GRP78 in the pathogenesis of ischemic stroke, possibly in the astroglial reaction and the activation/recruitment of microglia/macrophages, in addition to its known role in neuronal cell death in response to ischemia-induced ER stress. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2017R1A2B4002922).

Keywords: 78-kDa glucose-regulated protein; Endoplasmic reticulum; Stroke; Neuron; Glial cells

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P114

Desmin Expression Profile In Reactive Astrocytes In The 3-Nitropropionic Acid–Lesioned Striatum Of Rat: Characterization And Comparison With Glial Fibrillary Acidic Protein And Nestin

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Desmin, the muscle-specific, type-III intermediate-filament protein, is reportedly expressed in astrocytes in the central nervous system. To elucidate whether desmin is regulated in reactive astrocytes in response to brain insults, we examined the spatiotemporal expression profiles of desmin and their relationship with two astroglial intermediate filaments, glial fibrillary acidic protein (GFAP) and nestin, in the striatum of rats treated with the mitochondrial toxin 3-nitropropionic acid (3-NP). Weak, constitutive immunoreactivity for desmin was observed in astrocytes generally, and in reactive astrocytes in the peri-lesional area, its expression increased in parallel with that of GFAP over three days post-lesion and was maintained until at least day 28. Desmin, GFAP, and nestin, in particular, show characteristic time-dependent expression patterns in reactive astrocytes

forming the astroglial scar; delayed and long-lasting expression of desmin and GFAP occurs in these astrocytes, while nestin induction is rapid and transient. In the lesion core, desmin is also expressed in two categories of vasculature-associated cells, nestin-negative and nestin-positive perivascular cells. These findings show that desmin, together with GFAP and nestin, is a dynamic component of intermediate filaments in activated astroglia, which may account for the dynamic structural changes seen in these cells in response to brain insults. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2017R1A2B4002922).

Keywords: Desmin, Glial fibrillary acidic protein, Nestin, Reactive astrocytes, Glial scar

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Mice Get More Stressed When Bullied in Group than Individual

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Bullying is a threat or physical use of force, aiming at the individual, another person, a specific community or group which can result in injury, death, physical damage, some development disorders or deficiency. There is a sharp increase in the number of news on bullying at school in mass media making it an issue that continues to receive attention from educators, parents, and students. We assumed that being bullied individually would get more stress than together in a group. To test our assumption we carried out experiments using female non-pregnant mice (~3 month-old, n=4 per group). After mice were accustomed for 2 min in a large ovale shaped, dark brown, plastic basket (90 cm L x 60 cm W x 60 cm H), a 3-month old cat was introduced and allowed her to access freely to mice for 2 min. This bullying-mimicking routine was repeated once in the morning and afternoon for 4 consequtive days. After last threat, mice were placed in the same basket with or without a shelter (16 cm L x 16 cm W x 10 cm H) and behavior during initial 2 min was vedeotaped for later analysis. In contrast to our assumption, mice bullied in group were more stressed as evidence by ~2-fold more stools than those individually bullied ones. There was no difference in times spent exploring the middle or peripheral area between two experimental groups nor against the unthreatened control group. However, when a shelter was placed in the center of the basket, group-bullied mice stayed squatting in the shelter significantly longer than those individually-bullied and control ones. Our data indicate that mice get more stressed when bullied in group than individual. *, These authors contributed equally to this study.

Keywords: bullying, cat, mouse, shelter, stress

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Effects of Inflammasome Activation on DICER Down-regulation in Astrocyte

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The inflammasome is a multiprotein oligomer consisting of caspase 1, PYCARD and NLRP. It's strongly expressed in immune cells but also in the various cells that participates in innate immune system. The inflammasome promotes activation of procaspase-1 to active caspase-1 and as a result caspase-1 is processing the inflammatory cytokines Interleukin 1β (IL-1β) and Interleukin 18 (IL-18) to mature form. Dicer, also known as endoribonuclease Dicer or helicase with RNase motif, is an enzyme cleaves double-stranded RNA (dsRNA) and pre-microRNA (pre-miRNA) into short double-stranded RNA fragments called small interfering RNA and microRNA. In various cancer, ovarian cancer, breast cancer and basal cell carcinoma, Dicer dysregulation is one of the component predict disease prognosis. Also stress conditions (eg. Hypoxia, inflammation, DNA damage ect.) regulates expression of Dicer. But the direct mechanism of downregulation of Dicer protein is no fully identified. Some

researchers report activated Caspase-3 can cleave Dicer to form truncated Dicer to reduces its RNase activity, however there is any reports caspase-1 reduces Dicer expression. In this study, we stimulate inflammasome activation in hypoxia/ viral infection condition in human T98G glioblastoma cell and mouse primary astrocyte cell and check Dicer expression. Treatment of caspase-1 inhibitor Ac-YVAD-cmk recovering Dicer protein level in those inflammasome activated astrocyte.

Keywords: Inflammasome, Astrocyte, Caspase-1, Dicer

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Upregulation of Parvalbumin and Glutamic acid decarboxylase-67 in ventral hippocampus of maternal separation adolescent mice

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Anxiety is affecting one-eighth of the total population of the world and has become a very important area of research interest in psychopharmacology in the past decade. Many individuals exposed to early life adversity go on to develop a variety of behavioral and psychiatric problems that persist well into adulthood. Several studies have proven that neonatal maternal separation (MS) is related to anxiety and depression. A positive relationship between anxiety and hippocampal inhibitory circuit development also has been well reported. So, in this study, we analyzed the relationship between the anxiety behavior and the inhibitory neuronal alteration in the developing ventral hippocampus by using MS animal model. Male mice pups were stressed by separating them from their mothers for 4 hours daily from postnatal day (PND) 2 to PND 20. To verify whether MS could induce behavior problems in adolescent mice, behavior test was conducted at PND 45. MS group displayed anxiety-like behavior (elevated plus maze) and aggressive-like behavior (tube-dominance test). However, MS did not affect learning and memory (Morris water maze). To determine the relationship between MS behavioral changes and hippocampal inhibitory circuit, glutamic acid decarboxylase-67 (GAD67) and parvalbumin (PV) immunohistochemistry was performed. The ventral hippocampus was divided into 6 areas (dentate gyrus (DG), conus ammonis (CA) 1, CA3, subiculum, presubiculum, and parasubiculum) and the areas were further segmented into 19 layers. The number of GAD67- or PV-immunopositive cells per unit area (1 mm2) were counted and compared with control group. As a result, compared with control groups, more than twice as many GAD67 positive neurons were identified in the DG molecular layer, CA3 stratum lucidum, presubiculum layer I~III, and parasubiculum layer I. PV positive neurons were also outnumbered in the DG granule cell layer, DG molecular layer, all layers of CA3, and parasubiculum layer II~III. These results suggest that the early life stress exposure, like as maternal separation, could change the inhibitory neuronal circuit in the ventral hippocampus which causes the behavioral disorders of adult life.

Keywords: Maternal separation, Anxiety, Hippocampus, GABA, GABAergic interneuron

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P118

Synaptic Deficits in Mice Brain caused by Long-Term High-Fat Diet induced Neurodegenerative Injury.

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There are increasing number of studies on the relationship between Alzheimer's disease (AD) and metabolic dysfunction. In our study, long term high-fat diet feeding of mice resulted in cognitive decline, accumulation of amyloid beta, and tau protein, suggesting that environment rich in fat could possibly work as the contributing factor

to AD.It is well known that cognitive dysfunction in degenerative brain diseases such as Alzheimer's disease features severe loss of synapse integrity and its proper function. The damage notably begins around the hippocampus, where neurons are under high energy demands, especially in sites where synaptic connections are abound. Therefore, we sought to make detailed morphological observations on changes in synaptic connections induced by long-term high-fat diet using electron microscopy technique, and importantly, in the synaptic-rich AD-vulnerable region of the brain.Male ICR mice (30–35 g, 7 weeks old) were fed either a normal diet (ND, 13% kcal fat) or high fat content diet (HFD, 60% kcal fat) for 24weeks. CA1, CA3, and dentate gyrus regions of hippocampus were isolated and prepared separately as TEM samples. The TEM results showed that the number synaptic connections were decreased in CA1(ND=56, HFD=25.53, p<.05) and CA3(ND=48.5, HFD=31.225, p<.05), but not in DG(ND=34.1, HFD=34.75, p>.05). Post-synaptic density was also notably decreased in high-fed mice hippocampus, compared to normal condition, though the number of synaptic vesicles per synapse did not report statistical significance. Western blot was conducted to quantify the synaptic proteins, PSD95, and synaptophysin. Interestingly, there also has been increased presence of astrocytes observed in high-fat condition, and increased connections made to the astrocytes. This was confirmed by the western blot data, reporting higher GFAP in high-fat mice brain. Immunohistochemical data also showed that the number of GFAP-positive astrocytes was high in high-fat fed brain. Overall, we suggest that long-term feeding of high-fat diet can induce a synaptic deficit, which hallmark the neurodegeneration such as in Alzheimer's disease. This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, Korea. (HI14C2173).

Keywords: Alzheimer's Disease, High-Fat Diet, Electron Microscopy, Synapse

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P119

Microcoil을 이용한 저혈류 모델의 뇌혈류 변화 분석 (Analysis of cerebral blood flow in Microcoil-induced hypoperfusion model)

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노화에 의한 뇌혈관 질환 및 퇴행성 질환의 근본원인은 뇌의 저혈류 (Hypoperfusion) 로 여겨진다. 이번 연구에서는 Microcoil을 이용한 뇌의 저혈류 모델을 제작하여 전통적인 결찰 방법과 뇌혈류 변화를 비교 분석하였다. 온목동맥 (Common carotid artery; CCA) 의 결찰방법에 따른 뇌혈류 변화를 비교하기 위해 직경 0.20mm의 microcoil을 생쥐(8weeks male balb/c mouse)의 온목동맥에 감아 Microcoil유도 저혈류 모델을 만들었으며 대조군으로 7-0 silk suture을 이용하여 양쪽 온목동맥을 결찰한 전형적인 뇌의 저혈류 모델을 만들었다. 각 그룹은 수술 후 1주 간격으로 형광조영제인 인도시아닌그린 (Indocyanine green; ICG) 을 꼬리정맥에 주사한 후 CCD 카메라로 160 ms의 단위로 촬영하여 영상을 획득하였다. 인도시아닌그린은 체내에 유입되면 근적외선 파장에서 형광을 내는 물질로서 실험동물의 꼬리정맥에 주사한 후 두개골을 투과하여 나오는 영상을 통해 뇌혈류 흐름을 파악할 수 있다. 획득한 영상은 BFI (blod flow index), MTT (mean transit time), Trising (the time between of the first appearance of ICG fluorescence) 과 같은 파라미터로 뇌혈류를 분석하여 결찰방법에 따른 뇌혈류 흐름 변화를 비교하였다.

Keywords: Hypoperfusion, Microcoil, 저혈류모델

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P120

Light-Emitting Diode treatment ameliorates amyloid pathology in the 5XFAD mouse model of Alzheimer's disease

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Backgroud: Low-level light emitting diode therapy (LED-T) can be rapidly applied in a safe and non-invasive way, acting on various pathways. This treatment is effective for chronic disease because it has fewer side effects than drugs. In this study, we aimed to investigate the effects of LED-T on activating cognitive neural network and inhibiting neuronal cell death to prevent cognitive impairment and dementia, and optimal timing of LED-T initiation for functional recovery.

Method: LLLT was applied by placing the skin-adhesive light-emitting probes onto the skin at two locations on the head (the right midpoint of the parietal bone and the posterior midline of the seventh cervical vertebra). Experimental groups receiving treatment are divided into early-treat group and late-treat group according to the time of starting LED-T [3 month (early group) or 6 month (late group)], and the mice of each groups received LED-T 3 times a week for 14 weeks, 20 minutes per session. Morris Water Maze, passive avoidance test, and elevated plus maze were evaluated at 10 month of age.

Result: Early-treat group but not late-treat group showed improved learning and memory, and reduced anxiety compared to the light-untreated group. Consistent with the behavioral results, amyloid plaque load was significantly decreased in the cortex, hippocampus and corpus callosum of early LED-T group, but not late LED-T group.

Conclusion: LED-T reduced the amyloid plaque in the 5XFAD mouse and alleviated the behavioral characteristics of Alzheimer's disease. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and future Planning (NRF-2016R1A2B2007862).

Keywords: Alzheimer's disease Dementia Low-level light emitting diode therapy LLLT Amyloid pathology

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P121

Calpain activation contributes prenatal stress-induced spasms in rat

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Infantile spasm (IS) is a serious epileptic syndrome that occurs in the early infantile age. Recent studies revealed prenatal stress exposure is a risk factor of IS. Our previous study showed that prenatal stress with betamethasone altered the maturation of GABAergic progenitors and resulted in the lack of GABA input, which in turn, decreased KCC2 expression and lowered the seizure threshold. However, the mechanisms on the seizure susceptibility to N-methyl-D-aspartate (NMDA)-triggered spasms on postnatal day still need to be clarified. Prenatal stress with betamethasone on gestational day 15 increased seizure susceptibility to NMDA-triggered spasms on postnatal day 15. Compared to the control group, the protein level of NMDA receptor 2B (NR2B) was not different, but the protein level of phosphorylated-NR2B/NR2B ratio was decreased in the cortex of the prenatally stressed model. We further confirmed increased expression levels of STEP, phosphorylation of p38, cleaved caspase-3, and decreased calpain2. Our study suggest that calpain2 and STEP pathway and downstream p38 are related with increased sensitivity of seizure threshold of prenatal stress-induced cortex, and it would be considered as a new treatment approach of infantile spasms.

