재단
법인 **한 곡 의 학 장 학 회**

Hankok Medical Science Foundation (since 1971)

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10. 16 (Wen.)	13:00	Check-In & Registration (호텔 1층 로비)		
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	17:00 ~ 20:00	제69차 대한해부학회 정기이사회 (Grand Ballroom B)		
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Time		Schedule		
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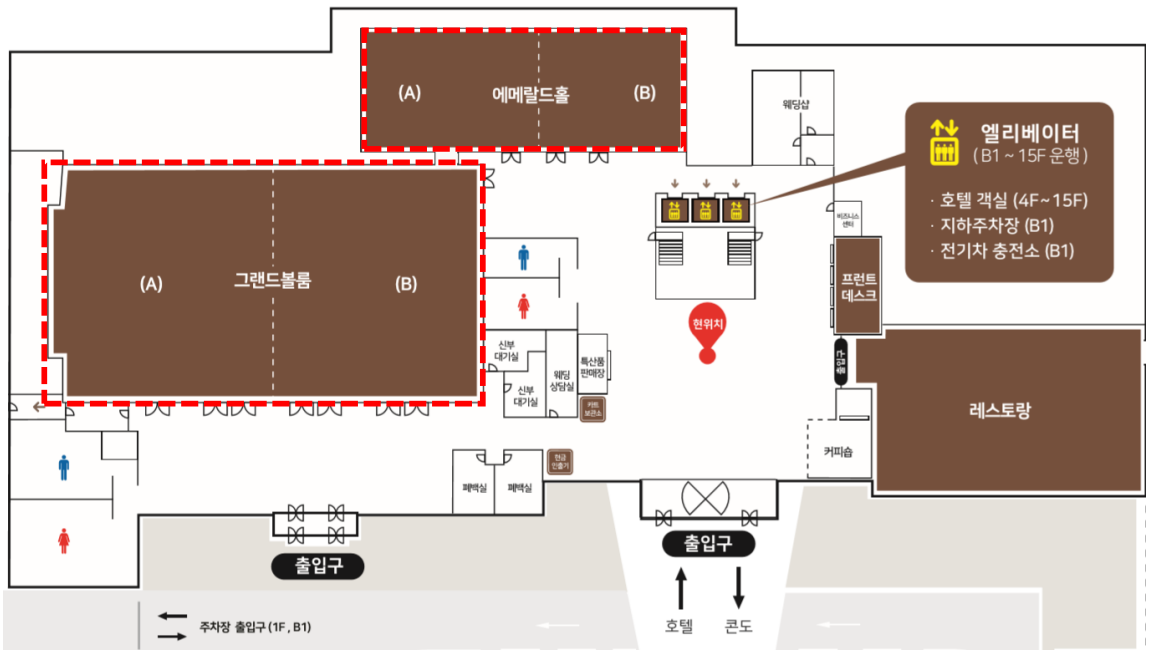
학술대회장 배치도



<그랜드 볼룸 A>

- Plenary Lecture I/II
- Special Lecture I/II
- Symposium I: Gross Anatomy

<그랜드 볼룸 B>

- Luncheon Symposium I/II
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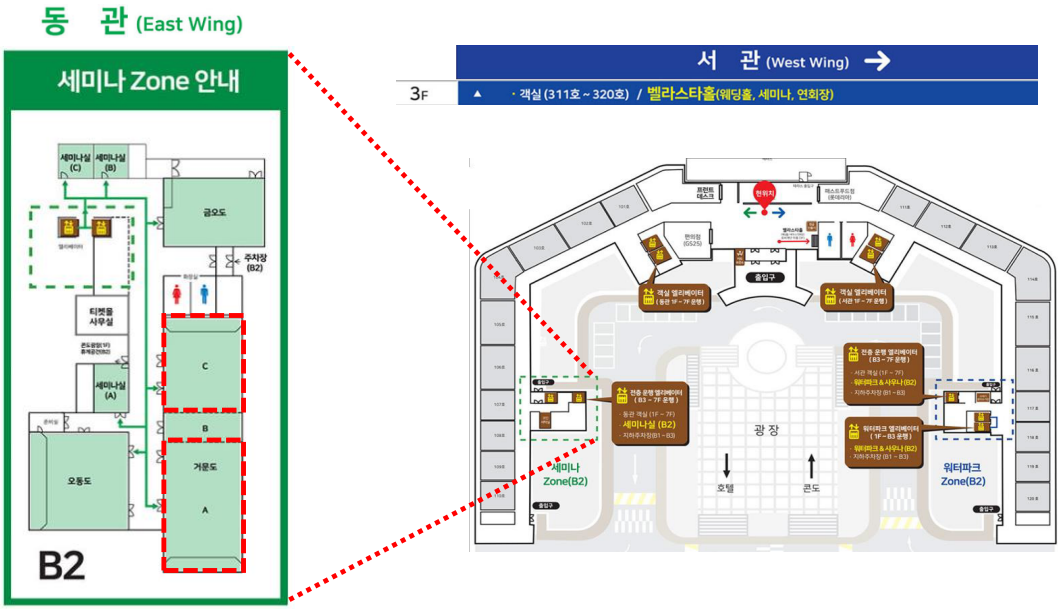
<에머랄드홀>

- Poster Presentation
- Exhibition



<거문도 A>

- Symposium IV: Physical Anthropology
- Symposium VII: Anatomy Education
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- Symposium VI: Cell Biology (I)
- Symposium IX: Cell Biology (II)
- Oral Presentation II and V

<벨라스타홀>

- Symposium V: Microscopy
- Symposium VIII: KAA-JAA Joint Symposium
- Oral Presentation V

Plenary Lecture I

2019년 10월 17일(목) 13:30 ~ 14:20
그랜드 볼룸 A

좌장 안규윤 전남의대

PL-1 **13:30-14:20**
What and How can "Nano" do for "Medicine?"
현택환 • 서울대학교 화학생물공학부

본 Plenary Lecture I은 (주)엔테라퓨틱스의 후원에 의해 진행되었습니다.

PL-1

What and How can "Nano" do for "Medicine?"

Taeghwan Hyeon[1,2]

[1]Center for Nanoparticle Research, Institute for Basic Science (IBS)
[2]School of Chemical and Biological Engineering, Seoul National University

Over the last 20 years, our laboratory has focused on the designed chemical synthesis, assembly and applications of uniform-sized nanocrystals. In particular, we developed a novel generalized procedure called as the "heat-up process" for the direct synthesis of uniform-sized nanocrystals of many metals, oxides, and chalcogenides.[1,2]

For the last 10 years, our group has been focused on medical applications of various uniform-sized nanoparticles.[3] Using 3 nm-sized iron oxide nanoparticles, new non-toxic MRI contrast agent was realized for high resolution MRI of blood vessels down to 0.2 mm. Very recently, we report on the biocompatibility evaluation and MR imaging of extremely small and uniform-sized iron oxide nanoparticles in large animal models including most clinically-relevant non-human primates. These biocompatible iron oxide nanoparticles are successfully used as T1 MR contrast agent for high-resolution MR angiography of macaque monkeys.[4] We reported the first successful demonstration of high-resolution in vivo three-photon imaging using biocompatible and bright Mn2+ doped ZnS nanocrystals.[5] We demonstrated that ceria nanoparticles and ceria–zirconia nanoparticles can work as therapeutic antioxidants to treat various nasty diseases including ischemic stroke, Alzheimer's disease, sepsis, and Parkinson's disease.[6]

I will present recent advances on the fabrication of ultraflexible & stretchable electronic & optoelectronic devices integrated with various functional nanomaterials and their applications to wearable & implantable healthcare devices.[7] We reported graphene-hybrid electrochemical devices integrated with thermo-responsive micro-needles for the sweat-based diabetes monitoring and feedback therapy.[8] We introduced electromechanical cardioplasty using an epicardial mesh made of electrically conductive and mechanically elastic Ag-Au core-shell nanowire-rubber nanocomposite to resemble the innate cardiac tissue and confer cardiac conduction system function.[9]

We report a highly sensitive and selective K+ nanosensor that can quantitatively monitor extracellular K+ concentration changes in the brains of freely moving mice experiencing epileptic seizures.[10]

1. "Ultra-Large Scale Syntheses of Monodisperse Nanocrystals," Nature Mater. 2004, 3, 891.
2. 2."Synthesis and Biomedical Applications of Multifunctional Nanoparticles." Adv. Mater. 2018, 30, 1802309.
3. "Large-Scale Synthesis and Medical Applications of Uniform-Sized Metal Oxide Nanoparticles." Adv. Mater. 2018, 30, 1704290.
4. "Iron oxide nanoclusters for T1 MRI of nonhuman primates," Nature Biomed. Eng. 2017, 1, 637.
5. "High-Resolution Three-Photon Biomedical Imaging using Doped ZnS Nanocrystals," Nature Mater. 2013, 12, 359.
6. "Ceria Nanoparticles that can Protect against Ischemic Stroke," Angew. Chem. Int. Ed. 2012, 51, 11039; "Mitochondria-Targeting Ceria Nanoparticles as Antioxidants for Alzheimer's Disease," ACS Nano, 2016, 10, 2860; "Ceria–Zirconia Nanoparticles as Enhanced Multi-Antioxidant for Sepsis Treatment," Angew. Chem. Int. Ed. 2017, 56, 11399; "Ceria nanoparticle systems for selective scavenging of mitochondrial, intracellular, and extracellular reactive oxygen species in Parkinson's disease," Angew. Chem. Int. Ed. 2018, 57, 9408.
7. "Designed Assembly and Integration of Colloidal Nanocrystals for Device Applications," Adv. Mater. 2016, 28, 1176; "Recent advances in flexible and stretchable bio-electronic devices integrated with nanomaterials," Adv. Mater. 2016, 28, 4203.
8. "A graphene-based electrochemical device with thermo-responsive microneedles for diabetes monitoring and therapy," Nature Nanotech. 2016, 11, 566; "Wearable/disposable sweat-based glucose monitoring device with multi-stage transdermal drug delivery module," Science Adv. 2017, 3, e1601314.
9. "Electromechanical cardioplasty using a wrapped elasto-conductive epicardial mesh," Science Transl. Med. 2016, 8, 344ra86; "Highly conductive, stretchable, and biocompatible Ag-Au core-sheath nanowire composite for wearable and implantable bioelectronics," Nature Nanotech. 2018, 13, 1048.
10. "Signal sorting and amplifying potassium nanosensors for monitoring epilepsy in freely moving mice," Nature Nanotechnol. 2019, in revision.

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Plenary Lecture II

2019년 10월 18일 (금) 11:00 ~ 11:50
그랜드 볼룸 A

좌장 조사선 가천의대

PL-2 **11:00-11:50**
Nanostructure and dynamics of dendritic spines
Shigeo Okabe • The University of Tokyo

PL-2

Nanostructure and dynamics of dendritic spines

Shigeo Okabe

Department of Cellular Neurobiology, Graduate School of Medicine, The University of Tokyo

Dendritic spines are small protrusions on the surface of neuronal dendrites. Spines receive most of the excitatory inputs to pyramidal neurons in the forebrain. Excitatory neural circuits are important for experience-dependent changes in brain functions, including postnatal sensory refinement and memory formation. Several lines of evidence indicate that synaptic efficacy is correlated with spine size and structure. It is essential to have precise and accurate technologies for the measurement of structural parameters and molecular dynamics of single spines. Recent advances in microscopic techniques have opened the way toward comprehensive analyses of spine structure and molecular dynamics. We developed methods of accurate measurement of spine nanostructure by super-resolution imaging and intra-spine molecular dynamics by fluorescence correlation technology, such as FCS and RICS. These techniques are useful in understanding (1) the correlation between spine nanostructure and the fate of individual spines, (2) extracting important morphological features associated with synapse plasticity, and (3) reorganization of intra-spine actin filaments immediately after induction of synaptic plasticity. We discuss the possible interplay between spine nanoscale morphology and molecular dynamics and how these two factors cooperate to determine the formation, activity-dependent modulation, and pruning of dendritic spines.