Keywords: Infantile spasms, Prenatal stress, NMDA receptor, Calpain

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P122

High ω3-Polyunsaturated Fatty Acids In Fat-1 Mice Prevent Scopolamine-Induced Amnesia Through BDNF Signaling

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ω-3 polyunsaturated fatty acids (PUFAs) are known to be critical for optimal brain health and psychiatric and neurological ailments. We have shown the effects of scopolamine on memory impairment in the omega-3 overexpressed fat-1 mouse hippocampus. y-maze and passive avoidance tests were performed to evaluate the memory function of mice after administering scopolamine to fat-1 mice. Fat-1 mice showed increased latency in the passive avoidance test and improved ameliorated alternation in y-maze. The effects of scopolamine on damaged hippocampal neurogenesis was confirmed by the increase of ki-67 and DCX positive stained cells in the fat-1 mice. Western blot analysis revealed that expression of brain-derived neurotrophic factor (BDNF) and phosphorylated cAMP response element-binding proteins (pCREB) was increased. We were able to confirm that omega-3 was effective for scopolamine-induced apoptosis by using the cleaved-Caspase 3 Western Blot. In conclusion, these findings indicate that scopolamine-treated fat-1 mice were protected from granular cell loss and exhibited increased BDNF signaling and decreased apoptosis signaling. These processes may underlie granular cell survival and maybe provide potential therapeutic targets for treatment of memory impairment.

Keywords: ω-3 Polyunsaturated Fatty Acids, Brain-Derived Neurotrophic Factor, Memory, Neurogenesis

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P123

Amelioration Of Cognitive Decline And Hippocampal Neuronal Loss By Novel Synthetic Risperidone-Ferulic Acid Hybrids In A Rat Model Of Vascular Dementia

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Vascular dementia (VD), which is caused by microvascular obstruction, is the common type of dementia together with Alzheimer's disease, and is commonly accompanied with cognitive impairment. In this study, we novelly synthesized Risperidone (RIS)-Ferulic acid (FA) hybrids (RIS-FA, HBU-#292) based on previously well-documented neuroprotective effects of both RIS and FA and evaluated whether RIS-FA might be therapeutically effective in cognitive impairment and hippocampal neuronal death using a rat model of vascular dementia. For this, 10-week-old male Sprague-Dawley rats were subjected to 4-vessel occlusion (4-VO) and randomly divided into three groups; a VEH (a rat group subjected with 4-VO and administrated with vehicle), RIS-FA-L [a rat group subjected with 4-VO and administrated with low dose (1 mg/kg) of RIS-FA], and RIS-FA-H [a rat group subjected with 4-VO and administrated with high dose (10 mg/kg) of RIS-FA]. For all experimental groups, RIS-FA was intraperitoneally administered daily for post-operative days (POD) 7. At POD 7, memory functions were assessed using Barnes maze, passive avoidance, and Y-maze test. To examine neuronal loss in the CA1 region of the hippocampus, we performed stains with Cresyl-Violet. To investigate the underlying mechanisms, chemical hypoxia was induced by CoCl2 on PC12 cell, a neuroblastoma cell line, and analyzed the apoptosis-related signal pathway using western blot. Compared with the VEH group, both RIS-FA-L and –H groups showed the significant attenuation of VD-related memory deficit in the behavioral tests in a dose-dependent manner. Additionally, RIS-FA also rescued the hippocampal neuronal loss as demonstrated by the histological assays. Finally, RIS-FA attenuated the chemical hypoxia-triggered apoptosis of PC12 cell, as demonstrated by observing increase of Bcl-2 and decreases of Bax expressions. Collectively, the results demonstrates that novelly synthesized

RIS-FA significantly alleviates VD-related cognitive decline and neuronal loss in the hippocampal CA1, at least in part, by inhibiting neuronal apoptosis.

Keywords: Vascular Dementia Four vessel occlusion Risperidone Ferulic acid

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Streptozotocin-induced neurodegeneration could be ameliorates through BDNF signaling and autophagy in fat1 transgenic mice

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Chronic degenerative brain disease in diabetes, known as 'diabetic encephalopathy', is a recognized complication that can occur due to long-standing diabetes in patients. The hippocampus appears vulnerable in diabetic subjects that have a higher risk of stroke, dementia, and cognitive decline. Although the decreased neurogenesis in the dentate gyrus was found streptozotocin (STZ)-induced diabetic mice, the effects of ω3-polyunsaturated fatty acids (PUFA) in diabetics have not been studied yet. Here, we report that high ω3-PUFA could ameliorate the hippocampal degeneration in STZ model, using fat-1 transgenic mice. When STZ was administrated to wild-type (WT) mice in order to induce diabetes, hyperglycemia was well induced after 14 days but not in STZ-treated fat-1 mice. To examine whether omega-3 could protect from the pyramidal cell loss in the dentate gyrus of hippocampus caused by STZ treatment, we immunostained with Ki67- or DCX antibodies. The number of Ki67- or DCX-reactive cells from STZ-treated WT mice was decreased, but not in the STZ-treated fat-1 mice. In addition, the level of expression of Brain-derived neurotrophic factor (BDNF) from hippocampal homogenates in STZ-treated WT mice was significantly decreased compared to untreated-WT mice. However, BDNF expression in STZ-treated fat-1 mice was comparable to STZ-treated WT mice. In conclusion, these findings indicate that ω3-PUFA may reduce the loss of proliferation and neuronal progenitors in the dentate gyrus of hippocampus in Type-2 diabetes by STZ.

Keywords: Diabetes, Fat-1, BDNF, Streptozotocin (STZ), Hippocampal degeneration

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Resveratrol Ameliorates Retinal Ischemia/Reperfusion Injury Induced Cell Death in C57BL/6J Mice by Downregulation of Caspase-8

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Retinal cell death is a common pathology in eye diseases and one of the major causes of retinal damage, which can ultimately lead to blindness. I/R injury model is well-established animal model for the retinal cell death. I/R injury induces apoptosis in RGCs. Resveratrol (Res) is a potent natural antioxidant with beneficial effects in many ocular diseases, such as diabetic retinopathy, and glaucoma. The caspase-8 expression is highly correlated with activation of the apoptotic pathway, and several regulators of caspase-8 have been identified, including p53, NF-κB, and HIF-1α. These proteins are not only associated with I/R injury, but also regulated by Res. It might be indirect evidence of increased transcription of caspase-8 in I/R injury. The present study aimed to determine whether Res regulates the expression of caspase-8 in I/R retinal injury model. C57BL/6J

mice were injected with Res before I/R retinal injury induced by increasing the intraocular pressure for 1 h. Res was then injected for several consecutive days. mRNAs and proteins were extracted in different time point after injury. The expression levels of caspase-8, p53 and NF-κB mRNA and HIF-1α protein were determined using RT-PCR and western blot analyses. I/R injury induced caspase-8, p53 and NF-κB mRNA expression increased. Res treatment reduced the the expression of caspase-8 mRNA. This result suggests that I/R injury induced caspase-8 reduced by Res. In conclusion, our data suggest that Res is suitable as a therapeutic agent for treating I/R-related ophthalmic diseases by targeting the expression of caspase-8.

Keywords: Ischemia/reperfusion injury, Caspase-8, Resveratrol, Retina, Cell death

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P126

Progressive ac cumulation of autofluorescent granules in macrophages in rat striatum after systemic 3 nitropropionic acid: a correlative light and electron microscopic study

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A variety of tissue biomolecules and intracellular structures are known to be autofluorescent. However, autofluorescent signals in brain tissues often confound analysis of the fluorescent markers used for immunohistochemistry. While investigating tissue and cellular pathologies induced by 3-nitropropionic acid, a mitochondrial toxin selective for striatal neurons, we encountered many autofluorescent signals confined to the lesion core. These structures were excited by blue (wavelength = 488 nm) and yellow-orange (555 nm), but not by red (639 nm) or violet (405 nm) lasers, indicating that this autofluorescence overlaps with the emission spectra of commonly used fluorophores. Almost all of the autofluorescence was localized in activated microglia/macrophages, while reactive astrocytes emitted no detectable autofluorescence. Amoeboid brain macrophages filled with autofluorescent granules revealed very weak expression of the microglial marker, ionized calcium-binding adaptor molecule 1 (Iba1), while activated microglia with evident processes and intense Iba1 immunoreactivity contained scant autofluorescent granules. In addition, immunolabeling with two lysosomal markers, ED1/CD68 and lysosomal-associated membrane protein 1, showed a pattern complementary with autofluorescent signals in activated microglia/macrophages, implying that the autofluorescent structures reside within cytoplasm free of intact lysosomes. A correlative light- and electron-microscopic approach finally revealed the ultrastructural identity of the fluorescent granules, most of which matched to clusters of lipofuscin-like inclusions with varying morphology. Thus, autofluorescence in the damaged brain may reflect the presence of lipofuscin-laden brain macrophages, which should be taken into account when verifying any fluorescent signals that are likely to be correlated with activated microglia/macrophages after brain insults.
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Keywords: Autofluorescence, Lipofuscin, 3-NP, Microglia, Macrophages

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Interactions between Microglia and Macrophages on Polarization and Chemotaxis Effect following Ischemic Stroke

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The inflammatory response following ischemic stroke is a well-known and widely studied phenomenon, but the mechanism is still unclear. After ischemic stroke, microglia and recruited macrophages play major roles in neuroinflammation after ischemic stroke. To characterize these roles, we explored how these cells affect counterpart's differentiation, polarization and infiltration or migration. BV2 (microglia cell line) were treated with lipopolysaccharides (LPS) or interleukin-4 (IL-4), and the supernatant was collected as M1 or M2 conditioned media of BV2. The supernatant of PMA differentiated THP-1 (monocyte cell line) followed by LPS treatment or interleukin-13 (IL-13) & IL-4 co-treatment was collected as M1 or M2 conditioned media of THP-1. After BV2 or THP-1 cultured in conditioned media, the activation and polarization were assessed by ICC and confocal microscopy for CD11b, CD86 and CD206. Transwell inserts of 3 and 8 μm pore membrane were used for THP-1 infiltration and BV2 migration assay. M1/M2 conditioned media of BV2 and THP-1 and the brain tissue of ischemic mouse model were assessed by proteome profiler array (PPA) to find target cytokine and chemokine. THP-1 and BV2 expressed CD206 in M2 conditioned media of BV2 or THP-1. M2 conditioned media of BV2 increased the infiltratory ability of THP-1 while M1 conditioned media of THP-1 enhanced BV2 migration. MIP-2 was significantly expressed in the M1 conditioned media of BV2 and MIP-1a was high in the M2 conditioned media of BV2. MIF and CCL5 were highly expressed in M1 and M2 conditioned media of THP-1, particularly in M1. After ischemic stroke, chemokines were significantly expressed at 3 days than at 7 days in the PPA and several spots were match to the conditioned media of BV2. Our study suggests a new insight into the interaction of microglia and monocyte through their ability to expression of cytokine and chemokine after ischemic stroke. Modulation of microglial and monocyte by key cytokine and chemokine represents huge potential for new therapeutic strategies in acute brain injury. "This research was supported by the Brain Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning(NRF-2016M3C7A1905098)"

Keywords: Macrophages, Microglia, Chemokine, Polarization

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P128

A New Behavior Test for Suicide Attempt based on impulsivity derived from chronic stress

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Suicide is a type of death, causing serious social problem in worldwide. Increased impulsivity in depression has been considered a cause of suicide attempt. However, the correlation between depression and suicidal behavior is not revealed yet, because experimental animal model is not available. Therefore, we tried to develop an experimental animal model, named as suicide attempt test (SAT). We tried to reveal the biological mechanisms underlying suicidal attempts of depressed animals. Mice were educated for life-threatening experience, subjected to chronic stress regimen to induce depressivenss, and tested for their impulsivity. The depressiveness was confirmed using sucrose preference test and tail suspension test. To validate correlations of SAT and previous clinical studies of depression suicidal attempts, corticosterone, ERK1/2, GFAP and glutamine synthetase (GS) were analyzed. In SAT, 25 % of depressed mice jumped into ice-cold water, a life-threatening environment, which could be considered as suicide attempt. This result is similar to statistics of suicidal attempts of depressed patients. Blood corticosterone level was elevated, GFAP expression and Erk1/2 phosphorylation were reduced with no significant difference in GS expression. These results were consistent with previous clinical reports. Therefore, these results suggest that SAT could be used as an experimental animal model in suicide study.

Keywords: Suicide, Depression, Neuroscience, Behavior test

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Electroacupuncture Enhances the Differentiation of Grafted Mesenchymal Stem Cells Overexpressing TrkB as well as Functional Recovery in a Mouse Model of Ischemic Stroke

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Transplantation with mesenchymal stem cells (MSCs) has been used to improve functional outcomes in a rodent model of ischemic stroke. This study attempted to graft TrkB gene-modified MSCs (TrkB-MSCs) into the ischemic penumbra and investigate whether therapeutic electroacupuncture (EA) stimulation could promote the survival and differentiation of grafted TrkB-MSCs. EA stimulation with 2 Hz was applied at two acupoints to Baihui (GV20) and Dazhui (GV14) in middle cerebral artery occlusion (MCAO) mice. CM-DiI labeled MSCs, which were isolated and purified from mouse bone marrow, were transplanted into the damaged brain at 5 days after MCAO. We performed behaviour tests after MCAO using corner, cylinder, rotarod, wire grip, and passive avoidance tests. TrkB-MSCs+EA group resulted in significantly improved motor function compared to MSCs+EA group. The largest number of grafted DiIlabeled MSCs were detected in TrkB-MSCs+EA group at 30 days after MCAO. Some of the differentiation into immature neuroblasts, or astrocytes was detected, however there was no significant differences between groups. TrkB-MSCs+EA treatment could lead to higher level of mature brainderived neurotrophic factor (BDNF) more than neurotrophin-4/5 (NT4) in the ischemic striatum. Furthermore, at 60 days poststroke, we observed that TrkB-MSCs+EA group was more differentiated into neuronlike cells than MSCs+EA group. To confirm the specific effects of TrkB, we showed that EA following MCAO+TrkB-MSCs with a selective TrkB antagonist, ANA-12, produced losses of both DiI-labeled MSCs and motor function ameliorated by EA. The present results suggest that grafted TrkB-MSCs combined with EA stimulation can promote the expression of mature BDNF and NT4 in the lesion sites, and further enhance the grafted TrkB-MSCs to differentiate into neuronlike cells, and improve behavioral functions after ischemic stroke.

Keywords: Electroacupuncture, Ischemic stroke, Mesenchymal stem cells, Neuronal differentiation, Neurotrophic factors

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노화 쥐의 뇌혈류저하에 대한 멜라토닌의 개선 효과

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노화는 뇌혈관변성 (Cerebrovascular degeneration) 과 뇌혈류저하 (Cerebral blood flow decrease) 를 유도하는데 이는 정상적인 사람에서도 발견되는 현상이다. 그러나 지속적인 뇌혈류저하는 혈관 확장성 (Vasodilatory capacity) 과 팽창성 (Distensibility) 을 감소시켜 신경 퇴행성 뇌질환(Neurodegenerative disease), 혈관성치매 (Vascular dementia)의 원인이 될 수 있다. 따라서 노화에 의한 뇌혈류저하를 개선하는 방안은 노령화가 진행되고 있는 우리나라에서 반드시 필요한 연구라 할 수 있다. 본 연구팀은 선행연구를 통해 정상적인 노화 쥐에서 연막 혈관 (Pial artery)의 변형과 뇌혈류저하를 확인하였고, 뇌혈관의 탄성을 구성하는 단백질인 콜라겐 (Collagen) 과 엘라스틴 (Elastin) 의 발현 변화를 보고하였다. 멜라토닌 (Melatonin) 은 송과선 (Pineal gland) 에서 분비되는 생체시계 (Circadian rhythm) 를 조절하는 호르몬으로 대표적인 Free radical scavenger, 항산화제 (Antioxidant)이기도 하다. 멜라토닌 수용체 (Melatonin receptor) MT1과 MT2를 통해 멜라토닌은 항산화 효과 외에도 혈관의 수축 (Vasoconstriction)과 확장(Vasodilation)에도 관여하는 것으로 밝혀졌다. 이에 본 연구는 12개월 된 수컷 BALB/c 마우스에 멜라토닌을 희석한 물 (10 mg/ml with ethanol; dilute in water) 을 4개월간 자유롭게 섭취할 수 있도록 하고 한달 간격으로 인도시아닌 그린 (Indocyanine green; ICG) 을 이용하여 혈류를 측정하였다. 혈류 측정은 일반적인 노화 쥐 (Normal aging mice; sham control) 그룹과 멜라토닌을 섭취한 노화 쥐 (Melatonin-treated aging mice) 그룹으로 나누어 실시한다. 이후 MTT (mean transit time), BFI (blood flow

index), Trising (the time between of the first appearance of ICG fluorescence) 와 같은 매개변수 (Parameter) 로 혈류를 분석한다. 분석결과 일반적인 노화 쥐 그룹보다 멜라토닌을 섭취한 노화 쥐 그룹에서 MTT와 Trising가 유의하게 감소하는 것을 확인하였다. BFI 또한 멜라토닌을 섭취한 노화 쥐 그룹에서 증가하는 것으로 보아, 멜라토닌이 노화 쥐에서 나타나는 뇌혈류저하를 개선할 수 있는 잠재적 가능성을 가진 것으로 사료된다. 이 연구는 2016년 정부 (교육부) 재원으로 한국연구재단의 기초과학지원사업의 지원을 받아 수행되었다 (NRF-2016R1A2B4011607).

Keywords: 노화, 멜라토닌, 인도시아닌그린, 뇌혈류저하

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Scalp-Acupuncture Enhances Functional Improvements via Proliferation and Differentiation of Neural Progenitor Cells in Neonatal Hypoxia-Ischemia of Rats

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Neonatal hypoxia-ischemia (HI) is a devastating perinatal injury resulting in severe neurological disabilities such as sensorimotor deficits and memory impairments. Scalp-acupuncture (SA) is one of several specialized acupuncture techniques, which a needles are used to penetrate specific stimulation areas on the cerebral cortex. We investigated whether SA stimulation with three intensities (1, 3, and 5 mA) could promotes functional improvement through proliferation and differentiation of neural progenitor cells in a neonatal HI model. In rotarod and cylinder tests, all SA groups resulted in improved motor function after HI. In particular, SA stimulation with 3 mA intensity (SA2) significantly enhanced functional outcomes including the recovery of depression and memory dysfunction compared to other groups by open field and passive avoidance tests. We found that SA2 group resulted in significantly increased thickness of the corpus callosum (CC) compared to HI. Moreover, SA2 group showed an increase in the number of BrdUdouble labeling positive cells with 2',3'cyclic nucleotide 3'phosphodiesterase (CNPase), glial fibrillary acidic protein (GFAP), or neuronal nuclei (NeuN) in CC, subventricular zone (SVZ) and dentate gyrus (DG), especially BrdU/NeuNpositive cells in the DG were remarkable. Our western blot analysis demonstrated that SA2 group resulted in significantly increased the expression levels of mature neuron and oligodendrocyte makers in the CC and DG, but not astrocyte marker. These results suggest that SA stimulation with 3 mA intensity may promote functional improvement through proliferation and differentiation of neural progenitor cells after neonatal hypoxic ischemia.

Keywords: Neonatal Hypoxia-Ischemia, Scalp-Acupuncture, Neurogenesis

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Localization of Calcium Binding Proteins Immunoreactivities in the Inferior Colliculus and Superior Olivary Complex of Circling Mice

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The circling mice are known as an animal deafness model with tmie gene mutation, which showed hyperactive circling movement. Recently, the reinvestigation of circling mouse was performed to check the inner ear pathology as a main lesion of early hearing loss. In this trial, the inner ear organs were not so damaged to cause the hearing deficit of circling (cir/cir) mouse at 18 postnatal day (P18) though auditory brainstem response (ABR) data indicated hearing loss of cir/cir mice at P18. Thus, another mechanism may be correlated with the early hearing loss of cir/cir mice at P18. Hearing loss in the early

life can disrupt the ascending and descending information in the superior olivary complex (SOC) regions, at which sound information from the two ears is integrated and mainly relayed to the nuclei of the lateral lemniscus and the inferior colliculus (IC). There were many reports that hearing loss could result in the changes in Ca2+ concentration by either cochlear ablation or genetic defect. However, little was known to be reported about the correlation between the pathology of IC and Ca2+ changes in circling mice. Therefore, the present study investigated the distribution of calcium binding proteins (CaBPs), calbindin D-28k (CB), parvalbumin (PV), and calretinin (CR) immunoreactivity (IR) in the SOC and IC to compare among wild-type (+/+), heterozygous (+/cir), and homozygous (cir/cir) mice by immunohistochemistry. The decreases of CaBPs IR in cir/cir were statistically significant in the neurons as well as neuropil of IC. Thus, this study proposed overall distributional alteration of CaBPs IR in the SOC and IC caused by early hearing defect and might be helpful to elucidate the pathology of central auditory disorder related with Ca2+ metabolism. Acknowledgments: This study was supported by Research institute for Convergence of biomedical science and technology (30-2016-000), Pusan National University Yangsan Hospital.

Keywords: Circling mice, Calbindin D28-k, Parvalbumin, Calretinin, Deafness

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Asarone improves motor functional recovery via promoting differentiation of transplanted neural progenitor cells in a mouse model of ischemic stroke

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Neural progenitor cells (NPCs) are able to proliferate and differentiate into diverse cell types of CNS, i.e. neurons, astrocytes, or oligodendrocytes. Transplantation of NPCs has also been shown to be effective for treating ischemic stroke. Our preliminary results show that asarone is capable of NPCs proliferation and differentiation into the neuronal cell types in vitro. This study investigated whether asarone could enhance functional improvement via the differentiation of transplanted NPCs in a mouse model of transient middle cerebral artery occlusion (MCAO). First, CM-Dil labeled NPCs, isolated from mouse embryos cortex, were infused unilaterally into ipsilateral striatum. We performed behavioral tests including corner test and rotarod at 14 and 28 days after MCAO. NPCs+asarone group resulted in synergistic effects on motor function improvement compared to NPCs or asarone alone group after stroke. The largest number of transplanted DiI-labeled NPCs were detected in NPCs+asarone group at 30 days after MCAO. Following immunofluorescent assay, we observed that asarone mainly promoted neuronal differentiation of the transplanted NPCs in the ischemic striatum, and some differentiated into astrocytes. These results indicated that asarone can promote NPCs proliferation and differentiation. The synergistic effect of NPCs and asarone resulted in differentiation into neurons in the ipsilateral striatum, and further enhance behavioral functions after ischemic stroke.

Keywords: Asarone, Ischemic stroke, Neural progenitor cells, Neuronal differentiation

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Neuroprotective Effect Of Grateloupia Elliptica Holmes On An Ischemic Stroke Via Inhibition Of Apoptosis

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The aim of the study is verifying the neuroprotective effect of extract of Grateloupia Elliptica Holmes (GEH) in vivo and in vitro model of ischemic stroke. To prove the hypothesis, male Sprague Dawley rats were orally administrated with GEH (100 and 500 mg/kg for low and high dose, respectively) for 3 days before the induction of permanent middle cerebral artery occlusion (pMCAO). At 24 and 48 hrs after pMCAO, extent of pMCAO-induced sensorimotor deficit were assessed using neurological deficit scoring, grip strength test, and wire hanging test. At the end of these (48 hrs after pMCAO), the infarct volume was evaluated with 2,3,5-Triphenyltetrazolium chloride (TTC) staining. To elucidate the underlying mechanisms, we investigated the involvement of possible modulation on glutamate-induced excitotoxic neuronal damage and subsequent apoptosis by GEH treatment using PC-12 cells, a rat neuroblastoma cell line. The in vivo results indicated that GEH treatment at a dose of 100 and 500 mg/kg significantly diminished the infarct volume. Furthermore, oral intake of GEH significantly attenuated the pMCAO-induced sensorimotor deficits at 24 and 48 hrs after pMCAO in a dose-dependent manner. In vitro results showed that GEH were not toxic up to the concentration of 50 mg/ml on PC-12 cells and pretreatment with 50 mg/ml GEH exerted the neuroprotective effects against excitotoxic neuronal death triggered by subsequent incubation with 7 mM glutamate for 24 hrs. Notably, while the incubation with 7 mM glutamate for 6 hrs elicited the apoptosis pathway in PC-12 cells, the pretreatment with 50 mg/ml GEH for 18 hrs significantly reduced the apoptosis as demonstrated in the results with flow cytometric analysis of Annexin-V/PI staining. Taken together, we suggest oral intake of GEH can exert the therapeutic action against ischemic stroke via a blockade of excitotoxicity-associated neuronal apoptosis.

Keywords: Grateloupia Elliptica Holmes, Permanent middle cerebral artery occlusion, Glutamate-induced excitotoxicity, Blood brain barrier breakdown, Mitochondria-dependent neuronal apoptosis

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Comparing Cellular Structures Between Neural Stem Cells And Cancer Stem Cells

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It has been hypothesized that the origin of brain cancer stem cells (CSCs) might be neural stem cells (NSCs), because there are many similar characteristics between brain CSCs and NSCs, which contain self-renewal, differentiation potential, and microenvironment. Despite of these similarities, the cellular structures between brain CSCs and NSCs have not been well defined. Previously, we reported the primary isolation and characterization of adult human multipotent neural cells (ahMNCs) which showed similar characteristics of NSCs. In this study, we investigated the ultra-structural differences between brain CSCs and ahMNCs using electron microscope. Moreover, we quantitated the size of cellular body using scanning electron microscope (SEM). As results, the shape, differentiation ratio, and the size of cellular body were similar, which suggested the structural similarities between brain CSCs and ahMNCs. Human derived neural stem cells(NSCs) and cancer stem cells(CSCs) were used three lines and cultured for 0 day to 5 days in 12well. Differentiated cell culture medium was added to IBMX. We observed the un-differentiation/differentiation cells using scanning electron microscope(SEM). we compared 4day cells about cell-body size, differentiation ratio. As a result, NSCs and CSCs were similar of the shape, differentiation ratio and cell-body size. Oligodendrocyte and astrocyte in differentiated NSCs/CSCs show more percentage than neuron. In other words, the relationship between NSCs and CSCs was found to be structurally related.