Key Words: Dendritic spine, Synapse, Super-resolution imaging, Actin, Fluorescence correlation microscopy

1. Obashi, K., Matsuda, A., Inoue, Y., and S. Okabe Cell Reports 2019, 27:1503-1515.
2. Kashiwagi, Y., Higashi, T., Obashi, K., Sato, Y., Komiyama, N., Grant, S. G. N. and S. Okabe Nature Communications 2019, 10:1285.
3. Isshiki, M., Tanaka, S., Kuriu, T., Tabuchi, K., Takumi, T. and S. Okabe. Nature Communications 2014, 5:4742.
4. Shin, E., Kashiwagi, Y., Kuriu, T., Iwasaki, H., Tanaka, T., Koizumi, H., Gleeson, J. G. and S. Okabe Nature Communications 2013, 4:1440.
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Special Lecture I

2019년 10월 17일 (목) 11:20 ~ 12:00
그랜드 볼룸 A

좌장 이영호 충남의대

SL-1 **11:20-12:00**
Metabolic dysfunction and Alzheimer Disease
이종은 • 연세대학교 의과대학

SL-1

Metabolic dysfunction and Alzheimer Disease

Jong Eun Lee

Department of Anatomy, BK21 Plus Project for Medical Science, Brain Research Institute, Yonsei University College of Medicine

The abnormal proteins deposits in the brain, including senile amyloid plaques(Aβ) and neurofibrillary tangles, has been recognized as the essential root of AD. However, recent imaging studies have shown that early, selective atrophy and glucose hypometabolism are detected in the medial temporal lobe of patient with early stage of AD, which suggests AD as a metabolic disease. Especially obesity and type 2 diabetes(T2D) are well known risk factors for Alzheimer's disease(AD). MRI imaging shows that obese men have smaller brain volumes and increase the risk for AD. People who don't engage in physical activity are at higher risk of developing cognitive decline over time. Also persons suffered with T2D are also at significantly increased risk for the development of Alzheimer's disease due to brain insulin resistance. It is well established that reduced insulin signaling in neurons leads to neuronal dysfunction, accumulation of Aβ and phosphorylation of tau.

In this study, we try to define the correlation between metabolic dysfunction and AD pathophysiology and detect early metabolic changes in AD brains using by hyperpolarized ^{13}C magnetic resonance spectroscopy, and define the metabolic changes in the brain of obese mice with AD pathology. We developed type 2 diabetes induced Alzheimer's disease mouse model that exhibits obesity and insulin resistance, and obesity induced AD animal model. Male ICR mice were fed a 60% high fat diet (HFD) for 12 weeks and injected streptozotocin (STZ, 100mg/kg, i.p.) at 4^{th} week for T2D-induced Alzheimer's disease model, and mice were fed a 60% high fat diet (HFD) for 24 weeks for obesity induced AD model. Blood glucose level and weights of high fat diet group were significantly increased compared with normal diet group over a period of time. Insulin downstream signaling was blunted and the amount of Aβ42 and phosphorylated tau proteins was increased in brain of STZ-HFD group. In behavior test, STZ-HFD group and HFD group showed cognitive impairment.

Imaging study revealed both the amounts and speed of lactate conversion in the hippocampal areas were drastically increased in the HFD mouse brain. Change of adiponectin level in the brain was induced by HFD and this change might lead brain metabolism causing cognitive decline.

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)

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Special Lecture II

2019년 10월 18일(금) 13:00 ~ 13:40
그랜드 볼룸 A

좌장 이왕재 서울의대

SL-2 **13:00-13:40**
The Future of Healthcare and Medical Education in the DPRK
노대영 • 평양과기대 의대 학장

본 Special Lecture II는 (주)엔테라퓨틱스의 후원에 의해 진행되었습니다.

SL-2

The Future of Healthcare and Medical Education in the DPRK

Daeyoung Roh /평양과기대 의대 학장

The current healthcare condition in the DRPK has been in a severe decline since the 1990s due to natural disasters, economic problems, food, and energy shortages. By the early 2000s, many of the North Korean hospitals and clinics lacked essential medicines, equipment, running water and electricity. The current life expectancy for females and the males are significantly lower for North Koreans than it is for South Koreans. Malnutrition in North Korea is rampant, with 20% of North Korean children have stunted growth.

There are several areas in which North Korea cannot solve their problems, requiring outside intervention, and one of these areas is in the field of medical education. The main reason for this is the lack of resource and their isolation from the international community. Many of the North Korean doctors severely lack basic knowledge, skills, and equipment to take care of the North Korean population appropriately.

The current medical education system is based on the policy of the former Soviet Union. The undergraduate medical school is a 4.5-year program. The basic science course which are offered in North Korea are as follows: Biochemistry, Biology, Molecular Biology, Human Anatomy, Neuroanatomy, Histology, Embryology, Physiology, Cell Biology, Pharmacology, Genetics, Epidemiology, Immunology, and Pathology. The text books are written by North Korean Professors. Very little Western books are available for the students. Each textbook are 30-40 years behind compared to the West. Also, students are taught basic science with very little clinical exposure. Once they graduate from medical school, students are placed into various hospitals for training and apprenticed to become full-time staff at the hospital. One of the major flaws with this type of system is the significant variability in the training which students receive. Currently, there are no standardized clinical training programs in DPRK. PUST College of Medicine is the first institution to initiate Western-based clinical training for medical students, with an Internship training program, Residency training program, and a Fellowship Training program.

Historically, medical education has played an essential role in the development of society. Education has always proven to be by far the most effective and efficient way to impact a nation. Education teaches one how to "fish." Within the context of education, medical education has an even more profound impact on society. Improved medical knowledge saves lives. Improving the current medical education system in the DPRK will directly impact the quality of healthcare delivery and will, in turn, enhance the healthcare of the people of DPRK. Improving medical education system will also have a positive impact on the economy and the quality of life.

In 2016, The Education Committee of the DPRK Party formally approved the establishment of a College of Medicine as a part of the Pyongyang University of Science and Technology. Currently, we have 45 undergraduate medical students enrolled in our medical school. Also, 15 postgraduate students who have graduated from other medical schools have been selected to receive clinical training in our program.

The main goal of our clinical training program is to develop an effective Western standard medical education model for DPRK to emulate. We want to build future leaders in medicine and the healthcare industry. We want to train our student physicians the Western values of compassion and empathy, which will have a positive influence in approach to healthcare in DPRK. To strategically accomplish our goal, we will proceed with the following 4 phases of strategic planning.

- The first phase will be to establish a functioning undergraduate medical school. Currently, we have 45 students enrolled in our medical school.
- The second phase is to develop a postgraduate medical training program in Pyongyang, including an internship, residency, and fellowship training program following international standards. Currently, we have 15 postgraduate students enrolled in our postdoctoral training program. We have selected two fellow candidates in Nephrology for 2020 and two fellow candidates in Surgery for 2020.
- The third phase is to establish a self-sustaining teaching hospital in Pyongyang. The teaching hospital will have centers of excellence with modern outpatient and specialty centers in the areas of CV disease, Orthopedic, and Spine Surgery, Neurosurgery, Gastroenterology, a Cancer Center, Urological and Renal Centers.
- Lastly, the fourth phase will be to partner with the business community to develop needed medical services such as pharmaceutical companies, medical device companies, and medical supply companies, to name a few.

One of the unique aspects of our program is that our students are taught in English as the primary language and that all of our faculties are recruited from Europe, Canada, Australia, and the United States.

In summary, we believe that our medical school and clinical training programs are needed in the DPRK. The PUST College of Medicine and the new clinical training programs will hugely improve the current medical education system in DPRK. We believe graduate students from our programs will have a very positive impact on healthcare delivery in the DPRK.

Key Words: Medical Education, Medical School, DPRK, Basic Science, Clinical Training

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Luncheon Symposium I

2019년 10월 17일 (목) 12:00 ~ 13:00
그랜드 볼룸 B

좌장 최형진 서울의대

LS-1 **12:00-13:00**
AI-powered modeling and visualization platform for medical anatomy education
박상준 • Medical IP

LS-1

AI-powered modeling and visualization platform for medical anatomy education

박상준 /Medical IP

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Luncheon Symposium II

2019년 10월 18일(금) 12:00 ~ 13:00
그랜드 볼룸 B

LS-2 **12:00-13:00**

ZEISS LSM 9 family with Airyscan 2: Your Next Generation Confocal for Fast and Gentle Multiplex Imaging

엄기수 • Carl Zeiss

LS-2

ZEISS LSM 9 family with Airyscan 2: Your Next Generation Confocal for Fast and Gentle Multiplex Imaging

엄기수 /Carl Zeiss

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Symposium I

2019년 10월 17일(목) 09:20 ~ 10:50
그랜드 볼룸 A

Gross Anatomy

좌장 정민석 아주의대 • 김홍태 대구가톨릭의대

SI-1 **09:20-09:35**
2차원 벡터 그림을 다루는 Adobe Illustrator
정민석 • 아주대학교 의과대학

SI-2 **09:35-09:50**
2차원 비트맵 그림을 다루는 Adobe Photoshop
윤관현 • 인천가톨릭대학교

SI-3 **09:50-10:05**
표면 3차원 영상을 다루는 Amira
김홍태 • 대구가톨릭의과대학

SI-4 **10:05-10:20**
표면 3차원 영상을 다루는 Maya (부록: 동영상을 만드는 PowerPoint)
정범선 • 아주대학교 의과대학

SI-5 **10:20-10:35**
부피 3차원 영상을 다루는 MRIcroGL (부록: 동영상을 편집하는 Adobe Premiere)
박진서 • 동국대학교 의과대학

SI-6 **10:35-10:50**
표면 3차원 영상과 부피 3차원 영상을 다루는 Mimics
박종태 • 단국대학교 치과대학

본 심포지엄 I은 경북대학교 치과대학 얼굴 신경-뼈 네트워크 연구센터 (CNBNRC)의 지원에 의해 진행되었습니다.

SI-1

2차원 벡터 그림을 다루는 Adobe Illustrator

정민석 /아주대학교 의과대학 해부학교실

해부학 만화(해부학 단순2차원 벡터 그림)를 어떻게 써먹었는지, 왜 그리고 어떻게 Adobe Illustrator로 그렸는지 알림으로써, 다른 해부학 선생님한테 도움 주고자 하였다.
저자는 단순 그림에 글을 보태서 해부학 학습만화와 명랑만화를 그렸다. 해부학 명랑만화를 누리통신망으로 퍼뜨린 덕분에 트위터에서 팔로우하는 사람이 30,000명쯤 되었다. 해부학 명랑만화를 모아서 책을 펴냈고, 건강상식 명랑만화를 그려서 신문에 연재하고 있다. 학습만화와 명랑만화를 영작해서 논문을 쓰기도 하였고, 의학 명랑만화를 그려서 SCI 학술지에 싣고 있다. 만화를 바탕으로 국소해부학, 계통해부학, 신경해부학 영어책을 만들었는데, 이중 신경해부학 영어책은 Elsevier에서 펴내기로 하였다.
Adobe Illustrator는 벡터 그림을 다루는데, 벡터 그림은 비트맵 그림과 달리 선의 집합이므로, 해상도와 관계 없이 파일이 작다. 벡터 그림은 아무리 확대해도 화소가 보이지 않는다. 벡터 그림은 복사한 다음에 쉽게 고쳐서 쓸 수 있고, 자기 뜻을 쉽게 담을 수 있다. 벡터 그림은 여러 사람이 덧그림을 그려도 한 사람이 그린 것처럼 한결같다. 벡터 그림은 배우기 어려울 것 같지만, 몇 시간 동안 꼭 필요한 것을 모두 배울 수 있다.
다른 해부학 선생님도 단순 그림을 Adobe Illustrator로 그려서 좋은 교육 자료를 많이 만들기 바란다.