Keywords: Neural stem cell, Cancer stem cell, Scanning electron microscope

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A Study on The Distribution of Multiple Neurons in Hypothalamic Arcuate Nucleus(ARC) and Lateral Hypothalamic Area(LHA): Comparative Study of Human and Mouse

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The hypothalamic Arcuate Nucleus(ARC) is well known as the area for homeostasis of appetite, and Lateral Hypothalamic Area(LHA) was identified as a critical neuroanatomical substrate for motivated behavior. Agouti-related peptide (AgRP) and Pro-opiomelanocortin (POMC) neurons are the major regulator of appetite in ARC. In a previous study with mouse hypothalamus, Glucagon-like peptide-1 receptor (GLP-1R) whose agonist has potent appetite reduction effect was co-localized with POMC neurons but not with AgRP neurons. Gamma-aminobutyric acids(GABA) neurons are the major regulator of reward system in LHA. Several rodent studies suggest that these GABA neurons expressing Leptin receptor (LeptinR) regulate food reward. However, only few studies investigated GLP-1R expression in AgRP and POMC neurons and LeptinR expression in GABA neurons in human hypothalamus. First, we investigated hypothalamic ARC and LHA by Nissl staining in human brain. Then we identified the POMC neurons, AgRP neurons, and LeptinR neurons in human hypothalamus by immunohistochemistry(IHC). We then investigated the distribution of GLP-1R in ARC and the co-localization of LeptinR with GABA neurons in LHA. As known from rodent studies, GLP-1R co-localizes with POMC neurons but not with NPY neurons although the intracellular distribution is diverse. Also, we found several GABA neurons with LeptinR in both rodent hypothalamic LHA and Human hypothalamic LHA. The neuronal distribution of GLP-1R and leptin receptor showed similar patterns in ARC and LHA, between mouse and human. Our findings imply conserved functionality between rodents and humans regarding neuronal regulation of metabolism.

Keywords: Neuroscience

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Combination of Electroacupuncture and Treadmill Training Enhances Motor Function via Oligodendrogenesis from Neonatal Hypoxia-ischemia Rat Model

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In neonatal hypoxia ischemia rat model, we investigated that combination of EA and TM (EATM) treatment have synergic effect to recovery behavior related to motor dysfunction. We also, investigated the expression of markers associated with oligodendrocyte in the corpus callosum (CC) and whether it was related to expression of brain-derived neurotrophic factor (BDNF). On postnatal day 7, rat pups were subjected to left common carotid artery ligation followed by 2h 30min of hypoxia (8% O2). After 14 days, EA treatment (2Hz, 1mA) performed three times per week and TM training performed five times per week for 3 weeks. For proliferative cell labelling, we performed intraperitoneal injection of 5-bromo-2'-deoxyuridine solution for a week. The motor dysfunction was evaluated by behavior tests, such as cylinder, rotarod and cat walk test. Histological and molecular change of EA and TM treatment on hypoxia ischemia were assessed by immunofluorescence staining and western blot analysis. EATM treatment significantly improved motor function compared to hypoxia ischemia rats. EATM treatment showed an increase of thickness and expression of myelin basic protein (MBP) in the CC compared to hypoxia ischemia rat. Proliferation of neuronal/glial antigen (NG2) and 2'3'-cyclic-nucleotide 3'-phosphodiesterase (CNPase)-positive cells was significantly increased, also phosphorylated cAMP-response element binding protein (pCREB)/NG2 and CNPase double positive cells was increased in CC compared to group treated EA or TM training only. Furthermore, expression level

of mature BDNF was increased in contralateral cortex. These data indicated that combination treatment of EA and TM training have synergic effect to enhance motor function, via oligodendrogenesis in neonatal hypoxia ischemia. It is due to increased expression of mature BDNF, and subsequent activation of transcription factor, CREB.

Keywords: Neonatal hypoxia-ischemia, Electroacupuncture, Treadmill, Oligodendrogenesis, Brain-derived neurotrophic factor

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Confirmation for behavioral and pathophysiological phenotype following the mild ischemic stroke by MCAo

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Stroke is the leading cause of morbidity and mortality worldwide. The most common causes of death in Korea is cancer, heart failure, and stroke. Among them, the ratio of stroke is increasing every year, thus, more and more people suffering from stroke as well. Especially, about 10% of stroke cases lead to epilepsy, and repeated strokes lead to vascular dementia. So, there is increasing interest in clearing the underlying pathological mechanisms and identifying possible treatment strategies. In rats, temporary occlusion of the middle cerebral artery (MCA) closely resembles reversible human ischemic stroke. The aim of this study is to investigate the phenotype after mild MCAo. The focal cerebral ischemia was induced by 30min of MCAo in adult rat. All rats were tested on a variety of functionality and electrophysiology over a period of two weeks following surgery. To confirm the infarct volume, TTC stain, Nissl stain, and immunohistochemistry were performed and locomotor activity was decreased in the open field test. Whereas, in a series of memory and cognition test, experimental group have had low cognition and spatial learning function, Moreover, in light-dark box and elevated plus maze tests, anxiety level is increased compared with control group. TTC stain was performed for checking the actual infarct size, and as a result, 17% of whole brain was infarcted. Indeed, we confirmed throughout Nissl stain because of cross-check with the TTC stain result. Immunoreactivities for glial fibrillary acidic protein (GFAP) was shown the absences of GFAP-positive astrocyte in core area, whereas its distributional pattern was changed as degraded morphological feature in the penumbra. Thus, our result using this animal as mild stroke model is suitable for clinical application of future experiments. Therefore, it may utilize as standard feature of phenotype following MCAo for our next step of clinical study. Support: This research was supported by the National Research Foundation of Korea(NRF) funded by the Korea government(NEST)(2017R1D1A1B05036195 and 2017R1C1B5017801)

Keywords: Stroke, MCAo, GFAP, Ischemia, Behavior

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Reversibility of Morphological Change of Dopaminergic Amacrine Cell in Strobe Rat Model

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We previously reported that morphology and number of dopaminergic amacrine cells were changed under continuous strobe light stimulation in rat model (daily 12 h strobe light (2 Hz)/dark cycle). This study was designed to test whether strobe light stimuli during limited time period also cause the changes of dopaminergic amacrine cells, and if so, how long does it takes to recovery under normal light. Forty litters of SD rats were used. From eye opening (postnatal days 12), a half of them (control group) were maintained on daily 12h light/dark cycle, while the remainder, strobe light reared group animals were raised under 12 h strobe light (2 Hz)/dark cycle for 2 weeks. After 2 weeks of strobe light stimulation, all the animals were raised under normal light (12h light/dark cycle). Retinas were

taken at postnatal days 28, 42, 56 and 70 (P 4, 6, 8 and 10 weeks, respectively). In strobe reared retina, type I TH-IR cell showed decreased number and larger somata in whole-mount preparation at P6w. However, number and morphology of type I TH-IR cell was not significantly different at P10w. Dopamine was decreased at P4w. These results demonstrate that strobe light during short period also cause morphological change of dopaminergic amacrine cells, but the changed cell can restore their morphology after stopping the strobe light.

Keywords: Strobe Light, Myopia, Dopamine

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Influence of behavioral and recognition in the hippocampus following chronic renal insufficiency

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Chronic kidney disease (CKD) is affected the structure and function of the kidney, lasting for more over 3 months, and lead to albuminuria and reduction in glomerular filtration rate (GFR). Theses CKD is either occurring naturally in humans or induced surgically in rat causes alterations in behavior and motor functions. Clinical studies have demonstrated a high risk for dementia and cognitive impairment in patients with CKD. Moreover, the evidence in animal studies indicates that uremia impairs synaptic transmission in the rat hippocampus. However, the effect of association to behavior, neuropathological and perturb synaptic function in the CKD is imprecision. Therefore in this study, we are identifying the mechanisms that psychomotor functional disorders by renal and synaptic malfunction at the CKD. In the results of this study, we were confirmed body weight and creatinine concentration in CKD models. Furthermore to characterize of behavioral disturbance by cognitive dysfunction, we were experimented behavior test. Compared to control, the CKD group was markedly suppressed locomotor activity and enhanced anxiety. And then working memory was similarly to control but, special working memory of hippocampus dependent was decreased then control and cross-check results of behavior test through local field potential (LFP). In addition, we were investigated field excitatory postsynaptic potential (fEPSP) in the hippocampus for identifying impairs synaptic transmission, observed that resultant slope of fEPSP was markedly reduced more than control level. Morphological investigations in the hippocampus showed sclerotic features of glomeruli by PAS stain and reducing of interneurons by cresyl violet staining at CKD group. Additionally, immunoreactivity of glial fibrillary acidic protein (GFAP) was enhanced that soma and proximal process compared with control. Therefore, our findings in present study indicated that elevations in uremic toxin levels functionally perturb synaptic function of the hippocampus and leads to neuronal cell death and subsequent cognitive dysfunction. Support: This research was supported by the National Research Foundation of Korea(NRF) funded by the Korea government(NEST)(2017R1D-1A1B05036195)

Keywords: Chronic kidney disease, Recognition, Hippocampus, Learning and memory, GFAP

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P141

Protective Effect of Indole-3-Carbinol on Primary Biliary Cirrhosis-induced Hepatic Encephalopathy Though Attenuation of Neuronal Oxidative Stress

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Primary biliary cirrhosis (PBC) commonly accompanies hepatic encephalopathy (HE), which caused by neuronal oxidative stress. Indole-3-carbinol (I3C), a natural dietary component found in cruciferous vegetables, has been reported to exert antioxidant effect. However, to date, protective effects of I3C on PBC-associated HE has not yet demonstrated. In the present study, we examined the protective effect of I3C on HE and its underlying mechanism using PBC rat model that were made with an operation, a bile duct ligation. Adult male Sprague-Dawley rats randomly divided into four groups: Sham (sham-operated), Veh (operated and administered with vehicle), I3C-L (operated and administered with I3C at a low dose), and I3C-H (operated and administered with I3C at a high dose). For I3C-L and –H groups, either 6 or 12 mg/kg of I3C were administered daily via intraperitoneal route for postoperative day (POD) 14, respectively. We revealed that HE was apparently induced in Veh, I3C-L, and –H groups at POD 14 as demonstrated by marked increases in sensorimotor deficit, leakage in blood-brain barrier (BBB), brain edema, and morphological derangement in brain vasculature when compared with Sham group. However, all the values associated with HE significantly attenuated in I3C-L, and –H groups compared with Veh group and these were dose-dependent. Furthermore, it is revealed that the operation triggered the neuronal oxidative damage at POD 14 in cortices of Veh, I3C-L, and –H groups as demonstrated by the results of immunohistochemistry using antibodies against 4-hydroxy-2-nonenal (4-HNE), a marker for lipid peroxidation, and 8-hydroxydeoxyguanosine (8-OHdG), a marker for DNA damage. However, when compared with that of Sham group, neuronal oxidative damage was markedly attenuated in cortices of I3C-L, and –H groups as demonstrated that their 4-HNE- and 8-OHdG-immunoreactivities were both significantly decreased. These were also dose-dependent. Finally, at POD 14, level of catalase, an endogenous antioxidant enzyme, and Akt / Nrf-2, the upstream regulators, were markedly increased in cortical homogenates of I3C-L, and –H groups compared with that of Sham group. Taken together, these data suggests that I3C can protect the brains against the PBC-associated HE, via reducing neuronal oxidative damage and these effects is due to upregulation of antioxidant defense mechanism.

Keywords: Primary biliary cirrhosis, Hepatic encephalopathy, Indole-3-carbinol (I3C), bile duct ligation, Oxidative damage, Nuclear factor erythroid 2–related factor 2 (Nrf-2)

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P143

Neuroprotective Effect Of Grateloupia Elliptica Holmes On A Transient Focal Cerebral Ischemia Via Attenuation Of Neuronal Oxidative Damage

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The aim of the study is verifying the neuroprotective effect of extract of Grateloupia Elliptica Holmes (GEH) against transient focal cerebral ischemia (tFCI). For this, male C57/BL6 mice were orally administrated with GEH (50 and 500 mg/kg for low and high dose, respectively) for 10 days before the surgery, a 2 h of middle cerebral artery occlusion and reperfusion (MCAO/R). At 24 h after MCAO/R, extent of sensorimotor deficits were assessed using neurological deficit scoring, grip strength test, and wire hanging test. At the end of these, the infarct volume were evaluated with 2,3,5-Triphenyltetrazolium chloride (TTC) staining. To elucidate the possible involvement of antioxidant activity of GEH as the underlying mechanism, expression of antioxidant enzymes i.e., superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), and nuclear translocation of their upstream modulator, the nuclear factor erythroid 2–related factor 2 (Nrf-2), were morphologically analysed using immunohistochemistry (IHC). The results indicated that oral intake of GEH at a dose of 50 and 500 mg/kg significantly diminished the infarct volume generated by 2 h of MCAO/R compared with that of vehicle. Furthermore, oral intake of GEH significantly attenuated the tFCI-induced sensorimotor deficits at 24 h after MCAO/R in a dose-dependent manner. Notably, IHC analysis for SOD, CAT, and GPX revealed that oral uptake of GEH for 10 days significantly increased the neuronal expression of Nrf-2 as well as its nuclear translocation. Taken together, we suggests long-term intake of GEH could be beneficial to prevent the tFCI through activation of endogenous antioxidative enzymes.