Key Words: 해부학, 학습만화, 명랑만화, 단순 그림, 벡터 그림, Adobe Illustrator

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SI-2

2차원 비트맵 그림을 다루는 Adobe Photoshop

윤관현 /인천가톨릭대학교대학원 바이오메디컬아트전공

논문이나 강의용 파일에서 세련된 이미지는 reviewer나 독자의 관심을 즉각적으로 끌수 있기 때문에 그 중요성은 점점 증대되고 있다. 여기에 쓰이는 이미지는 도표, 일러스트, 사진 또는 이들이 서로 혼합된 형식의 figure, 그리고 표지디자인 등이 있다. 최근들어 일부 논문에서는 graphical abstract(또는 visual abstract)의 형식을 요구하기도 한다. 이러한 이미지를 새롭게 만들거나 편집할 때 Adobe Photoshop은 매우 유용한 그래픽 프로그램 중 하나로 가장 널리 알려져 있다. 포토샵은 비트맵 방식으로 본래는 사진 편집에 최적화된 프로그램이었으나 최근에는 Adobe Illustration과 함께 디지털 드로잉으로도 그 쓰임새가 확장되고 있다. 이렇게 유용한 도구임에도 불구하고 포토샵을 시작하기 위해서는 펜마우스(stylus pen)나 테블릿 같은 추가적인 장비를 준비해야하거나, 오랜 기간 숙련이 필요하다는 점 때문에 많은 이들이 망설이곤 된다. 하지만 간단한 사진 편집이나 단순한 일러스트를 제작하는 것은 비교적 간단하며, 이러한 몇 가지 예시들을 소개하고자 한다.

Key Words: 해부학 일러스트, 논문 그림, 비트맵 그림, Adobe Photoshop

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SI-3

표면 3차원 영상을 다루는 Amira

김홍태 /대구가톨릭대학교 의과대학 해부학교실

우리 몸을 구성하는 모든 구성요소는 그 크기와 상관없이 입체적인 구조를 하고 있으므로 제대로 된 모양을 분석하기 위해서는 3차원 영상기술이 필요하다. 입체구조의 3차원 영상분석을 위해서는 표본의 모든 부분에 대한 2차원 평면 영상 정보를 모으고, 각각의 정보를 이어 붙여 3차원 정보를 담아내는 재구성(reconstruction) 후 3D 이미지화 과정을 거치게 된다. 재구성과 3D 이미지화를 위해서는 소프트웨어가 필요하며 이미 건축, 영화, 공학 뿐만 아니라 의생명 영역에 특화된 소프트웨어가 개발되어 있다.
Amira는 Zuse Institute Berlin (ZIB)와 Thermo Fisher Scientific사가 협력하여 개발한, 생명과학과 의생명 영역의 다양한 영상정보의 3D 이미지화 뿐만 아니라 모델링, 분석, 커뮤니케이션, 프레젠테이션 등이 가능한 고성능 소프트웨어 솔루션이다. 다양한 의생명 표본의 3차원 영상분석 연구에 Amira를 사용할 수 있도록 이 소프트웨어의 구성, 특징, 사용법을 소개하고자 한다.

Key Words: 3D 이미지화, 3차원 모델링, 3차원 영상분석, Amira

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SI-4

표면 3차원 영상을 다루는 Maya (부록: 동영상을 만드는 PowerPoint)

정범선 /아주대학교 의과대학 해부학교실

해부학 구조물의 표면3차원영상을 어떻게 만들고 다듬을 수 있는지, 왜 그리고 어떻게 Maya로 작업했는지 알림으로써, 다른 해부학 선생님한테 도움 주고자 하였다.
저자는 시신의 절단면영상에서 해부학 구조물을 구역화한 것을 바탕으로, 표면3차원영상을 만들었다. 연속절단면영상과 표면3차원영상을 함께 볼 수 있게 함으로써, 의과대학 학생과 의사들이 단면해부학과 입체 해부학을 쉽게 이해하게 하였다. 관련된 임상 내용을 덧붙여 다양한 임상 해부학 논문을 썼다.
Maya가 다루는 표면3차원영상은 벡터 그림의 일종이라서, 부피3차원영상과 달리 아무리 확대해도 화소가 보이지 않는다. 기본적으로 표면3차원영상은 시신의 실제 빛깔이 아닌 그린 사람이 지정한 빛깔을 나타내지만, 시신의 실제 빛깔을 담은 절단면영상을 표면에 씌울 수 있다. 또한 절단면영상과 표면3차원영상을 겹쳐서 보게 할 수 있다.
다른 해부학 선생님도 표면3차원영상을 Maya로 그려서 좋은 해부학 자료를 많이 만들기 바란다.

Key Words: 해부학, 표면3차원영상, Maya

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SI-5

부피 3차원 영상을 다루는 MRIcroGL (부록: 동영상을 편집하는 Adobe Premiere)

박진서 /동국대학교 의과대학 해부학교실

병원에서는 환자의 의료영상(컴퓨터단층사진, 자기공명영상)으로 부피3차원영상을 만든다. 부피3차원영상은 연속된 의료영상의 모든 정보를 하나로 담고 있기 때문에 수평면, 관상면, 시상면뿐 아니라 의사가 필요한 기울기의 단면을 마음대로 잘라보아도 환자 몸 속 정보를 그대로 볼 수 있다. 이러한 부피3차원영상은 환자의 질병 진단에 큰 도움이 되고, 따라서 의료영상으로 부피3차원영상을 만드는 소프트웨어가 많이 개발되고 있다.
이 발표에서는 다양한 부피3차원영상제작 소프트웨어 중에서 MRIcroGL을 소개한다. 대부분의 소프트웨어처럼 MRIcroGL도 회색빛깔 의료영상만을 다룰 수 있게 설계되었지만, 일부기능을 쓰면 실제빛깔 절단면영상으로 실제빛깔 부피3차원영상을 만들 수 있고, 각 구조물을 마음대로 잘라보고 골라볼 수도 있다.
다른 해부학 선생님도 자신이 만든 의료영상, 절단면영상, 조직학영상 등 연속된 단면영상을 MRIcroGL 소프트웨어로 부피3차원영상을 만들어서 자신의 연구와 교육에 쓸모있게 쓰기를 바란다. 더불어 Adobe Premiere 소프트웨어를 써서 강의와 실습 동영상을 편집하는 방법도 함께 소개한다.
본 연구는 산업통상자원부와 한국산업기술진흥원의 "국제공동기술개발사업"의 지원을 받아 수행된 연구결과임. (과제 번호: N0002249)

Key Words: Visible Human Projects, Cross-Sectional Anatomy, Three-Dimensional Imaging, Computer Simulation

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SI-6

표면 3차원 영상과 부피 3차원 영상을 다루는 Mimics

Jong-tae Park
Department of Oral Anatomy, Dankook University College of Dentistry

As the use of 3D software increases in the medical field, the utilization of 3D printers such as patient-specific surgical guides and patient-specific implants is increasing. This requires 3D software that can make the structure and position of the human body in 3D more precisely. Since the Mimics software which is based on DICOM file can obtain the desired part of the human body in 3D format, it can work on specialized functions of the professional field. Therefore, images generated in various situations, such as Medical CT, MRI images, and Microscopy images, can be imported and utilized quickly. The imported file can be created in a 3D model by separating the ROI area through the Thresholding operation. In addition, only the desired area can be generated in 3D models or the parts within one object can be separated. The generated 3D model can measure Surface and Volume, and can measure Distance, Angle, and Density in 2D image and 3D view. Lastly, the generated 3D model can be converted to STL file to produce the model through 3D printing. Currently, we are conducting research through the Mimics software and developing patient-specific guides, implants, VR, and so on by the use of the generated 3D patient model. So the Mimics software can be studied in various fields. Thus, through this presentation, we hope that research and educational materials using the Mimics software will greatly contribute to the development of anatomy in the future.

Key Words: CBCT, 3D, 3D Printing, Mimics, Medical

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Symposium II

2019년 10월 17일(목) 09:20 ~ 11:00
그랜드 볼룸 B

Neuroscience

좌장 이종은 연세의대 • 이지연 서울의대

SII-1 **09:20-09:45**
Investigating cell type specific role of RAS signaling pathway in learning and memory in mice
이용석 • 서울대학교 의과대학

SII-2 **09:45-10:10**
Mechanosensory neurons control sweet taste in Drosophila
정용택 • 고려대학교 의과대학

SII-3 **10:10-10:35**
The chick embryo as a model to study neural development
송미령 • 광주과기원

SII-4 **10:35-11:00**
Piezo channel PEZO-1 regulates intestinal motility in C. elegans
김규형 • DGIST

본 심포지엄 II는 연세대학교 치과대학 미각연구센터(TRC)의 지원에 의해 진행되었습니다.

SII-1

Investigating cell type specific role of RAS signaling pathway in learning and memory in mice

Yong-Seok Lee
Department of Physiology, Biomedical Sciences, Seoul National University College of Medicine

RAS signaling is an ubiquitous signaling pathway playing critical roles in multiple cell types including neuron and glia. Mutations in the genes in RAS signaling pathway are associated with neurodevelopmental disorders collectively called RASopathy which includes neurofibromatosis and Noonan syndrome. Cognitive deficits such as learning disabilities and autism are common in RASopathy. Interestingly, RASopathy affects distinct neuronal cell types: neurofibromatosis type 1 affects inhibitory neurons, while Noonan syndrome affects excitatory neurons. In this talk, I will share our finding that distinct RAS signaling network in each neuronal type may explain these cell type-specific pathophysiology in RASopathy in mouse models of RASopathy. Furthermore, I will also present our recent finding that RASopathy-associated Raf mutations impair learning and memory by selectively affecting astrocyte. Our findings strongly suggest that identifying cell types affected in individual disease is critical to developing treatment strategies for cognitive disorders.

Key Words: MAPK, Synaptic plasticity, Learning, Memory, Mutant mice

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SII-2

Mechanosensory neurons control sweet taste in Drosophila

Yong Taek Jeong
Department of Pharmacology, Korea University College of Medicine

Animals discriminate nutritious food from toxic substances using their sense of taste. Since taste perception requires taste receptor cells to come into contact with water-soluble chemicals, it is a form of contact chemosensation. Concurrent with that contact, mechanosensitive cells detect the texture of food and also contribute to the regulation of feeding. Little is known, however, about the extent to which chemosensitive and mechanosensitive circuits interact. Here, we show Drosophila prefers soft food at the expense of sweetness and that this preference requires labellar mechanosensory neurons (MNs) and the mechanosensory channel Nanchung. Activation of these labellar MNs causes GABAergic inhibition of sweet-sensing gustatory receptor neurons, reducing the perceived intensity of a sweet stimulus. These findings expand our understanding of the ways different sensory modalities cooperate to shape animal behavior.