Keywords: Grateloupia Elliptica Holmes, transient focal cerebral ischemia, middle cerebral artery occlusion and reperfusion, antioxidative enzymes, Nuclear factor erythroid 2–related factor 2

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P144

Glycan Diversity in the Olfactory Mucosa and Vomeronasal Organ of Rats

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Glycans in the epithelium and glands play an important role in cell-to-cell communication and adhesion. The aim of this study was to characterize glycoconjugates in the olfactory mucosa and vomeronasal organs of rats using lectin histochemistry. Glycoconjugates identified by lectin histochemistry were grouped as follows: N acetylglucosamine (s-WGA, WGA, BSL-II, DSL, LEL, STL), mannose (Con A, LCA, PSA), galactose (RCA120, BSL-I, Jacalin, PNA, ECL), N-acetylgalactosamine (VVA, DBA, SBA, and SJA), fucose (UEA-I) and complex type N-glycan (PHA-E and PHA-L) groups. The free border of the olfactory epithleium and vomeronasal sensory epithelium (VSE) was positive for all 21 lectins. However, some lectins were bound on each receptor cells, supporting cells and basal cells with a varying intensity. In the vomeronasal non-sensotry epithelium (VNSE) of rats and other animals, the free border showed staining for all 21 lectins examined, while some lectins were labeled on the ciliated cells. Collectively, we postulate that a variety of glycoconjugates were detected on both olfactory epithelium and VSE, which include N-acetylglucosamine, mannose, galactose, N acetylgalactosamine, fucose, and complex-type N-glycans.

Keywords: Rat, Glycoconjugate, Olfactory Mucosa, Vomeronasal Organ

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P145

Regulation of eye morphogenesis by chemokine signaling

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Collective cell migration is a key mechanism underlying organogenesis, but extracellular signals that regulate this type of cell movement are largely unknown. During vertebrate eye morphogenesis, continuous lateral migration of the neuroepithelial sheet from the ventral midline places the prospective ventral retina in its proper position. Here we show that the chemokine controls this process in Xenopus.

Keywords: central nervous system, morphogenesis

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P146

Comprehensive assessment of human cell quantification injected in mice using immunohistochemistry, real-time PCR, and digital PCR

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In the course of biological therapy development, bio-distribution of human cells sometimes has to be assessed both in investigational new drug application (IND) and in new drug application (NDA) steps. Usually, quantitative real-time PCR (RT-PCR) has been a gold standard method for detection of human cells in experimental animals (bio-distribution study) by Korea Food and Drug Administration (KFDA). However, more accurate and faster methods are needed. In this study, we compared the efficiency and efficacy of immunohistochemistry (IHC), real-time PCR (RT-PCR), and digital PCR (dPCR) in this respect Mice were sacrificed one week after

administration of human immune cells intravenously. Main organs where the cells would be lodged such as the spleen, lymph node, and the lung were obtained. These organs were subjected to paraffin embedding in part and prepared for DNA extraction in part. RT-PCR was performed following the KFDA protocol, and dPCR was conducted using QuantStudio™ 3D digital PCR System. Based on the PCR results, copy number of human DNA (hDNA) were calculated. Tissues were immuno-stained for human immune cells using the avidin-biotin complex (ABC) detection system As results, RT-PCR and dPCR showed similar sensitivity for hDNA detection in animal tissues. However, time consumption was different between these two cases. In dPCR, the copy number could be immediately obtained as automatically calculated by the dPCR System. However, in the case of RT-PCR, certified reference material was needed to calculate the copy number. Quantification of the staining results was difficult. However, information about the exact location of human cells in animal tissues could be easily obtained. Thus, it is desirable to use the immuno-staining, dPCR, and RT-PCR appropriately in combination according to the specific purpose. Acknowledgement: This work was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2015M3A9E6028677).

Keywords: Bio-distribution, Alu, DNA Quantification

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P147

Generation Of Electrical Power Under Human Skin By Subdermal Solar Cell Arrays For Implantable Bioelectronic Devices

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Medical electronic implants can significantly improve people's health and quality of life. These implants are typically powered by batteries, which usually have a finite lifetime and therefore must be replaced periodically using surgical procedures. Recently, subdermal solar cells that can generate electricity by absorbing light transmitted through skin have been proposed as a sustainable electricity source to power medical electronic implants in bodies. However, the results to date have been obtained with animal models. To apply the technology to human beings, electrical performance should be characterized using human skin covering the subdermal solar cells. In this paper, we present electrical performance results (up to 9.05 mW/cm2) of the implantable solar cell array under 59 human skin samples isolated from 10 cadavers. The results indicate that the power densities depend on the thickness and tone of the human skin, e.g., higher power was generated under thinner and brighter skin. The generated power density is high enough to operate currently available medical electronic implants such as pacemakers that require tens of microwatt.

Keywords: Solar cell, Implantable, Medical electronic implants, Human skin, Bioelectronic devices

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P148

PKCK2/STAMP2/FSP27-mediated Sequestration Of Free Fatty Acids In Lipid Droplets Rescues Chondrocytes

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Although several previous studies reported a causal relationship between free fatty acids (FFAs) and osteoarthritis pathogenesis, the mechanism by which FFAs exert lipotoxicity in articular chondrocytes remains largely unknown. We here observed that oleate at the usual clinical range does not exert lipotoxicity while oleate at high pathological ranges exerted lipotoxicity through apoptosis in articular chondrocytes. By investigating the differential effect of oleate at toxic and nontoxic concentrations, we revealed that lipid droplet

(LD) accumulation confers articular chondrocytes the resistance to lipotoxicity. Using high fat diet-induced osteoarthritis models and articular chondrocytes treated with oleate alone or oleate plus palmitate, we demonstrated that articular chondrocytes gain resistance to lipotoxicity through protein kinase casein kinase 2 (PKCK2)-, six-transmembrane protein of prostate 2 (STAMP2)- and fat-specific protein 27 (FSP27)-mediated LD accumulation. We further observed that the exertion of FFAs-induced lipotoxicity was correlated with the increased concentration of cellular FFAs freed from LDs, whether FFAs are saturated or not. In conclusion, PKCK2/STAMP2/FSP27-mediated sequestration of FFAs in LD rescues osteoarthritic chondrocytes. PKCK2/STAMP2/FSP27 should be considered for interventions against metabolic OA.

Keywords: FSP27, Lipid droplet, Osteoarthritis, PKCK2, STAMP2

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P149

Cilostazol Improves HFD-induced Hepatic Steatosis and Insulin Resistance Through Modulation of Hepatic STAMP2

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Background & Aims: Nonalcoholic fatty liver disease (NAFLD) is an increasingly recognized condition that may progress to end-stage liver disease. Although NAFLD was first described in 1980, a complete understanding of the mechanism and causes of the disease is still lacking. A previous study suggested STAMP2 as a suitable target for NAFLD. Because there is no first-in-class for NAFLD, yet, I performed focused drug-screening to discover STAMP2 augmentor and found that cilostazol could be a potential candidate. In this study, I examined whether cilostazol alleviates NAFLD through STAMP2.
Methods: In vitro pharmacological efficacy of cilostazol on STAMP2 expression and lipid accumulation was analyzed in HepG2 cell lines. For in vivo study, male C57BL/6 mice which were fed 15 weeks after standard diet (SD) or high-fat-diet (HFD) were randomly divided into four groups: (1) mice fed SD with vehicle; (2) mice fed SD with cilostazol; (3) mice fed HFD with vehicle; (4) mice fed HFD with cilostazol. Vehicle (DMSO) or cilostazol (30 mg/kg) was orally administered once daily for 9 weeks.
Results: Cilostazol reverted oleic acid-induced downregulation of STAMP2 expression in HepG2 cells in vitro. Cilostazol treatment ameliorated lipid accumulation induced by oleic acid and this effect was diminished when STAMP2 was silenced by small interference RNA. Cilostazol significantly enhanced hepatic STAMP2 expression in vivo. Cilostazol administration attenuated hepatic steatosis and insulin resistance in HFD-fed mice.
Conclusions: Cilostazol ameliorated hepatic steatosis and insulin resistance through enhancing hepatic STAMP2 expression. Enhancing STAMP2 expression with cilostazol represents a potential therapeutic avenue for treatment of NAFLD.

Keywords: Nonalcoholic fatty liver disease (NAFLD), Cilostazol, STAMP2, High-fat-diet (HFD), HepG2

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The study of ancient DNAs from human skeletons

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The biological remains excavated from burials or soil have been studied recently for the analysis of genetic informations. Two DNA types are widely used, ie mitochondiral DNA and nuclear DNA. The nuclear DNAs are composed with autosomal and sex chrosomes. The genetic markers mainly studied are STR and SNP. SNP markers are mutating elements over long time duration. And STR markers are mutating with short time duration. STRs markers have been used for two decades. There two types of STR markers: autosomal STR and Y chromosomal STR. the mitochondrial DNA are inherited only through maternal lineage. The Y chromosomal DNA is inherited only through pateral lineage. We have studied with ancient human DNA from the skeletons. The extracted and highly purified

DNAs with least PCR inhibitors are essential for successful PCR results. We present some results of our study with one decads including mitochondrial haplotypes, Y chromosome haplogroups, autosomal STR, Y STR, some genetic variations of color phoenotypes and kinship analysis.

Keywords: Ancient Human DNA Mitochondria Nucleus

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P151

GlcNAc Kinase Increases O-GlcNAc Level and Beating Rate of NRVM and Reduces ROS in H9C2 Cells

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O-linked N-acetyl-β-D-glucosamine (O-GlcNAc) is a dynamic post-translational modification of serine and/or threonine residues in diverse nucleocytoplasmic and mitochondrial proteins. Since recent studies have indicated that the sugar moiety O-GlcNAc is further phosphorylated to produce O-GlcNAc-6-phosphate, we investigated the effects of GlcNAc kinase (NAGK) in cultured cardiomyocytes. Exogenous expression of DsRed-tagged NAGK in neonatal rat ventricular myocytes (NRVMs) increased GlcNAc immunocytochemial signals and the beating rate. The primary NRVM and L6 myogenic line were very resistant to hypoxia (12 hr in 1% O2, 37°C). In contrast, H9C2, a myocardiocyte cell line, was relatively susceptible to hypoxia and thus appropriate for assessing the cytoprotective effects of NAGK in hypoxia/reoxygenation (H/R) injury. Exogenous expression of NAGK reduced the reactive oxygen species (ROS) levels after H/R in H9C2 cells, and this effect was abolished by a short hairpin (sh) RNA to NAGK. Scatter plots revealed that the ROS levels of each cell was in a linear descending or ascending trend with the expression levels of DsRed-NAGK or shRNA, respectively. NAGK increases intracellular O-GlcNAc level and the beating rate of NRVM, which helps the H9C2 cells overcome hypoxic shocks by reducing ROS levels.

Keywords: H/R injury, NAGK, NRVM, O-GlcNAc, ROS

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Fluorescent Labeling of Protein Using Blue-Emitting BODIPY derivatives

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Fluorescence is the emission of light by a substance that has absorbed light, and has been widely used in basic science; biology, chemistry, bioimaging, anatomy, and so on. In a part of application, a protein labeling based on fluorescence has come into spotlight in many research field because of its simplicity and high sensitivity with reliability. Visualization of protein movements has a great potential to reveal protein functions, dynamics, and behaviors. So far, a variety of protein labeling technics and materials have been developed. In this study, we disclosed a new protein labeling material that have bright blue fluorescence. The development of blue-emitting material for protein labeling have been rarely explored while it is important for studying biological system. A new blue-emitting material, 8-amino-BODIPY (boron-dipyrromethane), showed valuable properties such as (i) sharp and intense absorption and fluorescence emission peaks, (ii) emission wavelengths insensitive to solvent, (iii) high photo-stability, (iv) compact structure, (v) selective labeling of specific amino acid such as cysteine or lysine, and (vi) mild labeling condition. We demonstrated the protein labeling using 8-amino-BODIPY derivatives for the bovine serum albumin (BSA) and lysozyme as model proteins, and verified the labeling via chromatography (HPLC) and mass spectroscopy (MALDI-TOF) analysis. We believe our new materials would be applicable for studying the protein dynamics in living cells and tissues, and fluorescence resonance study with intrinsic fluorescent biomolecules.

Keywords: Protein labeling, Fluorescence labeling, BODIPY dye, Blue-emitting BODIPY

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Methylglyoxal-Induced Apoptosis Is Dependent On The Suppression Of c-FLIPL Expression Via The Downregulation Of p65 In Endothelial Cells

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Methylglyoxal (MGO) is a reactive dicarbonyl metabolite of glucose and its plasma levels are elevated in diabetic patients. Studies have shown that MGO combines with the amino and sulfhydryl groups of proteins to form stable advanced glycation end products (AGEs), which are associated with vascular endothelial cell (EC) injury and may contribute to the progression of atherosclerosis. In the present study, MGO induced apoptosis in a dose-dependent manner in HUVECs, which was attenuated by a pretreatment with z-VAD, a pancaspase inhibitor. Treatment with MGO increased the ROS levels, which was followed by the dose-dependent down-regulation of c-FLIPL. In addition, a pretreatment with the ROS scavenger, NAC, prevented the MGO-induced downregulation of p65 and c-FLIPL, and the forced expression of c-FLIPL attenuated MGO-mediated apoptosis. Furthermore, MGO induced apoptotic cell death in the endothelium isolated from mouse aortas. Finally, MGO was found to induce apoptosis by downregulating p65 expression at both the transcriptional and posttranslational levels, and thus, to inhibit c-FLIPL mRNA expression by suppressing the NF-kB transcriptional activity. Collectively, this study showed that MGO-induced apoptosis is dependent on c-FLIPL down-regulation via ROS-mediated downregulation of p65 expression in endothelial cells.