Key Words: Taste, Mechanosensation, Synapse, in vivo Calcium imaging

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SII-3

The chick embryo as a model to study neural development

Mi-Ryoung Song

School of Life Sciences, Gwangju Institute of Science and Technology

The chick embryo is a classical animal model that has been used to study neural development for decades. It has many advantages over other models since it can be easily accessible for visualization and manipulations *in ovo*. For instance, misexpression or knockdown of genes within the neural tube is readily achieved by *in ovo* electroporation. Here we investigate the roles of transcription factors in motor neuron development within chick embryos. By testing the reporter activity of motor neuron-specific enhancers with major transcription factors for spinal cord development, we found that complex interplay between transcription factors and enhancers controls motor neuron diversification. Furthermore, misexpression or knockdown of these genes resulted in altered motor neuron identity, cell body position and axon projection errors. Together, our findings suggest that combinations of transcription factors establish cell-type specificity and functional diversity in terms of motor neuron identities and/or axon development.

Key Words: Chick embryo, In ovo electroporation, Neural tube

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SII-4

Piezo channel PEZO-1 regulates intestinal motility in C. elegans

Jihye Yeon, YeonJi Park, Jinmahn Kim, Seoyoung Jun, and Kyuhyung Kim
Department of Brain and Cognitive Sciences, DGIST

Piezo ion channel is an evolutionarily conserved mechanosensitive channel (Coste et al., 2010). Mammalian genomes encode two PIEZO genes, *Piezo1* and *Piezo2*, of which functions have been shown to be involved in mechanosensation (Woo et al., 2014, Nonomura et al., 2017, Li et al., 2014, Rode et al., 2017). *C. elegans* genome has a single PIEZO gene, *pezo-1*, which encodes 14 isoforms. The molecular function of PEZO-1 in *C. elegans* has yet to be determined. To examine *pezo-1* function, we grouped 14 isoforms into short or long isoform depending on the mRNA length and observed their expression patterns. While promoter region of short isoforms is expressed in the several head neurons and intestinal cells, that of long isoforms is specifically expressed in the pharyngeal-intestinal valve which is predicted to mediate intestinal peristalsis (Avery and Thomas, 1997). Next, to examine whether *pezo-1* has a role in intestinal peristalsis, we performed intestinal motility assay by feeding animals with GFP-microsphere and found that *pezo-1* mutant animals show excess accumulation of GFP-microsphere in the intestine lumen. Expression of long isoform PEZO-1 under the control of its endogenous promoter restore the peristalsis defect of *pezo-1* mutant animals. We also found that pharyngeal-intestinal valve exhibits calcium transient during peristalsis and the optogenetic activation of valve cells induce peristalsis by contracting pharynx muscles via gap junctions. Furthermore, ectopic expression of mouse PIEZO1 is sufficient to restore defect of *pezo-1* mutant animals. Currently, we are investigating whether PEZO-1 is activated upon pressure by performing electrophysiology in a heterologous system. These results demonstrate that *C. elegans* PIEZO channel *pezo-1* is required for intestinal peristalsis, and it provide insights to understand function of mammalian PIEZO channels which have shown to be expressed in intestine.

Key Words: Piezo channel, *pezo-1*, *C. elegans*, Intestinal motility

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Symposium III

2019년 10월 17일(목) 09:20 ~ 11:00
벨라스타홀

Organoid

좌장 김동운 충남의대 • 홍성태 충남의대

SIII-1 **09:20-09:45**
Expandable and Functional Human Pluripotent Stem Cell–Derived Hepatic organoids
손명진 • 한국생명공학연구원

SIII-2 **09:45-10:10**
Organoid Medicines; Tools for drug discovery and regeneration
유종만 • 차의과대학

SIII-3 **10:10-10:35**
Human organoids: new opportunities for biomedical research
김철훈 • 연세대학교 의과대학

SIII-4 **10:35-11:00**
Establishment and Characterization of Human Cancer Organoids
구자록 • 서울대학교 의과대학

SIII-1

Expandable and Functional Human Pluripotent Stem Cell-Derived Hepatic organoids

Seon Ju Mun[1], Jae-Sung Ryu[1], Mi-Ok Lee[1], Ye Seul Son1, Soo Jin Oh[2], Hyun-Soo Cho[1], Mi-Young Son[1], Dae-Soo Kim[1], Su Jung Kim[2], Hyun Ju Yoo[2], Ho-Joon Lee[1], Janghwan Kim[1], Cho-Rok Jung[1], Kyung-Sook Chung[1]* and Myung Jin Son[1]*

[1]Korea Research Institute of Bioscience and Biotechnology,
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The development of hepatic models capable of long-term expansion with competent liver functionality in a personalized setting is technically challenging. Stem cell-based organoid technologies can provide an alternative source of patient-derived primary hepatocytes. However, self-renewing and functionally competent human pluripotent stem cell (PSC)-derived hepatic organoids are still lacking. We developed a novel method to efficiently and reproducibly generate functionally mature human hepatic organoids derived from PSCs, including human embryonic stem cells and induced PSCs. The maturity of the organoids was validated by a detailed transcriptome analysis and functional performance assays. The organoids were applied to screening platforms for predicting toxicity and evaluating drugs that target hepatic steatosis through real-time monitoring of cellular bioenergetics and high-content analyses. The organoids exhibited significant toxic responses to clinically relevant concentrations of drugs that had been withdrawn from the market due to hepatotoxicity and recapitulated human disease phenotypes such as hepatic steatosis. Our organoids may provide a versatile and valuable platform for physiologically and pathologically relevant hepatic models in the context of personalized medicine.

Key Words: Liver, Organoids, Pluripotent stem cells, Drug toxicity, Disease modeling

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SIII-2

Organoid Medicines; Tools for drug discovery and regeneration

Jongman Yoo
Department of Microbiology and Organoid Research Center, School of Medicine, CHA University

Organoids are three-dimensional in-vitro-grown cell clusters with near-native microanatomy that arise from self-organizing stem cells. Organoid based models can provide breakthrough platforms for studying pathophysiology, screening drug efficacy, and predicting drug toxicity. In addition, the organoids are capable of regenerative therapeutics that can restore the damaged organ functions when injected into animal models such as inflammatory bowel diseases. However, there are many limitations to the application of organoids. A high cost for organoid expansion, low viability after cryopreservation, inefficient expansion by spontaneous differentiation and using Matrigel as an extracellular matrix are major obstacles in the clinical and industrial applications. Here I present the current limitations for clinical and industrial application of organoids, and introduce our challenges.

Key Words: Organoid, Regeneration, Disease model, Cell therapy, Screening

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SIII-3

Human organoids: new opportunities for biomedical research

Chul Hoon Kim
Department of Pharmacology, Yonsei University College of Medicine

The introduction of organoid technology that allows us to grow human tissues from stem cells with their 3D architectures has the enormous potential to push forward the boundaries of biomedical research. The aim of this presentation is to enhance the understanding of how cerebral organoid technology can be used to study human physiology and diseases.

김철훈 | 연세대학교 의과대학 • KIMHOON@yuhs.ac

SIII-4

Establishment and Characterization of Human Cancer Organoids

구자록 /서울대학교 의과대학

An organoid is a miniaturized and simplified version of an organ produced in vitro in three dimensions that shows realistic micro-anatomy. Organoids as well as cell lines are important because they provide a consistent renewable source of cell material for study. Organoids like as cell lines can be also established from original tumor tissues, metastatic tumor tissues, PDX, ascites, pleural effusions or circulating tumor cells of cancer patients.

Cancer cells that are grown in organoid culture system retain cell-cell and cell-matrix interactions that more closely resemble those of the original tumor compared with cells grown in two dimensions on plastic. Utilizing organoid culture system, high-throughput drug screening (HTS) from patient-derived tumor samples offers a unique opportunity to identify effective cancer drugs for individual patients.

Over 450 human cancer organoids derived from colorectal, pancreatic, breast, gastric, ovarian cancers, hepatocellular carcinoma and renal cell carcinomas have been established since 2016 in our laboratory. The characteristics of these human cancer organoids have been analyzed (DNA fingerprinting analysis, mycoplasma contamination test, cell viability test for anticancer drugs and NGS (WES and RNA seq.) for detections of mutations and expressions of genes. We have been conducting anticancer drug screening assay on these cancer organoids and also these human cancer organoids will be available in the future thorough the KCLB (Korean Cell Line Bank, https://cellbank.snu.ac.kr).

Key Words: Cancer, Organoid, 3D culture, Patient derived, HTS, Biobanking

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Symposium IV

2019년 10월 17일(목) 16:20 ~ 18:25
거문도A홀

Physical Anthropology

좌장 신동훈 서울의대 • 홍종하 경희대

SIV-1 **16:20-16:45**
생물인류학 연구 차원에서 본 동물고고학의 학술적 의미
신동훈 • 서울대학교의과대학

SIV-2 **16:45-17:10**
Multi-isotope investigation of horse breeding in Japan
Uetsuki Manabu • Teikyo University

SIV-3 **17:10-17:35**
고고학 발굴현장에서 수집한 조선시대 말 뼈 미토콘드리아 DNA D-loop 서열에 대한 유전학적 분석
홍종하 • 경희대학교 한국고대사 · 고고학연구소

SIV-4 **17:35-18:00**
분묘유적에서의 동물유존체 출토 양상과 그 의미
고은별 • 서울대학교 고고미술사학과

SIV-5 **18:00-18:25**
삼국시대 생활유적 출토 동물뼈
김헌석 • 국립경주문화재연구소

SIV-1

생물인류학 연구 차원에서 본 동물고고학의 학술적 의미

Dong Hoon Shin and Jong Ha Hong

Lab of Bioanthropology Paleopathology and History of Disease, Department of Anatomy and Cell Biology, Seoul National University College of Medicine

Biological anthropology has rapidly developed in recent years, entering a new stage to better understand our ancestors' physical and pathological traits in history. However, the development of biological anthropology is not limited to the studies on human remains collected from archaeological sites. Rather, various kinds of specimens of parasites, insects, and animals also become the subjects of bioanthropological researches. Despite the trends, there has not been much opportunities for bioanthropologists to see recent outcomes of zooarchaeology from anthropological perspectives. In this presentation, we thus present the current trends in this attractive subject to improve our understanding of the domesticated or wild animals over time, as well as their interaction with human society in history. The zooarchaeological study will be fundamental basis for forthcoming zooarchaeological studies that would be performed on various specimens collected from excavation sites in Korea. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2017R1D1A1B03030127).

Key Words: Zooarchaeology; Anthropology; Archaeology; Excavation

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SIV-2

Multi-isotope investigation of horse breeding in Japan

Manabu Uetsuki[1] Takashi Gakuhari[2]

[1]Research Institute of Cultural Propetries, Teikyo University, [2]Institute for Frontier Science Initiative, Kanazawa University

The result of isotopic analysis of tooth enamel from archaeological horse remains in Japan and how it can contribute to understanding the history of horse breeding will be discussed. Oxygen isotopes (18/16O) and strontium isotopes (87/86 Sr) reflect the geographical area of origin. Carbon isotopes (13/12C) reflect diet, namely, the ratio of C3 and C4 plants. The latter is rare in natural environment in Japan and consist mainly of millets, implying artificial feeding. Horse teeth enamel contains information of up to 5 years of age, when the mineralization completes. A sequential sampling will also enable us to track geographical movement or change in diet.

In traditional horse breeding areas of inland central Japan and pacific coasts of northeastern Japan, δ18Ooxygen and 87/86Sr values from classic to medieval period remains were limited. This is in contrast with the result from 7th century Nara, the location of the central palace, where the values were more varied and many exhibited exotic values. Some of these matched afore mentioned values from breeding areas of central Japan. The fact corresponds with the tribute of horses from this region to the central palace recorded in later documents.

The analysis of carbon isotopes has revealed a high frequency of C4 plant consumption among horses in inland central Japan and pacific coasts of northeastern Japan. The result coincides with the fact that these areas were also traditional millet cultivation zone and suggests strong relationship between the production of millet and development of horse breeding. Sequential sampling has revealed a significant rise in C4 plant consumption around 3 years of age among some individuals. This is in accordance with historic records prescribing millet feeding to fine horses. On the contrary, some individuals exhibited a constant high intake of C4 plant, which may reflect another form of feeding such as a year-round breeding in barns. Isotopic analysis is a rich source of information on horse usage and breeding techniques. Our next task is to study and compare Korean and Japanese remains to understand the origin, spreading, and transition of these techniques.

Key Words: Horse, Zooarchaeology, Isotope, Oxygen, Strontium, Carbon

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SIV-3

고고학 발굴현장에서 수집한 조선시대 말 뼈 미토콘드리아 DNA D-loop 서열에 대한 유전학적 분석

Jong Ha Hong[1,2,*], Jieun Kim[1], Sun Kim[3], Dong Hoon Shin[1]

[1]Lab of Bioanthropology Paleopathology and History of Disease, Department of Anatomy and Cell Biology, Seoul National University College of Medicine, [2]Institute of Korean Archaeology and Ancient History (IKAA), Kyung Hee University, [3]Research Institute of Buddhist Cultural Heritage

Ancient DNA (aDNA) analysis have become broadly used to obtain genetic information from the ancient animal bones discovered at archaeological sites of late. Nevertheless, despite of the close relations of ancient animals to human culture and society of long-term in Korea, intimate genetic history could not be inferred from aDNA analysis. In this study, we thus performed the research on the ancient DNA recovered from horse bones excavated in South Korean 15th or 16th century archaeological site. We used femur of ancient horse specimen (SNU-A001) for amplification, cloning and sequencing of genus *Equus* aDNA. In NCBI/ BLAST search, the current ancient horse specimen was analyzed to be similar to the modern domesticated *Equus caballus* DNA reported from Korea. however, *Equus asinus* (donkey) sequence has been figured out to be genetically distant with the current sequence. And also, our results from current ancient horse DNA study induced genetical affinity to the domesticated *E. caballus*, but not as so with wild *E. caballus* sequence reported in GenBank (from Mongolia). Since horse had historical significance in dimensions of transportation and weapons and had interred in the ancient societies, their bones will be studied increasingly for future anthropological investigations in Korea. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2017R1D1A1B03030127).

Key Words: *Equus caballus*; Ancient DNA; Phylogenetic analysis; Horse; D-loop; DNA

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SIV-4

분묘유적에서의 동물유존체 출토 양상과 그 의미

고은별 /서울대학교 고고미술사학과

한국 고고학 유적 가운데 분묘유적에서 동물유존체가 출토되는 경우는 대부분 삼국시대, 그 중에서도 5-6세기를 전후한 백여년에 집중된다. 그 이전과 그 이후 시기에도 분묘 유적에서 동물유존체가 출토되는 경우가 있지만 소수에 불과하고, 그 양도 많지 않다. 반면 5-6세기를 중심으로 신라, 가야 지역에서 고총고분이 세워지던 시기에는 후장문화의 영향하에 많은 동물이 부장, 희생되었고, 그 결과 많은 동물유존체가 잔존할 수 있게 되었다. 이를 가리켜 동물공희라는 용어를 사용하는데 그 성격과 의미에 따라 동물부장과 동물희생으로 구분된다. 먼저 분묘 내부, 즉 무덤의 주인이 묻히는 주곽과 부장품이 매납되는 부곽 내부에 공물의 의미로 묻히는 경우는 동물부장으로 분류되는데, 조류, 어류, 패류, 포유류 등 식용되는 동물이 토기 등의 용기에 담겨 부장되는 형식이다. 동물부장의 다음 단계는 분묘 내부 또는 개석 위, 봉토 등에 용기류에 담겨져 매납된 공물로, 이는 분묘 축조 과정이나 이후 제사 과정에서 행해진 의례에 이용된 祭需 음식을 주로 주 · 부곽의 외부에 매납한 경우다. 마지막은 의례 과정에서 의미가 부여되어 희생된 제물이 매납된 경우로, 살아있는 존재의 목숨을 앗는다는 행위에 초점이 맞추어진 것이며 이는 동물희생으로 분류할 수 있다. 이 동물들은 분묘 축조 과정 혹은 그 이후의 제사 과정에서 행해진 의례에서 희생되어 개석 위, 호석 주변, 인접한 독립매장유구 등 분묘 외부에 매납되는데 흔히 말무덤, 마갱 등으로 불려왔던 사례들이 이에 해당한다. 굴광이나 정지 작업 외에 별도의 시설 없이 매납되고 이때 용기류에 담긴 사례는 드물다. 이처럼 동물부장, 제수의 매납, 동물희생 등 동물공희의 종류에 따라 부여된 의미가 상이하기 때문에 그 목적에 따라 선택되는 동물의 종류도 달라지고 매납 방식에서도 차이가 나타난다. 임당 유적에서 공물로서 부장 매납된 동물은 식용되는 종이 주를 이루며 조류, 어류, 패류, 포유류가 모두 확인되는 반면 제물로 희생되는 동물은 상징적인 가치가 부여되거나, 재산으로서의 가치가 부여된 말이나 개와 같은 사육종 포유류 동물이 선택된다. 부장품으로 분묘 내부에 동물이 매납되는 동물부장과 달리 분묘 외부에서 이루어지는 동물희생과 제수의 매납은 의례 과정에 혼재되어 있고 그 결과 고고학적으로 그 공간이 중첩되기도 해 조사 과정에서 그 맥락에 대한 면밀한 주의가 요구된다고 하겠다.

Key Words: 동물유존체, 동물공희, 공물, 동물희생, 의례

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SIV-5

삼국시대 생활유적 출토 동물뼈

Hunsuk Kim*, Moonjung Choi, Jonghoon Lee
Gyeongju National Research Institute of Cultural Heritage

In the Korean Peninsula, animal remains are found mainly in shell middens and wetlands. Wolseong, Gyeong-ju, considered as the royal palace of Silla(5- 7C), is surrounded by water moat where a large number of animal remains were excavated.
Identified species in Wolseong include mammals such as boar, cattle, horse, dog, deer, bear and sea lion. In terms of fish and birds, only shark and pheasant were recorded. Mammals constitute the majority of faunal remains in Wolseong except for a little amount of fish and birds. Among mammals, boar (30%) comprise the largest proportion of identified animals. Cattle, horse and dog are also noticeable with approximately 10% each.
Fauna in Wolseong is distinctive from other palace sites in Korea where the majority of animal remains is deer.
Further research is required to address whether this difference is due to temporal changes, the environmental differences or the differences in political development

Key Words: Wolseong, Fauna, Royal palace of Silla(5- 7C), Gyeong-ju, Animal remain

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Symposium V

2019년 10월 17일(목) 16:20 ~ 18:00
벨라스타홀

Microscopy

좌장 유임주 고려의대 • 현영민 연세의대

SV-1 **16:20-16:45**
Two-Photon Microscopy Imaging of Synapses, Glia and Neuronal Calcium in Living Mouse Brain for Neuroscience and Pain Research
김선광 • 경희대학교 한의과대학

SV-2 **16:45-17:10**
Multi-dimensional Imaging with Correlative Super-Resolution Microscopy
김두리 • 한양대학교 화학과

SV-3 **17:10-17:35**
Application of Structured Illumination Microscopy to Chromosome Morphogenesis and Localization of Replication Protein A during Mammalian Meiosis
김근필 • 중앙대학교 생명과학과

SV-4 **17:35-18:00**
Trend in deep molecular imaging with tissue clearing
하창만 • 한국뇌연구원

SV-1

Two-Photon Microscopy Imaging of Synapses, Glia and Neuronal Calcium in Living Mouse Brain for Neuroscience and Pain Research

Sun Kwang Kim
Department of Physiology, College of Korean Medicine, Kyung Hee University

Recent advances in two-photon microscopy, fluorescence labeling techniques and genetically encoded calcium indicators have enabled us to directly see the structural and functional changes in neurons and glia, and even at synapses, in the brain of living animals. Long-term *in vivo* two-photon imaging studies have shown that some postsynaptic dendritic spines in the adult cortex are rapidly eliminated or newly generated, in response to altered sensory input or synaptic activity, resulting in experience/activity-dependent rewiring of neuronal circuits. *In vivo* two-photon Ca^{2+} imaging studies have revealed the distinct, input-specific response patterns of excitatory neurons in the brain. These updated *in vivo* approaches are now being widely used for the study of pathophysiological mechanisms of neurological diseases. In this talk, I will introduce my previous and ongoing works in the last decade, focusing on *in vivo* two-photon microscopy imaging of synaptic structures, glia, and neuronal calcium in living mouse brain during various types of pathological pain. Based on those results, I will show in detail how plastic changes in synaptic structure and function contribute to chronic pain conditions, like neuropathic and inflammatory pain.

Key Words: Two-photon microscopy, Synapse, Glia, Calcium, Brain, Pain

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SV-2

Multi-dimensional Imaging with Correlative Super-Resolution Microscopy

Doory Kim
Department of Chemistry, Hanyang University

The rise of super-resolution microscopy (SRM, Research field of the Nobel Prize in Chemistry 2014) over the past decade has drastically improved the resolution of light microscopy to ~10 nm, thus creating exciting new opportunities and challenges for correlative microscopy. Correlative microscopy, the integration of two or more microscopy techniques performed on the same sample, produces results that emphasize the strengths of each technique while offsetting their individual weaknesses. The new opportunities afforded by correlative SRM have hence motivated extensive new research, providing multidimensional, multi-scale, and corroborated information about a system regarding morphology, functionality, dynamics, cellular context, and chemical composition. In this presentation, I will talk about our technology development and recent applications of correlative SRM and other microscopy techniques, including electron microscopy, live-cell imaging, and spectroscopy. Using this approach, we studied filamentous influenza viruses, the purine biosynthetic enzymes organization complex called purinosomes, and the ring-opening reaction of photochromism molecules.

Key Words: Super-resolution microscopy, Correlative microscopy, Stochastic Optical Reconstruction Microscopy (STORM), Electron microscopy, Live-cell imaging

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SV-3

Application of Structured Illumination Microscopy to Chromosome Morphogenesis and Localization of Replication Protein A during Mammalian Meiosis

Keun Pil Kim

Department of Life Science, Chung-ang University

An important event enabling meiotic prophase I to proceed is the close juxtaposition of conjoined chromosome axes of homologs and their assembly via an array of transverse filaments and meiosis-specific axial elements into the synaptonemal complex (SC). During meiosis, recombination requires the establishment of a platform for recombinational interactions between the chromosome axes and their subsequent stabilization. This is essential for ensuring crossover recombination and proper segregation of homologous chromosomes. Thus, well-established SCs are essential for supporting these processes. The regulation of recombination intermediates on the chromosome axis/SC and dynamic positioning of double-strand breaks is not well-understood. Here, using super-resolution microscopy (Structured Illumination Microscopy), we determined the localization of replication protein A (RPA) complex on the chromosome axes in the early phase of leptonema/zygonema and within the central elements of SC in the pachynema during meiotic prophase in mouse spermatocytes. RPA, which marks the intermediate steps of pairing and recombination, appears in large numbers and is positioned on the chromosome axes at the zygonema. In the pachynema, RPA foci are reduced, but do not completely disappear; instead, they are placed between lateral elements. Our results reveal the precise structure of SC and localization dynamics of recombination intermediates on meiocyte chromosomes undergoing homolog pairing and meiotic recombination.