Keywords: Methylglyoxal, HUVECs, c-FLIPL, p65, ROS

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P154

Proangiogenic Capacity of RGD-SLAY-containing Osteopontin Icosamer in the Endothelial Cells and in the Postischemic Brain

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Osteopontin (OPN) is a phosphorylated glycoprotein that is secreted into body fluids by various cell types. OPN contains arginine-glycine-aspartate (RGD) and serine-leucine-alanine-tyrosine (SLAY) motifs, which bind to several integrins and mediate a wide range of cellular processes. In the present study, the authors examined the pro-angiogenic effects of a 20 amino acid OPN peptide (OPNpt20) containing RGD and SLAY motifs in human umbilical vein endothelial cells (HUVECs) and in a rat focal cerebral ischemia model. It was found OPNpt20 exerted robust pro-angiogenic effects in HUVECs by promoting proliferation, migration, and tube formation. However, these effects were significantly reduced in OPNpt20-RAA (RGD->RAA)-treated cells but only slightly reduced in OPNpt20-SLAA (SLAY->SLAA)-treated cells. Interestingly, a mutant peptide without both motifs failed to induce the above-mentioned pro-angiogenic processes, indicating the RGD motif is crucial and SLAY also plays a role. In OPNpt20-treated HUVEC cultures, AKT and ERK signaling pathways were activated, but activations of these pathways and tube formation were suppressed by anti-αvβ3 antibody, indicating that OPNpt20 stimulates angiogenesis via αvβ3 integrin/AKT and ERK pathways. The pro-angiogenic function of OPNpt20 was further confirmed in a rat middle cerebral artery occlusion (MCAO) model. Total vessel length and vessel densities were markedly greater in OPNpt20-treated ischemic brains and this was accompanied by inductions of pro-angiogenic makers. Together these results demonstrate that the 20-amino acid OPN peptide containing RGD and SLAY motifs exerts pro-angiogenic effects, wherein both motifs play important roles, and suggest these effects contribute to the neuroprotective effects of this peptide in the post-

ischemic brain.

Keywords: Osteopontin icosamer, RGD, SLAY, Pro-angiogenesis, MCAO

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3D Culture of Thymic Epithelial Cells on Bioactive Fish Collagen/ Polycaprolactone Composite Nanofibrous Scaffolds

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Bioactive electrospun nanofibrous scaffolds have been gaining increasing attention as a promising strategy for 3D cell culture and for tissue engineering applications. We constructed a novel composite marine collagen-based (MC/PCL) nanofibrous scaffold by electrospinning method to develop scaffolding materials with outstanding biocompatibility and favorable mechanical strength for 3D culture of thymic epithelial cells (TECs). Nanofibrous scaffolds were characterized using a scanning electron microscope (SEM), and it was revealed that the nanofiber diameters decreased with increasing MC content in the MC/PCL composite nanofibers. The cytocompatibility of the MC/PCL scaffolds was evaluated by SEM, WST-1 assay, confocal microscopy, western blot, and RT-PCR. It was found that the scaffolds not only facilitated the adhesion, spreading, protrusions, and proliferation of TECs but also effectively stimulated the expression of genes and proteins involved in cell adhesion and T cell development. Therefore, these results suggest that the composite MC/PCL nanofibrous scaffolds will be a useful model of 3D cell culture for TECs, and may have wide applicability in the future for 3D cell culture of various cell types and for tissue engineering.

Keywords: Nanofiber, Marine Collagen, Electrospinning, 3D Cell Culture

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A comparison of condyle size in maloc clusion skeletal patterns: using 3D program

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This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government (2016R1D1A1B01008853) This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government(2016R1D1A1B01008853) The condyle is an important part of the temporomandibular joint(TMJ), and its shape and size are related to the development and treatment of temporomandibular joint disorders(TMD). The condyle plays an import role as the primary center of growth in the mandible and serves as the pivot end of the jaw rotating in the skull. Condylar size and volume can be related to final dimensions of the mandibular. The purpose of this study was to assess condylar size in volumetric 3D imaging in patients with class I, class II, class III malocclusions. Our study included 60 patients(mean age 22.8) with skeletal class I, class II and class III(20 patients for one class) of Dankook university dental hospital. CBCT data images were imported and reconstructed into 3D models by an interative medical image control system, Mimics 17.0 software. We evaluated the condylar volume, surface size, width, height, length. The analysis of the condylar measurements of class I patients showed significant gender-wise differences in all the values($p < 0.05$). In class II, there was a significant difference in values of width, length, volume, and surface area between both the genders. In class III, the condylar measurements of men and woman had significant differences in the length, volume, and surface area values. To evaluate the differences among the three experimental groups, the condylar values of men were analyzed. There was a significant difference in the measured values of height, volume, and surface area. Among the three experimental groups, the condylar measurements in women

showed significant differences in height, width, volume, and surface area. we used the Mimics software to check the occlusal state of the patient and measure the size of the condyle by creating a 3D model. it allows the observation of small and narrow areas of the TMJ at multiple angles and provides more accurate measurement results. Through this process, a more accurate classification of malocclusion was possible, and the surface area and volume were measured. This study is expected to be used for determining the connection between malocclusion and condyle as a base line data. This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government(2016R1D1A1B01008853)

Keywords: 3D program, TMJ, Condyle, Malocclusions, Mimics

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In vivo visualization and 3D modeling of the paramagnetic materials using pFMMD

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We designed an experiment to visualize in vivo paramagnetic materials using the two dimensional frequency mixing magnetic detection (2D-FMMD) technique and construct 3D modeling based on 2D images. The middle cerebral artery occlusion (MCAO) and reperfusion injury animal model was prepared and the infarction area was confirmed by 2,3,4-triphenyltetrazolium chloride (TTC) staining. Immunofluorescence labeling against infarcted brain section was conducted by using paramagnetic nano-particle conjugated OX6 (activated microglia marker) antibody. The production of the reactive oxygen species (ROS) from the activated microglia was also demonstrated by means of hydroethidine histochemistry. Finally, we applied 2D-FMMD system to acquire images against infarct brain section treated with the paramagnetic nano-particle conjugated OX6 antibody. After that, 3D modeling was constructed and compared with MRI images. As a result, the infarcted area visualized with TTC staining was consistent with both areas of OX6 immunofluorescent images and of the 2D-FMMD images. These results postulated that FMMD system successfully visualized the paramagnetic materials in the tissue sections. Furthermore, the 3D model obtained from 2D-FMMD images was well consistent with 3D model obtained from MRI images. In this study, we have successfully visualized paramagnetic materials by using our 2D-FMMD system and we could present the promised application of our FMMD system in situ measurement of free radicals from biomaterials.

Keywords: Paramagnetic, Frequency Mixing Magnetic Detection, 3D modeling, Middle cerebral artery occlusion and reperfusion injury

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Development of Virtual Realty Contents for Third Molar Extration

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Medical technology has seen great improvement in recent years with the use of 3D technology. The purpose of this study is to develop dental treatment models and educational simulations for dental procedures such as third molar extraction, which is almost impossible to practice, through optimized dental modeling standardization. In this study, the entire surgical environment, including the operator and the dental hygienist along with the patient at the center, was filmed in a 360° VR format using three GoPro Hero5 Black (4k, 30fps) cameras equipped with Entaniya 220° angle-of-view lenses. In addition, a 3D parallel camera was used to acquire intraoral super close-up images. To compensate for the drawbacks of VR imaging, a stereoscopic image was acquired in the same direction as the viewer's line of vision by directly mounting the 3D head-mounted camera on a 3D printed head strap. 3D video tracks were edited and displayed in a side-by-side format using the Vegas program. Kolor Autopano Video Pro and Autopano Giga were used to sync and stitch the 360° VR clips and to render the clips in 4K (4096*2160,

30fps) resolution through color correction. The final 3D images and 360° VR clips were replayed on Samsung Gear VR. This study consists of the entire process of third molar surgical extraction including the pre-operative procedure, the surgical procedure, and the post-operative procedure. The practical training process is composed of three stages; the first stage when the demonstrator demonstrates the procedure at an appropriate speed without the explanation of an instructor; the second stage when the instructor explains each part of the surgical extraction; and the third stage when the learner acquires the procedure and principle of the procedure while listening to the explanation of the instructor. Through this three-stage process, the learner can check the entire medical procedure. Such a composition enables the learner to confirm conceptual information, detailed surgical procedure and step-by-step procedures as needed. With the development of simulation-based educational model, this study is expected to suggest a new paradigm of future dental industry. This research was financially supported by the Ministry of Trade, Industry and Energy(MOTIE) and Korea Institute for Advancement of Technology(KIAT) through the Research and Development for Regional Industry(R-0006275)

Keywords: VR, Virtual Realty, 3D Images, Third molar extraction, Advanced Dental Industry

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Morphological Characteristics Of The Posterior Malleolus Fragment Ac cording To The Ankle Fracture Patterns: A Computer Tomography Based Study

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Ankle fractures commonly occurred with an overall age- and sex-adjusted incidence rate of 187 per 100,000 at years. Trimalleolar fracture with the posterior malleolus fragment (PMF) accounted for 7% of ankle fracture. Clinical studies have shown that the presence of a posterior malleolus fragment (PMF) is important as prognostic factor or functional outcome in the treatment for ankle fracture. In the few studies to understand morphology of this PMF which have examined using computed tomography (CT), the authors included PMFs arising from ankle fracture and pilon fracture. Also, no study included morphological characteristics of the PMF according to the ankle fracture pattern. The aim of the present study was to evaluate the morphological characteristics of the posterior malleolus fragment (PMF) according to the ankle fracture pattern by Lauge-Hansen classification on the basis of a comprehensive computer tomography. We retrospectively analyzed computer tomography data of 107 patients (107 ankles) who underwent surgery for trimalleolar fracture from January 2012 to December 2014. A total of 76 ankles belong to Supination-^external rotation stage IV (SER group), 31 belong to Pronation-external rotation stage IV (PER group). The type of PMF of two groups was respectively assessed by Haraguchi and Jan Bartonicek classification. The cross angle (α), fragment length ratio (FLR), fragment area ratio (FAR), sagittal angle (θ) and fragment height (FH) were measured as morphologic assessments. Inter- and intra-observer reliabilities were obtained for all radiographic parameters using the intra-class correlation coefficient (ICC). A p-value of <0.05 was="" considered="" statistically="" significant="" span="">The Pearson's chi-square test and Student's t-test were used to compare sex, age and radiologic measurements between SER group and PER group. The Fisher's exact test was used to compare morphological difference according to the previous two classification system for PMF morphology of ankle fracture between two groups. p-values on comparison radiologic measurements between SER group and PER group are calculated by analysis of covariance adjusted for age and Jan Bartonicek. The study was completed with appropriate institutional review board approval. Intraclass correlation coefficients (ICCs) were generated for all radiographic measurements. All measurements were higher than 0.75 (indicating acceptable reliability) and were employed in the study. There was no significant difference in sex, but age was significantly different between the SER and PER groups. When two groups were only categorized using the Jan Bartonicek classification, there was significant difference between the SER and PER groups. The PMF type in SER group had mainly the posterolateral shape, while that in PER group had mainly the psoteromedial two parts or large, posterolateral triangular shape (p= 0.02). The mean cross angle (α) was no significant difference between two groups (SER group = 19.4°, PER group = 17.6°). The mean fragment length ratio and the mean fragment height in PER group were significantly larger than that in SER group (p= 0.024, p=0.006). The mean fragment sagittal angle (θ) in PER group was significantly smaller than that in SER group (p=

0.017). In conclusion, morphological characteristics of the posterior malleolus fragment (PMF) in trimalleolar fracture may differ according to ankle fracture pattern classified by the injury mechanism. With regard to the articular involvement, volume and the vertical nature, the supination-external rotation (SER) type fracture tends to have smaller fragment by rotational force, while pronation-external rotation (PER) type fracture tends to have larger fragment by a combination of rotational and axial forces.

Keywords: Ankle, Posterior Malleolus Fractures, Morphology, Computed Tomography

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Biomimetic 3D Tumor Spheroids to Regulate Malignancy of Human Prostate Cancer Cells

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Conventional 2D prostate cancer cell culture models do not reflect the true biological activities of prostate cancer cells in vivo, and thus drug screening and testing in 3D prostate cancer cell culture models are more effective than conventional 2D monolayer culture system. In the present study, we established a hydrogel-based 3D prostate cancer culture system using various human prostate cancer cell lines (LNCaP, DU145 and PC3). It was found that cells cultured in the hydrogels grow as tumor-like clusters in 3D formation when compared to cells cultured in 2D monolayer culture. Histological examination of all the three types of prostate cancer cells demonstrated the formation of spheroids, whereas none of the cell types in 2D formed any spheroids. RT-PCR, Western blot, drug resistance and immunofluorescence staining analyses revealed that the expression of various genes related with prostate cancer malignancy was significantly up-regulated in all the three types of cells in 3D cell culture when compared to 2D cell culture. Furthermore, increased migration and invasion in all three types of the human prostate cancer cells were observed in cells cultured in 3D compared to those in 2D. Therefore, this study provides a novel hydrogel-based 3D culture technique for human prostate cancer cells that closely mimicked in vivo cancer progression. Furthermore, our data may provide a useful platform technology to develop functional, biocompatible, three-dimensional scaffolds for 3D culture of various cancer cells.