Key Words: Meiosis, Structured illumination microscopy, Replication protein A, Recombination, Synaptonemal complex

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SV-4

Trend in deep molecular imaging with tissue clearing

Hye Ryeong Lim, Youngjae Ryu and Chang Man Ha
Research Division and Brain Research Core Facilities of KBRI

Biological tissues are intrinsically opacity and consist three dimensional structure; for this reason, scientists have always tried to extend tissue imaging to thick specimens. Many optical clearing techniques developed for fluorescent proteins in the past few years and we can take the deep tissue imaging such as mouse whole brain. The optical clearing techniques can clarify to 4 families based on the main physical mechanism: organic solvents, aqueous solutions with high refractive index, protein hyperhydration, and tissue transformation with hydrogel embedding. However, these tissue imaging for clearing have several problems such as huge data handling, light scattering and limitation of resolution. Here we are introduce that simple tissue clearing method for fluorescent overexpressed tissue or immunostained samples compare with the commercial clear methods. We further discuss what we need to solve the issue for clearing methods and how we can apply tissue clearing methods to our research interest.

Key Words: Tissue clearing, Deep molecular imaging, Brain tissue, Lage image tiling

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Symposium VI

2019년 10월 17일(목) 16:20 ~ 18:25
거문도C홀

Cell Biology (I)

좌장 허대영 인제의대 • 장용석 전북대

SVI-1 **16:20-16:45**
Mucosal immune system and antigen-specific mucosal immune enhancement
장용석 • 전북대학교 의과대학

SVI-2 **16:45-17:10**
T cell receptor signaling related primary immune disorder
박성규 • 광주과기원

SVI-3 **17:10-17:35**
A peptide-based vaccine for Mycobacterium avium subspecies paratuberculosis
박건택 • 인제대학교 바이오테크놀로지학부

SVI-4 **17:35-18:00**
p38 stabilizes Snail by suppressing DYRK2-mediated prime phosphorylation required for GSK3β-βTrCP-induced Snail degradation
유지윤 • 경상대학교 자연과학부

SVI-5 **18:00-18:25**
Proteomic and metabolomic analysis of plasma samples from autism patients
김민식 • DGIST

SVI-1

Mucosal immune system and antigen-specific mucosal immune enhancement

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Various pathogens initiate their infection through the mucosa. Therefore, induction of mucosal immunity against pathogenic antigens is an important aspect to develop successful protective measures against the pathogens. Despite the importance of mucosal immune induction against various pathogens, very few oral mucosa vaccines are currently available. Limited availability of mucosal vaccines can be attributed to the difficulty in inducing efficient mucosal immune responses because it is achievable only following antigen entry into the mucosal immune inductive site such as Peyer's patches (PPs) and antigen-specific immune induction. Moreover, mucosal epithelial cells tightly restrict the influx of luminal antigens and predominantly induce the tolerogenic immune response. The follicle-associated epithelium of the PPs contains M cells, which are epithelial cells specialized to internalize luminal antigens. The high transcytotic activity of M cells makes them attractive targets for mucosal antigen delivery. However, it remains unclear whether antigen delivery to M cells alone can guarantee the effective induction of a mucosal immune response. Consequently, our research interest is focused on developing strategies that efficiently targets antigens to M cells and enhances the efficiency of mucosal immune induction against the antigens. The role of M cell-targeting ligand that we identified and its receptor, complement 5a receptor, and the mechanisms underlying its action on mucosal immune induction will be discussed.

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SVI-2

T cell receptor signaling related primary immune disorder

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Undiagnosed inflammatory diseases are sometimes associated with de novo variations in immune related genes. Here we found a de novo variant associated with chronic inflammatory disease. The first example is a new variant for cytotoxic T-lymphocyte antigen 4 (CTLA-4). The functional defect of CTLA-4 due to de novo variation was tested by in vitro experimental systems and we report the direct effect of CTLA-4 dysfunction in humans. In patients with severe autoimmune features, CTLA-4-Ig has been used clinically for CTLA-4-Ig immunoreactivity to enhance the CTLA-4 mediated signal, resulting in significant clinical improvement. Another example is the de novo variant of transmembrane protein 173 (TMEM173) encoding the stimulator of the interferon gene (STING). Changes in the functional properties of STING caused by de novo mutations wer e also tested by an in vitro experimental system, and we observed infants with STING-related vascular disease induced by two genetic changes of STING successfully treated with Janus kinase Tofacitinib, an inhibitor, improved skin lesions in patients. Thus, in addition to identifying de novo variant, proper functional testing of de novo variants is an important step in guiding patient care.

Key Words: Inflammation, CTLA-4, STING, CTLA-4-Ig, Tofacitinib

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SVI-3

A peptide-based vac cine for Mycobacterium avium subspecies paratuberculosis

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Mycobacterium avium subsp. *paratuberculosis* (*Map*) is primarily causing a chronic inflammatory enteritis in ruminants (Johne's disease). However, a zoonotic potential of *Map* has been debated for more than a century due to the similarity of lesions in the intestine of patients with Crohn's disease and with those in *Map* infected cows. The recent accumulated data support the possibility of *Map* as a zoonotic pathogen. However, the development of efficient vaccine to control the spread of *Map* has been impeded, partly due to the lack of methods to fully evaluate the efficacy of candidate vaccines before testing in target animals. A reduction in the capacity to survive in macrophages or mice has not predicted the efficacy of mutant candidates in animal challenges. To address this problem, we developed an ex vivo platform to analyze host immune responses and evaluate candidate vaccines using bovine blood dendritic cells (bDC)/monocyte derived dendritic cells (MoDC)/ monocyte derived macrophages (MoMΦ). A flow cytometric assay was used to analyze the proliferative response to antigens presented by MoDC pulsed with candidate vaccines. A 6 hr killing assay was developed and used to measure the killing activity of effector T cells against *Map* present within MoMΦ. Using the ex-vivo system, we demonstrated *relA* gene deletion mutant of *Map* and a 35 kDa *Map* membrane protein can induce cytotoxic CD8 T cells, effectively killing intracellular *Map*, by co-culture with MoDC pulsed with each antigen, respectively . As presented here, the unique co-culture platform has potential for use in assessing efficacy of candidate vaccines and host immune responses to *Map* ex vivo.

Key Words: Bovine, Crohn's disease, Dendritic cell, Ex-vivo experiment, *M. paratuberculosis, Vaccine*

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SVI-4

p38 stabilizes Snail by suppressing DYRK2-mediated prime phosphorylation required for GSK3β-βTrCP-induced Snail degradation

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Snail is a key regulator of epithelial-mesenchymal transition (EMT) which is a major step in tumor metastasis. While the induction of Snail transcription precedes EMT, post-translational regulation especially phosphorylation of Snail, is critical for determining Snail protein levels or stability, subcellular localization, and the ability to induce EMT. To date, several kinases are known that enhance the stability of Snail by preventing its ubiquitination, however, the molecular mechanism(s) underlying this are still unclear. Here, we identified p38 MAPK as a crucial post-translational regulator that enhances the stability of Snail. p38 directly phosphorylated Snail at Ser107, this effectively suppressed DYRK2-mediated Ser104 phosphorylation which is critical for GSK3β-dependent Snail phosphorylation and βTrCP-mediated Snail ubiquitination and degradation. Importantly, functional studies and analysis of clinical samples established a crucial role for the p38-Snail axis in regulating ovarian cancer EMT and metastasis. These results indicate the potential therapeutic value of targeting the p38-Snail axis in ovarian cancer.

Key Words: Epithelial-Mesenchymal Transition, Snail, p38, DYRK2, GSK3β, βTrCP

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SVI-5

Proteomic and metabolomic analysis of plasma samples from autism patients

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Department of New Biology, DGIST

Autism spectrum disorder (ASD) is a type of neurological and developmental disorders that affect communication and behavior. Since symptoms generally begins in the first two years of life, early diagnosis is essential for early treatment that allows children with ASD to learn language and social skills. However, clinical molecular tests for ASD are currently unavailable and, because of this, a great number of children are not diagnosed with ASD in their early stage that would result in inadequate early intervention. In this study, we aimed at discovery of potential biomarkers from mass spectrometry-based integrative metabolomics and proteomic analysis. Plasma samples collected from children with ASD and normal patients with close ages were analyzed using high throughput tandem mass spectrometry. Metabolomic data was collected using AbsoluteIDQ technology to absolutely quantitate 180 circulating metabolites while proteomics data was acquired using label-free high resolution mass spectrometry platform combined with iBAQ-based quantitative technology. As a result, a few lipid classes and proteins were found to be altered in ASD patients. The result will be discussed in more detail. This list of molecules can be further studied for development of clinical tests for the early diagnosis of ASD.

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Symposium VII

2019년 10월 18일(금) 09:00 ~ 10:40
거문도A홀

Anatomy Education

좌장 송창호 전북의대 • 허영범 경희의대

SVII-1 **09:00-09:25**
Effect of alternate dissection on anatomy learning
황영일 • 서울대학교 의과대학

SVII-2 **09:25-09:50**
Digital anatomy table을 활용한 실습경험 및 미국 해부학교육 소개
최형진 • 서울대학교 의과대학

SVII-3 **09:50-10:15**
임상의학에서 academic medicine의 구현-가톨릭의대 사례
정대철 • 가톨릭대학교 의과대학

SVII-4 **10:15-10:40**
해부학 교육(자)의 현황과 전망
송우철 • 건국대학교 의과대학

SVII-1

Effect of alternate dissection on anatomy learning

이지연[1], 김도환[2], 황영일[1]
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해부실습에 있어서, 특히 머리목 부위의 실습은 혼잡할 수 밖에 없으며, 의도하지 않게 실습에서 배제되는 학생이 생길 수 있다. 이 문제를 해결하기 위해서 우리 대학에서는 2014년부터 머리와 목 부위의 실습에 있어서 분반 교대실습을 도입하였고, 2016년에는 팔다리 부위까지 확대하였다.
한 시신에 배정된 학생을 두 조(A, B)로 나누었다. A조가 먼저 실습을 시행하고, 다음 실습에 B조에게 이전 실습결과를 설명한 후 자유시간을 가졌다. B조는 A조에 이어서 실습을 시행하고, 다음 실습시간에는 A조에 실습결과를 설명한 후 자유시간을 가졌다.
2016년 분반 교대실습에 대한 학생들의 인식과, 교대실습이 학생들의 학습에 미치는 영향을 분석하여 해부학회 학술대회에서 포스터 발표한 바 있으며, 이후 2019년에 추가로 학생들의 의식과 성적 변화를 알아보았다.
교대실습에 대한 긍정적 반응은 2014~2016년과 2019년에 각각 65.4%, 68.6%, 81.0%, 88.5%(팔다리)와 90.6%(머리목)로 점차 증가했으며, 부정적 반응은 2019년에 4.2%(팔다리)와 3.1%(머리목)로 최소화 되었다. 앞 조의 설명에 대한 평가는 2014~2016년에 각각 56.9%, 72.8%, 82.6%에서 2019년에는94.7%(팔다리)와 91.6%(머리목)로 증가하였다. 실습을 직접 하지 않은 부분에 대해서는 2~4%의 학생이 많은 어려움을 표하였으며, 실습시험에 지장이 많았다는 응답은 1~2%였다. 특이하게, 몸통 부위에 대한 교대실습 시행에 대해서 2016년에는 56.3%만이 찬성한 반면에 2019년에는 82.1%가 찬성하였다.
2011~2019년까지의 해부학시험 성적을 분반 교대실습 이전과 이후로 나누어 비교해 본 결과, 필기시험 성적은 팔다리, 몸통, 머리목 등 모든 부위에서 상승한 경향을 보였으며 실기시험 성적은 팔다리와 머리목 부위에서는 다소 상승한 양상을, 몸통에서는 다소 감소한 양상을 보였다. 이 결과는 교대실습에 대한 정서적 불안감과는 달리 새로운 실습 방식이 학생들 학습에 부정적 영향을 끼치지는 않는다는 것을 보여준다.
결론적으로, 해를 거듭하면서 학생들은 분반 교대실습에 점차 적응하는 모습을 보였고, 막연한 우려와는 달리 교대실습이 학생들 성적에 악영향을 끼치지는 않아서, 이 방법은 해부실습실의 복잡성을 줄여줄 적절한 방법으로 생각된다.

Key Words: 맨눈해부학, 해부학교육, 해부실습, 분반 교대실습, 학습효과

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SVII-2

Digital anatomy table을 활용한 실습경험 및 미국 해부학교육 소개

최형진 /서울대학교 의과대학 해부학교실

Digital anatomy 은 가상의 카데바 신체를 디지털화한 3차원 입체 구조 정보를 사용하여 구성된 가상신체 카데바를 해부하거나, 3차원 공간에서 보고, 상호작용하며 공간지각적 이해를 할 수 있는 도구이다. 현재 사용되고 있는 형태는, 실제 1:1 신체 크기를 바탕으로 한 table 형태의 하드웨어로 구현한 경우도 있고, 스마트폰, 테블렛, 데스크탑에서 구현되는 형태도 있다. 다양한 수준과 형식의 contents, interface, software, hardware 가 학생, 교수, 기관에서 무료 혹은 유료로 사용되고 있다. 하지만, 아직도 기존 해부학 수업과 실습에 어떻게 이런 digital anatomy 를 적용하는 것이 적절한 유용성이 있을지는 잘 알려져 있지 않다.

이번 발표에서는, 개인적으로 해부학 수업과, 실습에 digital anatomy table 을 활용하기 위해, 기존 hardware, software, contents 를 사전작업을 하여 제작하고, 실제 수업과 실습에 어떻게 적용하였는지 개인적인 경험을 나누려고 한다. 기존 해부학수업에서 사용하던 2차원, 3차원 그림들이 가지는 한계를 극복하여, 반투명한 시각화와, 장기들을 3차원 공간에서 이동하며 보여주는 방식으로, 공간지각적인 각 장기의 위치와 서로 위치관계를 설명하고, 학생의 이해도를 높일 수 있었다. 실제 카데바 실습과 연관하여, dissection 할 장기들이 어느 위치에 어떤 크기, 방향으로 존재하고, 주변 구조물과의 관계를 digital virtual space 에서 설명하여, 통합적인 공간지각이 높은 상태에서, 카데바 dissection 을 할 수 있도록 도울 수 있었다.

미국 해부학교육 현실을 알기 위해, Cleveland Clinic Lerner College of Medicine, Stanford University School of Medicine, Mayo Clinic College of Medicine 을 방문하여, 해부학 교육이 실제로 이루어지고 있는 현장을 탐방하였고, 해부학교실 교수, 교육자들과 면담을 통해, 어떤 목적으로 어떤 형태의 해부학교육을 제공하고 있는지 탐방하였다. 미국 해부학교육 탐방을 통하여 적용점으로 생각한 점은 다음과 같다. 탐방했던 모든 의과대학에서는 카데바 실습을 의과대학 학생이 실시하고 있었다. 학생이 직접 dissection 을 전신에 대해서 하는 경우가 일반적이었다 (의사 과학자 양성 목표 대학인 Cleveland Clinic만 학생이 직접 dissection 을 하지 않았음). 교육 내용과 목표에서 Clinically oriented anatomy 교육을 지향하고, dissection 을 위한 dissection 은 하지 않는 교육목표를 가지고 있었다 (수술 연습은 등 dissection skill을 기르는 것은 해부학실습이 아닌 다른 선택적 특화수업이 있었음). 실제 진료현장을 반영하는 CT/MRI 영상과 직접 연동된 해부학수업을 운영하고 있었고, 카데바의 CT를 촬영하여, 카데바 dissection 과 함께 보면서, 구조적인 지식 습득과, 실제 진료현장의 적용을 연계하였다. 일방향 지식 전달 수업 보다는, Case 위주의 통합적인 수업으로 구성되어 있었으며, 직접 학생이 참여하여 발표하는 형식의 해부구조 지식 습득 수업들이 있었다. First Patient 라는 개념으로 인문 사회적 소양을 기를 수 있도록 하였다. 의대 학부생 선배들을 조교로 활용하고, 이 조교활동을 포트폴리오에 남겨서, 향후 전공의 지원에 반영될 수 있게 하였다. 모두 Pass/ non-pass 로 진행하였다. 신경해부는 해부학교실이 아닌 신경과학과정에서 수행하고 있었다.

Key Words: Digital Anatomy Table, Virtual Reality Education, USA Anatomy Education

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SVII-3

임상의학에서 academic medicine의 구현-가톨릭의대 사례

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Medicine provided health for individual, happiness for patients and their family, and prevention and care for disease. Academic medicine composed of three components: patient care, research and effective medical education. The good patient care is developed from research and continuous medical education, although there are not balanced for academic medicine in Korea due to various medical environments. Now, we entered into environment of 4th industrial revolution. New situation need the change for our thought, concept, and performance. In 21st century, we try to increase the '6' competencies for education: Collaboration, Communication, Contents, Critical thinking, Creative innovation, and Confidence. In Korea, the medical education changed to outcome based education since 2000, and KAMC proposed the outcomes for basic medical education.

In our institute, we are changing entire medical education curriculum after evaluation about OMNIBUS curriculum. We developed program outcome, phase outcome, and considered the application of education techniques. Also, we used Blackboard system as learning management system (LMS), which provide the information about lecture, laboratory works including education outcome. We have 'Applied clinical anatomy' for 4th year medical students at beginning of 2nd semester. Medical students and training doctors cannot perform directly invasive procedures for patients due to social limitations. This course contained emergency skills and surgical procedures for 2 days. The outcomes in this course are as follow: student can perform the life threatening emergency skills, and clinical significance and implementation process of major surgical procedures in practical field. The senior residents or junior clinical fellows attended in this course. Also, several clinical workshops using cadaver were opened under the collaboration between department of Anatomy and other clinical departments. These workshop help to improve the surgical processing for patient care. Recently, we have simulation based workshop for various clinical situations.

Now, we concern the new situation for student characteristics, 4th industrial revolution, and medical environment changes. We meet time for change the concept and thought. Academic medicine result from education, research, and patient care. Medicine is applied to patients, but based on the education and research. Patient care is closely related with research and continuous effective education.

Key Words: Academic medicine, Education, Research, Patient care

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SVII-4

해부학 교육(자)의 현황과 전망

송우철 /건국대학교 의학전문대학원 해부학교실

우리 대한해부학회에 등록된 국내 해부학자는 학술대회에 꾸준히 참가하는 경우 서로 잘 알고 있지만 우리나라 전체에 직급별로, 또는 세부전공별로 어느 정도 구성되어 있는지는 잘 알지 못한다. 2018년에 대한해부학회 회원이름책 여섯째 판이 새로이 발간되었고 이를 바탕으로 학회의 동의를 얻어 국내 해부학자의 현황을 보고하고자 한다. 국내 의과대학(54교실) 및 치과대학(9교실)에 소속된 해부학자는 2018년 현재 418명으로 남자 253명과 여자139명이다(모름 26명). 직급별로 교수 197명, 연구교수(박사후과정 포함) 55명, 대학원생(조교 및 연구원 포함) 125명, 기사 41명이다. 대학원생은 박사과정 24명, 석박사통합과정 13명, 석사과정 37명, 조교 38명, 연구원 13명 등이다. 교수의 구성은 각각 교수 134명, 부교수 33명, 조교수 30명이며, 전체 교수는 성별로 남자 156명, 여자 41명이다. 교수의 나이구성 중 50대 후반이 가장 많았다. 교수의 강의분야는 구분 없는 해부학(79), 조직학(40), 맨눈해부학(38), 신경해부학(19), 발생학(12) 순이었다. 교수의 연구분야로는 신경과학(55), 맨눈해부학(42), 조직학(33), 세포생물학(13), 발생학(11) 순이었다. 이번 조사로 전국적인 해부학자의 현황을 파악할 수 있었고 국내 해부학의 미래를 전망해 볼 수 있는 기회로 삼았으면 한다.

Key Words : 해부학, 해부학자, 교육분야, 연구분야, 교수, 대학원생

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Symposium VIII

2019년 10월 18일(금) 09:00 ~ 11:00
벨라스타홀

KAA-JAA Joint Symposium

좌장 한승호 중앙의대 • Satoshi Waguri Fukushima University

SVIII-1 **09:00-9:20**
Relevance of HOXB13 developmental protein to prostate cancer malignancy
Chaeyong Jung • Chonnam National University

SVIII-2 **09:20-9:40**
Three-dimensional structure of mouse seminiferous tubules
Hiroki Nakata • Kanazawa University

SVIII-3 **09:40-10:00**
Therapeutic effects of novel Tau antibody for Alzheimer's disease
Seung-Yong Yoon • Ulsan University

SVIII-4 **10:00-10:20**
The role of cohesin in the central nervous system
Yuki Fujita • Osaka University

SVIII-5 **10:20-10:40**
Neutrophil-Gated Immune Response: To drive or To be driven?
Young-Min Hyun • Yonsei University

SVIII-6 **10:40-11:00**
Hyperosmotic stress induces unconventional autophagy independent of the Ulk1 complex
Naoki Tamura • Fukushima Medical University

SVIII-1

Relevance of HOXB13 developmental protein to prostate cancer malignancy

Chaeyong Jung
Department of Anatomy, Chonnam National University Medical School

Androgen signaling plays a critical role in the development of prostate cancer (PCa) and its progression. However, androgen-independent PCa cells emerge after hormone ablation therapy, resulting in significant clinical problems. Transcription factor HOXB13 has an important role in development of normal prostate and PCa. HOXB13-mediated growth modulation of PCa involves both androgen-dependent signals and –independent signals. This talk will cover on HOXB13's role in PCa growth modulation through modulation of several well-known oncogenic pathways, including androgen receptor, RB/E2F1, β-catenin/TCF, NF-κB. This talk will also uncover HOXB13's regulation of PCa malignancy through altering intracellular zinc.