Keywords: 3D Culture, Hydrogel, Tumor Spheroid, Prostate Cancer

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LIF, a novel myokine, protect amyloid-beta-induced neurotoxicity via Akt-mediated autophagy signaling in hippocampal cells

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Leukemia inhibitory factor (LIF) a novel myokine, is known to associate with neural function, however, its underlying molecular mechanism is not clear. Here, we reported that LIF increased Akt phosphorylation in Phosphoinositide 3-kinase (PI3-K) dependent manner in hippocampal cells. LIF also increased the phosphorylation of Mechanistic target of rapamycin (mTOR) and its downstream S6K. In addition, LIF stimulated to phosphorylation of Signal transducer and activator of transcription (STAT) in Extracellular signal-regulated kinases (ERK) dependently. LIF increased Fos expression in both Akt and ERK dependently. Moreover, LIF blocked amyloid β-induced neural viability suppression. Amyloid β-induced glucose uptake impairment was recovered by LIF via blocking amyloid β-mediated insulin receptor downregulation. Furthermore, LIF blocked amyloid β-induced autophagy marker microtubule-associated protein 1A/1B-light chain 3(LC3). In primary prepared hippocampal cells, LIF stimulated of Akt and ERK, demonstrating that LIF has physiological relevance in vivo. Inhibition of amyloid β accumulation and suppression of autophagy marker, LC3 by LIF was observed in a Drosophila Alzheimer model. These results demonstrate that LIF protect amyloid β-induced neurotoxicity via Akt/

ERK-mediated c-Fos induction and thus suggest that LIF could be used as a potential anti-Alzheimer agent.

Keywords: LIF, Akt, autophagy, myokine, Alzheimer's disease

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Mitochondrial NADP+-dependent Isocitrate Dehydrogenase (IDH2) Deficiency Augments Cisplatin-induced Acute Kidney Injury

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Mitochondrial NADP+-dependent isocitrate dehydrogenase (IDH2) is a major producer of NADPH, which plays a critical role in the maintenance of cellular redox balance. Cisplatin is a widely used for the treatment of solid tumors. However, its nephrotoxicity has restricted the use. Here, we investigated the role of IDH2 in cisplatin nephrotoxicity. IDH2 gene-deleted (IDH2-/-) or wild type (IDH2+/+) littermates were treated with cisplatin, intraperitoneally, with or without Mito-TEMPO, a specific scavenger of mitochondrial superoxide. Cisplatin reduced IDH2 activity and expression and NADPH levels in the kidney. IDH2 deficiency aggravated renal functional and morphological impairments after cisplatin administration. Mito-TEMPO reduced those cisplatin-induced renal functional and morphological impairments in both IDH2-/- and IDH2+/+ mice and this reduction was greater in the IDH2-/- mice than in the IDH2+/+ mice. Cisplatin increased hydrogen peroxide levels, lipid peroxidation, and mitochondrial oxidative stress. These increases were greater in the IDH2-/- mouse kidneys than IDH2+/+ mouse kidneys. Mito-TEMPO attenuated those cisplatin-induced changes and the Mito-Tempo effect was greater in IDH2-/- mice than IDH2+/+ mice. These results indicate that cisplatin impairs mitochondrial redox balance, and IDH2 plays a critical role to maintain the mitochondrial redox balance, suggesting that IDH2 could be a critical target molecule to protect cisplatin nephrotoxicity.

Keywords: Cisplatin, Antioxidant, Mitochondria, Acute Kidney Injury

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Scopoletin Partially Stimulates Melanogenesis via p38 Activation

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Scopoletin was recently shown to stimulate melanogenesis through cAMP-response element-binding protein (CREB) phosphorylation. We investigated the molecular events of melanogenesis-induced by scopoletin. After exposure to scopoletin, the protein levels of tyrosinase and tyrosianse related protein-1 (TRP-1) were significantly increased in B16F10 cells. cAMP production and phosphorylation of p38 mitogen-activated protein kinase (MAPK) were increased by scopoletin treatment. Scopoletin-mediated increase of intracellular melanin and tyrosinase expression were significantly attenuated by PKA inhibitors (H-89 and KT5720), while a PKC inhibitor (Ro-32-0432) had no effect and a p38 MAPK inhibitor (SB203580) partially blocked the scopoletin-induced intracellular melanin and tyrosinase expression. Moreover, scopoletin synergistically with cell-permeable cAMP analog (dibutyryl cAMP) significantly induced tyrosinase activity and melanin content in B16F10 cells. The silencing of p38 MAPK by siRNA decreased the scopoletin-induced tyrosinase expression in B16F10 cells. These results suggest that scopoletin could induce melanin synthesis through the cAMP/PKA pathway and partially p38 MAPK activation in B16F10 cells.

Keywords: Scopoletin; Tyrosinase; cAMP; p38 MAPK; p38 MAPK siRNA

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Wheat Sprouts Extract Stimulate Cell Proliferation via Phosphorylation of ERK and Akt in Human Dermal Papilla Cells

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Wheat Sprouts contain a very high level of organic phosphates and a powerful cocktail of antioxidant molecules. We investigated the effect of Wheat Sprouts MeOH extract (WSM) on cell proliferation and analyzed the molecular mechanism in human hair dermal papilla cells (HHDPCs). After exposure to WSM in HHDPCs, cell proliferation was increased compared with minoxidil-treated cells. Treatment with WSM led to phosphorylation of extracellular signal-related kinase (ERK) and Akt. Moreover, WSM-mediated increase of cell proliferation was attenuated by PD98059, ERK inhibitor, and LY294002, Akt inhibitor. These results suggest that WSM induced cell proliferation in HHDPCs through activation of ERK and Akt.

Keywords: Wheat Sprout, HHDPCs, Cell Proliferation, ERK, Akt

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Induction of Inflammation In Vivo by Electrocardiogram Sensor Operation Using Wireless Power Transmission

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Prolonged monitoring by cardiac electrocardiogram (ECG) sensors is useful for patients with emergency heart conditions. However, implant monitoring systems are limited by lack of tissue biocompatibility. Here, an implantable ECG sensor for monitoring ventricular fibrillation in real time was developed, and its biocompatibility was evaluated using an animal model. The implantable sensor comprised transplant sensors with two electrodes, a wireless power transmission system, and a monitoring system. The sensor was inserted into the subcutaneous tissue of the abdominal area and operated for 1 h/day for 5 days using a wireless power system. Importantly, the sensor was encapsulated by subcutaneous tissue and induced angiogenesis, inflammation, and phagocytosis. In addition, we found that inflammation-related markers were upregulated according to the wireless power transmission and ECG sensor. In particular, the Th-1 cytokine interleukin-12 was significantly increased. The experimental results demonstrated that the induced tissue damage was associated with the use of wireless power sensors. We also explored research strategies for the prevention of adverse effects caused by lack of tissue biocompatibility of a wireless power ECG monitoring system and provided information regarding the clinical applications of inflammatory reactions according to implant treatment using the wireless power transmission system.

Keywords: Biocompatibility, Electrocardiogram, Implantable sensor, Wireless power

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Expression and location of HDAC2 in ischemic brain

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It is well defined that epigenetic modification is deeply related with the regulation of gene transcription. Histone acetyltransferases (HATs) and HDACs are two major groups of enzymes modulating histone acetylation. Recent studies indicate that histone deacetylases (HDACs) might be involved in the pathophysiology of stroke. In many studies using HDAC inhibitors including valproic acid (VPA), it seems to be a potential therapeutic candidate against brain ischemia. Especially, VPA, known as a class I HDACs inhibitor, showed neuroprotective

effects in reducing infarct volume and neurological deficits. And also, VPS has been shown to induce the cell survival signaling through inhibition of HDAC. In spite of intensive research, the molecular mechanisms underlying the therapeutic effects of HDAC inhibitors remain unclear. Moreover, we still do not have clear information about the expression and localization of each HDACs in brain. Therefore, in the present research, we investigated the expression and localization of HDAC2 in the normal and ischemic brain. Interestingly, HDAC2 was differentially located in neurons and endothelial cells of normal brain area. In many reports, class I HDACs including HDAC1 and HDAC2, they are generally located in the nucleus. Then, surprisingly, when we performed immunofluorescence analysis, HDAC2 was detected in the nucleus of neuron, but, HDAC2 expression was definitely indicated in cytosol of endothelial cells not nucleus. Moreover, we found that HDAC2 can translocate in ischemic brain neurons, but not in endothelial cells. Especially, nuclear HDAC2 of neurons translocated into the cytosol in neurons of penumbra area. In addition, the expression of HDAC2 was slightly reduced after ischemia in cDNA microarray analysis. Because endothelial HDAC2 was particularly located in cytosol, we tried to inhibit the expression of HDAC2 in endothelial cells using siRNA treatment. When HDAC2 was knockdown, many inflammatory factors including chemokine (C-C motif) ligand 3, chemokine (C-X-C motif) ligand 1, and interleukin 8 were strongly increased. This increased pattern expression coincides with the result from ischemic brain. Based on all of our data, we found that the particular location of HDAC2 in brain endothelial cells and translocation of neuronal HDAC2 in penumbra area of ischemic brain. In addition, change of brain enddothelial HDAC2 expression can affect on the inflammatory factors expression.

Keywords: Brain ischemia, Stroke, Histone Deacetylase, neuron, endothelial cell

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Efficacy of APX-115, a pan-NADPH oxidase inhibitor, on Streptozotocin-induced Rat models

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Objective: Dye eye syndrome (DE) was common ocular disorder of diabetic patients. The symptoms of DE include decreased tear volume, itchy eye, aching sensations, and dryness sensation. We recently reported that APX 115, pan-NADPH oxidase inhibitor, may have an effect on EBV-infected retina epithelial cells, but it's role in DE has not been determined. Therefore, we investigated whether APX 115effected on diabetic rat models with dry eye in this study.
Method: Diabetic rat models was induced in male Sprague Dawley rats by intraperitoneal injection of streptozotocin, and then we treated eyeballs of diabetic rats with eye drop solution contained APX-115 or control solution. Tear secretion was measured with phenol red thread tear test. Morphology of eyeball and lacrimal gland tissues was stained with H&E. In addition, the localization of NADPH oxidase 2 (NOX2), NADPH oxidase 4 (NOX4) and VEGF in the Eyeball and lacrimal gland tissues were detected for immunohistochemistry. The mRNA expression level and protein expression level for NADPH oxidase 2(NOX2), NADPH oxidase 4 (NOX4), and VEGF were measured by real-time PCR and western blot.
Results: APX 115 treatment was no effect on body weight, blood glucose level and sizes of the eyeballs and lacrimal glands. However, morphological changes were found on a component ratio of serous cells and mucous cell in lacrimal glands of diabetic rat and diabetic rat with APX 115. In immunohistochemistry, NOX2 expression level and VEGF expression level were decreased in diabetic rat with APX 115, whereas the outcome of mRNA expression level and protein expression level made no odds.
Conclusion: APX 115 improved the tear secretion and demonstrated positive effects from histological changes, but could not draw molecular changes. These findings suggest that APX 115 indicate a potential therapeutic role for DE.

Keywords: Diabetes Mellitus, Dry eye syndrome, NOX2, VEGF, APX 115

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Methyl Gallate Inhibits Osteoclast Formation and Function by Suppressing Akt and Btk-PLCg2-Ca2+ Signaling and Prevents Lipopolysac charide-Induced Bone Loss

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In the field of bone research, various naturalderivatives have emerged as candidates for osteoporosis treatment by targeting-abnormally elevated osteoclastic activity. Methyl gallate, a plant-derivedphenolic compound, is known to have numerous pharmacological effects againstinflammation, oxidation, and cancer. Our purpose was to explore the relationbetween methyl gallate and bone metabolism. Herein, we performed screeningusing methyl gallate by tartrate resistant acid phosphatase (TRAP) staining andrevealed intracellular mechanisms responsible for methyl gallate-mediated regulationof osteoclastogenesis by western blotting and quantitative reversetranscription PCR (RT-PCR). Furthermore, we assessed the effects of methylgallate on the characteristics of mature osteoclasts. We found that methylgallate significantly suppressed osteoclast formation through Akt andBtk-PLCγ2-Ca2+ signaling. The blockade of these pathways wasconfirmed through transduction of cells with a CA-Akt retrovirus and evaluationof Ca2+ influx intensity (staining with Fluo-3/AM). Indeed, methylgallate downregulated the formation of actin ring-positive osteoclasts andresorption pit areas. In agreement with in vitro results, we found thatadministration of methyl gallate restored osteoporotic phenotype stimulated byacute systemic injection of lipopolysaccharide in vivo according tomicro-computed tomography and histological analysis. Our data strongly indicatethat methyl gallate may be useful for the development of a plant-based antiosteoporoticagent.

Keywords: Methyl gallate, Osteoclast, Akt, Ca2+ signaling, Bone resorption, Osteoporosis

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The Inhibition of Rac1-GTPase Attenuates Kidney Ischemia/reperfusion Injury by Inhibiting Inflammatory Cell Migration

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Rac1, a member of the Rho-family of small GTPases, acts as a regulatory subunit of reduced nicotinamide-adenine dinucleotide phosphate (NADPH) oxidase, which produces reactive oxygen species (ROS). Here, we examined that Rac1 effects cytokine production and the inflammatory response contributing to ischemia/reperfusion (I/R) injury. After I/R, Rac1 expressions in the kidney gradually increased over time. Rac1 expression was greater in the outer medulla, which is most injured part following I/R. During repairing after I/R, Rac1 expression increased in in the interstitial cells which are positive to F4/80, a marker of macrophage, antibody. NSC23766, an inhibitor of Rac1, attenuated renal histological and functional damage after I/R. In addition, NSC23766 attenuated infiltration of inflammatory cells into the damaged site after I/R. NSC23766 inhibited chemoattractant cytokine-induced migration of Raw 264.7, a mouse monocyte/macrophage. These results indicate that Rac1 plays a critical role in infiltration of macrophage to injured part, suggesting that Rac1 represents a potentially useful target for the treatment of acute kidney injury.

Keywords: Rac1-GTPase, Ischemia/reperfusion, NADPH oxidase, Inflammation, macrophage

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Anti-inflammatory and Anti-osteoporotic Effects of Isoflavone-enriched Soybean (Glycine max) Leaf Extracts

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Postmenopausal osteoporosis is a skeletal disease thatis mainly caused by oestrogen deficiency and is generally accompanied by inflammation.Dietary isoflavones have been gaining attention for the treatment of postmenopausalosteoporosis. To investigate the beneficial effects of isoflavone-enrichedsoybean leaves (IESLs) on postmenopausal osteoporosis, lipopolysaccharide(LPS)-stimulated RAW 264.7 cells and ovariectomized (OVX) rats were used toinvestigate the anti-inflammatory and anti-osteoporotic effects of IESLs. The aglycones daidzein and genistein significantly inhibitedLPS-induced inflammation by suppressing the mRNA expression of iNOS, COX-2, IL6,and IL1β.Additionally, the oral administration of IESLs to OVXrats significantly ameliorated OVX-induced bone loss. The anti-osteoporoticactivity of IESLs may contribute to the decrease in osteoclastogenesis bydownregulating the mRNA expression of bone-specificgenes, such as RANKL/OPG, OC, and cathepsin K, as wellas inflammation-related genes, such as IL6, NF-κB, and COX-2. Theseresults demonstrate that IESLs, as functional foods, may protect against postmenopausalosteoporosis.

Keywords: Soybean leaves, Inflammation, Osteoporosis, Ovariectomized rats

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Anti-Osteoporotic Effect of Claudin-11 on Bone Metabolism through Dual Actions on Osteoblast and Osteoclast

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Claudins (Cldns) are well-established components of tight junctions (TJs) that play a pivotal role in the modulation of paracellular permeability. Several studies have explored the physiologic aspects of Cldn family members in bone metabolism. However, the effect of Cldn11, a major component of central nervous system myelin, on bone homeostasis has not been reported. In this study, we demonstrate that Cldn11 is a potential target for bone diseases therapeutics, as a dual modulator of osteogenesis enhancement and osteoclastogenesis inhibition. We found that Cldn11 played a negative role in receptor activator of nuclear factor kappa B ligand-induced osteoclast (OC) differentiation and function by downregulating the phosphorylated form of extracellular signal-regulated kinase (ERK), Bruton's tyrosine kinase, and phospholipase C gamma 2, in turn impeding c-Fos and nuclear factor of activated T cells c1 expression. The enhancement of osteoblast (OB) differentiation by positive feedback of Cldn11 was achieved through the phosphorylation of Smad1/5/8, ERK, and c-Jun amino-terminal kinase. Importantly, this Cldn11-dependent dual event in bone metabolism arose from targeting EphrinB2 ligand reverse signaling into OC and EphB4 receptor forward signaling into OB. In agreement with these in vitro effects, subcutaneous injection of Cldn11 recombinant protein exerted anti-resorbing effects in a lipopolysaccharide (LPS)-induced calvaria bone loss mouse model and increased osteogenic activity in a calvarial bone formation model. These findings suggest that Cldn11 is a novel regulator in bone homeostasis.

Keywords: Claudin-11, Osteoclast, Osteoblast, EphrinB2, EphB4

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P172

Metformin induces cell death through crosstalk between AMPK phosphorylation and O-GlcNAcylation in HeLa cell

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Cancer and diabetes have something in common which need high glucose condition. Recently, anti-diabetes drugs that decrease the blood glucose are known as effective in cancer treatment. Metformin, a diabetic drug, has an effect of reducing blood glucose and there are many researches discussing the effects of metformin in cancer. In this study, we investigated to see whether metformin induces more cell death in cervical cancer cells than in normal keratinocytes. HeLa and HaCaT cell were used in our study. We first performed methyl tetrazolium(MTT) assay to find metformin effect of cell death. Next, we compared the apoptotic cell death of metformin between HeLa cells and HaCaT cells and we found that cancer cell was more sensitive to metformin compared to normal cells using Fluorescence-activated cell sorting(FACS) and western blot analysis. Then, we confirmed cross talk between AMPK phosphorylation and O-GlcNAcylation using immunoprecipition and sWGA. Our data indicated that metformin induced cell cycle arrest by reducing O-GlcNAcylated AMPK. Put together, metformin is effective in regulating of O-GlcNAcylation which are key metabolitic modification in cancer cells and could be used as anti-cancer drug.

Keywords: Metformin, O-GlcNAcylation, AMPK, Cell death, HeLa cell

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Umbelliferone Suppresses Receptor Activator of Nuclear Factor-Kappa B Ligand-induced Osteoclast Differentiation and Bone Resorption In vitro and Restores Lipopolysac charide-Mediated Bone Erosion In vivo

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Umbelliferone (Umb) also known as 7-hydroxycoumarin is a fragrant organic chemical compound derived from plants including Angelica species. Umb has been reported to suppress expression of the pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-a) that have a crucial role in regulation of osteoclast differentiation and bone resorption. However, the effect of umb on bone metabolism has not yet been identified. In this study, we showed that umb suppressed receptor activator of nuclear factor-κB (NF-κB) ligand (RANKL)-induced osteoclast differentiation of bone marrow macrophages (BMMs) and the bone-resorbing activity of mature osteoclasts in osteoblast/osteoclast co-culture system without affecting any cytotoxicity. In agreement with this negative action, umb down-regulated phosphorylation of Akt in RANKL-dependent early signaling pathways and subsequently decreased mRNA level of osteoclast-specific marker genes, such as OSCAR, TRAP, Atp6v0d2, and Cathepsin K. Through using CHX, an inhibitor of protein synthesis and MG132, a selective proteasome inhibitor, we found that umb negatively regulated expression level of c-Fos and NFATc1 by targeting protein degradation of both c-Fos and NFATc1 post translational modification stage with no affecting mRNA level of these two transcription factors. Moreover, oral administration of umb showed marked attenuation of lipopolysaccharide (LPS)-induced bone erosion without any symptom of toxicity in comparison with PBS-treated control group by using micro-computed tomography (m-CT) and histologic analysis of femurs. Accordingly, our study indicates that umb is worth considering as a potential drug which is proven safe to treat metabolic bone diseases, such as osteoporosis.

Keywords: Umbelliferone, Osteoclast, RANKL, c-Fos, NFATc1

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Quercetin induces apoptosis in cervical cancer cell line via inhibiting O-GlcNAcylation

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Quercetin is a naturally occurring dietary flavonoid and has been recognized to reduce risk of chronic diseases such as diabetes and cancer, but the precise mechanism of cancer suppression by quercetin is still unclear. The aim of this study is to investigate the effect of quercetin in cervical cancer. Quercetin induces ctotoxicity in cervical cancer cell line through inhibiting cell proliferation. However, this effect of quercetin was limited in immortalized human keratinocyte cell line. Our results also demonstrated that quercetin inhibits expression of O-linked β-N-acetylglucosamine transferase (OGT) and then, activates AMPK by down regulating its O-GlcNAcylation. Next, we found that hyper-O-GlcNAcylation induced by Thiamet G decreased the activation and phosphorylation of AMPK and hypo-O-GlcNAcylation induced by DON increased the activation and phosphorylation of AMPK. In conclusion, our data suggest that inhibition of AMPK O-GlcNAcylation by quercetin could induce cell death in cervical cancer cell line

Keywords: Quercetin, O-GlcNAcylation, OGT, cervical cancer cell

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Exercise-induced secreted myokine, Chitinase-3-like protein 1, regulates glucose metabolism; implications for an anti-diabetic role

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Chitinase-3-like protein 1 (Chi3l1) is a novel myokine, but the underlying molecular mechanisms are not clear. Here, we report that Chi3l1 stimulates glucose uptake in skeletal muscles in an AMP-activate protein kinase- (AMPK) dependent manner, and increases intracellular calcium levels via protease-activated receptor 2 (PAR2). This increase in calcium was not observed after thapsigargin, Ca2+-ATPase inhibitor, but was still observed in calcium-free media, indicating that the calcium originated from intracellular spaces. Inhibition of calcium/calmodulin-dependent protein kinase kinase (CaMKK) blocked Chi3l1-mediated glucose uptake. In addition, Chi3l1 stimulated glucose uptake through the PI3K-dependent Akt pathway. Inhibition of AMPK did not affect Akt phosphorylation, and vice versa, suggesting that AMPK and Akt are activated independently, but both are involved in glucose uptake. Chi3l1 stimulated phosphorylation of AS160 and p38 MAPK. Knockdown of AMPK and Akt suppressed AS160 phosphorylation, and inhibition of AMPK suppressed p38 MAPK phosphorylation. In primary myoblast cells, AMPK and Akt stimulation was observed in response to Chi3l1. Chi3l1 mRNA levels were elevated in response to electric pulse stimulation in an exercise mimic in vitro model. Moreover, circulating Chi3l1 levels were increased in mice after chronic or acute exercise. These results identify Chi3l1 as a potential anti-diabetic agent for the treatment of type 2 diabetes.

Keywords: Chi3l1, Myokine, Skeletal muscle, AMPK, Glucose uptake

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Exercise-induced ECM Molecule Stimulates AKT Pathway and Improves Metabolic Parameters in Type 2 Diabetes

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The novel muscle-secreted myokine, ECM molecule, is a member of the small leucine-rich proteoglycans (SLRPs) and is potentially involved in glucose metabolism. ECM molecule stimulated L6 glucose uptake in a calcium- and AMPK-dependent manner. ECM molecule-stimulated increase in calcium concentration involved the release of intracellular calcium stores. Inhibition of calcium/calmodulin-dependent protein kinase kinase (CaMKK) blocked ECM molecule-induced AMPK phosphorylation and glucose uptake. ECM molecule also stimulated Akt and AS160 phosphorylation, and knockout of Akt suppressed AMPK phosphorylation, suggesting that Akt acts upstream of AMPK. ECM molecule increased the translocation of GLUT4 to the plasma membrane. Similar results were observed in primary myoblast cultures. The ECM molecule mRNA levels were increased by exercise-mimicking conditions, and amount of ECM molecule were also increased in the serum of exercised mice. Hence, ECM molecule may be a potential therapeutic for the treatment of diabetes.

Keywords: ECM molecule, AKT, Metabolism, Exercise

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Apelin-16, novel myokine, affect insulin sensitizing through AMPK-small GTPase pathway in myoblast cell

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Muscle differentiation is involved in many kinds of biological situation. However this mechanism is very complicated and unclear. Some cytokine is classified as myokine recently. Myokine play for a role in identification of myogenesis. The aim of our study is to identify novel myokine which regulates myogenesis. In results, we found that Apelin-16 increased Ect2, Rac GEF, expression AMPK dependently. In addition, we observed that Apelin-16 increased the expression of LC-3B, autophagy marker. Inhibition of AMPK and knockdown of Ect2 blocked Apelin-16-mediated muscle differentiation. Now, we are currently observing the fact that Apelin-16 enhance insulin-mediated glucose uptake. We hope to understand pathophysiological mechanism of myogenesis regulation role of Apelin-16, and thus to provide to provide the molecular target for the development of treatment drug for related diseases, such as diabetes.

Keywords: AMPK, Small GTPase, Myokine, diabetes

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Development of New Assistant Device for the Stress Radiography and Its Usability Study for the Knees

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In recent years, the knee ligament rupture (KLR) event has been frequently occurred due to the increased population of outdoor activity. To decide criteria of the medical treatment level and disability for KLR patient, the x-ray examination is considered as precise technic. TELOS is a kind of examination equipment for knee stress monitoring, and has been widely used to check stress of bilateral knees. In this study, we developed a new assistant device that can monitor the stress of both side knees at once, and compared the results with TELOS from normal and abnormal cases. We compared the x-ray film, exposure dose and test time from normal and abnormal cases by using the developed device and TELOS. In the x-ray comparison, the images from normal and abnormal patient were not significantly different. The results from a new device, however, the radiation

exposure dose and test time for patient was reduced by 50% and 60%, respectively. In case of the patient with KLR, both results were accurate and easy to compare with the normal and ruptured knees. Moreover, the x-ray result proved that the equal input forces on each knee. Aligned with the normal patient case, they showed 50% of the exposure dose reduction and 65% of the test time. Bilateral knee ligament stress test is an important test for the rupture that can be seen indirectly knee ligaments. So far, TELOS equipment has been used for bilateral knee ligament test, but it is high-priced and show patient's condition dependency such as non-equal input power to both knee. By using our new device, we can reduce the test time and x-ray exposure dose for patient with relieve work strength. Moreover, we also can expect the high accuracy and reliable radiography with affordable price.

Keywords: Varus, Valgus, Assistant Device, X-ray, TELOS

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