Key Words: HOXB13, Prostate cancer, Androgen receptor, Zinc

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SVIII-2

Three-dimensional structure of mouse seminiferous tubules

Hiroki Nakata

Department of Histology and Cell Biology, Graduate School of Medical Sciences, Kanazawa University

Seminiferous tubules develop from sex cords, which are embryonic structures with simple C-shaped arches. Our group recently reported the high-resolution three-dimensional (3D) structure of all seminiferous tubules in an adult mouse testis. The method involved manual segmentation of the outlines of seminiferous tubules in serial paraffin sections, tracing continuous tubules from section to section with different colors, and 3D reconstruction of individual tubules using serial high-performance reconstruction software. We found 11 seminiferous tubules, 28 connections with the rete testis, 9 branching points and one blind end in one testis. Each tubule ran along circular paths within the testis while making convolutions with cranial and caudal hairpin turns. The cranial turns of all tubules were in contact with the tunica albuginea, whereas the caudal turns were not, resulting in funnel-shaped networks of these tubules with tapered caudal portions. The caudally located networks surrounded the preceding cranially located networks from the bottom and outside, similar to stacked paper cups. Next, in order to reduce the time and labor required for 3D reconstruction, we made the segmentation step semi-automatic by labeling the basement membrane of seminiferous tubules with fluorescent immunohistochemistry or PAS staining. Using this improved method, we further analyzed all seminiferous tubules in 9 testes from 9 different mice, 3 each at 0, 21 and 90 days (adult) postpartum. The 3D structure of seminiferous tubules, including the number and length of tubules as well as the number of connections with the rete testis, branching points and blind ends, was assessed accurately. Although tubules showed marked variations among individual mice, their overall structure was regular and retained from newborn to adult mice. In a representative testis at 21 days, the sites at which spermatids initially occurred were examined by labeling acrosomes and were found to be preferentially distributed in the upper and medial portions of the testis close to the rete testis. In a representative adult testis, 76 complete waves with an average length of 16.9 mm were found and their directions were analyzed. The methods used in our study will be useful for investigating the structure and function of seminiferous tubules in mice and humans under normal and pathological conditions, such as infertility.

Key Words: Seminiferous tubules, Testis, Three-dimensional reconstruction, Wave, Mouse

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SVIII-3

Therapeutic effects of novel Tau antibody for Alzheimer's disease

Seung-Yong Yoon[1,2]

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Although various pathogenic molecules and mechanisms have been suggested to be involved in Alzheimer's disease (AD), the two indispensable pathogenic molecules of AD are β-amyloid (Aβ) and tau. In the meantime, majority of the mechanism studies of AD pathogenesis were focused on the Aβ, which leads big pharmaceutical companies to develop therapeutic drugs targeting Aβ. However, all the clinical trials targeting Aβ have been failed up to now, hence, tau, another inevitable pathogenic molecule, has received attention as a real treatment target for AD. To develop therapeutic antibody targeting tau, we first screened protective effects in tau-P301L transgenic mice by active immunization with several tau peptides of different residues and modifications. Among these tau peptides, we found one epitope with specific residues and modifications to show the best memory improving effects. We then screened and developed the antibody to target this epitope with high affinity and high specificity. We further confirmed the therapeutic effects of this antibody in tau-P301L transgenic mice by passive immunization. This antibody improved memory impairments and AD-related pathology in tau-P301L mice. We anticipate this antibody to be a novel pipeline for the AD therapeutics.

Key Words: Dementia, Alzheimer's disease, Frontotemporal dementia, Tau, Antibody

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SVIII-4

The role of cohesin in the central nervous system

Yuki Fujita[1,2] and Toshihide Yamashita[1-4]

[1]Department of Molecular Neuroscience, Graduate School of Medicine, Osaka University, [2]WPI Immunology Frontier Research Center, Osaka University, [3]Graduate School of Frontier Bioscience, Osaka University, [4]Department of Neuro-Medical Science, Graduate School of Medicine

Spatial chromatin organization and nuclear architecture play key roles in regulating gene expression during cellular proliferation and differentiation in the central nervous systems. Here, we focus on the role of cohesin complex, which is chromosome-associated multi-subunit protein. Cohesin complex is composed of four subunits, Smc3, Smc1, Scc3, and Scc1/Rad21, and has a role in sister chromatid cohesion, which is crucial for accurate chromosome segregation. Cohesin is also known to be involved in chromatin organization by forming chromatin loops at particular loci and regulates gene expression in postmitotic cells.

Disruption of cohesin network results in 'cohesinopathies' such as Cornelia de Lange syndrome. These diseases cause higher brain dysfunction, suggesting the role of cohesin in gene regulation rather than chromosome segregation in the postmitotic neurons. To investigate the potential role of cohesin in terminally differentiated cells in vivo, we generated conditional Smc3-knockout mice. We observed increased dendritic complexity and decreased spine density in cortical neurons of heterozygous Smc3-knockout mice. Neuron-specific Smc3-knockout mice showed the same phenotype. Heterozygous Smc3-knockout mice exhibited increased anxiety-related behavior, a symptom of Cornelia de Lange syndrome, also caused by disruption of cohesin. Thus, neuronal cohesin contributes to neural network formation, presumably by modulating gene expression, and cohesin deficiency leads to higher brain dysfunction.

Key Words: Central nervous system, Brain, Development, Chromatin, Genome

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SVIII-5

Neutrophil-Gated Immune Response: To drive or To be driven?

Young-Min Hyun

Dept. of Anatomy and Brain Korea 21 Plus Project for Medical Science, Yonsei University College of Medicine

For efficient immune response to be initiated by neutrophil extravasation during infection, 1) spatiotemporal regulation for neutrophil migration is critical for host defense and 2) subsequently precise trafficking of activated effector T cells to infection sites is key to their protective functions. Recent studies illuminated that neutrophils have interactions with endothelial cells, endothelial basement membrane, and pericytes as well as perivascular macrophages in the extravasation cascade. Thus, precise regulation of interactions of neutrophils with other cell populations and extracellular matrix would be essential for spatiotemporal migration of leukocytes. The real-time dynamics of cell surface adhesion receptor reflect leukocyte migration and trafficking in various tissues, providing valuable insight into the evolving events of the immune response. Up-to-date imaging techniques including two-photon intravital imaging and 3-dimensional images of transparently cleared tissue provide actual phenomenon of motility and morphology in leukocyte migration cascade. In this study, we provide evidences of cell to cell interaction and the function of adhesion molecules and cochlin-cleaved LCCL in leukocyte migratory strategy during bacterial infection. Especially, the finding of the critical role of cochlin-cleaved LCCL in innate immune cell migration suggests that the LCCL may be a potential therapeutic target to prevent bacterial infection-induced detrimental symptom

Key Words: Inflammation, Immune cell migration, Neutrophil, Two-photon microscopy, Intravital imaging

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SVIII-6

Hyperosmotic stress induces unconventional autophagy independent of the Ulk1 complex

Naoki Tamura, Satoshi Waguri
Anatomy and Histology, School of Medicine, Fukushima Medical University

Autophagy is considered an adoptive mechanism against hyperosmotic stress. Although the process has been reported to be triggered by the inhibition of mTORC1, the precise downstream mechanisms remain elusive. Here, we demonstrate that hyperosmotic stress-induced autophagy is different from conventional macroautophagy in mouse embryonic fibroblasts (MEFs) and human T24 cells. Our results indicated that cytoplasmic puncta for isolation membrane markers WIPI2 and Atg16L increased after hyperosmotic stress. They were found to partially colocalize with puncta for a selective autophagy substrate, SQSTM1/p62, and were shown to be diminished by inhibitors for phosphatidylinositol 3-kinase (PI3K), or by knockdown of hVps34, a component of PI3K. In addition, flux assays showed that SQSTM/p62 and NcoA4 were degraded by the lysosomal pathway. Surprisingly, Ulk1 that is essential for starvation-induced macroautophagy, remained inactivated under hyperosmotic stress, which was partially contributed by mTOR activity. Accordingly, the Ulk1 complex was not nucleated under hyperosmotic stress. Finally, autophagy proceeded even in MEFs deficient in FIP200 or Atg13, which are components of the Ulk1 complex. These data suggest that hyperosmotic stress-induced autophagy represents an unconventional type of autophagy that bypasses Ulk1 signaling.

Key Words: Autophagy, mTOR, osmotic stress, ClassIII PI3K

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Symposium IX

2019년 10월 18일(금) 09:00 ~ 10:45
거문도C홀

Cell Biology (Ⅱ)

좌장 한기환 이화의대 • 김인범 가톨릭의대

SIX-1 **09:00-09:35**
Primary cillia in the kidney function and disease
박권무 • 경북의대 해부학교실

SIX-2 **09:35-10:10**
Extracellular matrix-derived exosomes promote cardiomyocyte growth and electrical activity in engineered cardiac atria
김민석 • 이화의대 약리학교실

SIX-3 **10:10-10:45**
Calcium Homeostasis in Mitochondria-ER-Lysosome Microdomain
박규상 • 연세의대 생리학교실

SIX-1

Primary cillia in the kidney function and disease

Kwon Moo Park
Department of Anatomy, School of Medicine, Kyungpook National University

The primary cilium is a microtubule-based non-motile organelle and plays as a mechano- and chemo-sensor. In kidney, a single primary cilium is recognized on the apical surface of all renal tubular epithelial cells, with the exception of intercalated cells. Primary cilia are associated with a number of kidney diseases including ADPKD. Here, we investigates the association of primary cilia length with kidney function and acute kidney diseases in mice and human. In ischemia/reperfusion acute kidney injury animal model, the primary cilia length changes dynamically; primary cilia lengths in the kidney tubule cells are either shortened or completely disappeared at the initial phase of injury, grown at the early phase of recovery, and then returned to normal range at the late phase of recovery. Ciliary protein amount in the urine increase after ischemia-reperfusion insult in mice. Furthermore, patients kidney-transplanted have large amounts of ciliary proteins in the urine. Primary cilia length in the mouse kidney is altered by the change of water supply. Results indicate that changes in primary cilia length and urinary ciliary protein amount are associated with renal function and damage, suggesting that primary cilia length and urinary cilia could be a new useful biomarker for the diagnosis of kidney diseases and evaluation for renal function.

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SIX-2

Extracellular matrix-derived exosomes promote cardiomyocyte growth and electrical activity in engineered cardiac atria

Minsuk Kim
College of Medicine, Ewha Womans University

Extracellular matrix (ECM) plays a critical role in the provision of the necessary microenvironment for the proper regeneration of the cardiac tissue. However, specific mechanisms that lead to ECM-mediated cardiac regeneration are not well understood. To elucidate the potential mechanisms, we investigated ultra-structures of the cardiac ECM using electron microscopy. Intriguingly, we observed large quantities of micro-vesicles from decellularized right atria. RNA and protein analyses revealed that these contained exosomal proteins and microRNAs (miRNAs), which we referred to herein as ECM-derived extracellular vesicles (ECM-EVs). One particular miRNA from ECM-EVs, miR-199a-3p, promoted cell growth of isolated neonatal cardiomyocytes and sinus nodal cells by repressing homeodomain-only protein (HOPX) expression and increasing GATA-binding 4 (Gata4) acetylation. To further explore the role of this miRNA, we isolated neonatal cardiac cells and recellularized into atrial ECM, referred here has engineered atria. Remarkably, miR-199a-3p mediated the enrichment of cardiomyocyte and sinus nodal cell population, and enhanced electrocardiographic signal activity of sinus nodal cells in the engineered atria. In conclusion, these results provide clear evidence of the critical role of ECM, in not only providing a scaffold for cardiac tissue growth, but also in promoting atrial electrical function through ECM-derived miR-199a-3p.

Key Words: ECM, miRNA, Extracellular vesicles, Heart

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SIX-3

Calcium Homeostasis in Mitochondria-ER-Lysosome Microdomain

Kyu-Sang Park[1,2]

[1]Department of Physiology, [2]Mitohormesis Research Center, Yonsei University Wonju College of Medicine

Ca^{2+} homeostasis in mitochondria, ER and lysosome is important for cellular functions including signal transduction and energy metabolism. Mitochondrial Ca^{2+} uptake mainly mediated by mitochondrial Ca^{2+} uniporter (MCU) activates oxidative phosphorylation and ATP synthesis. In addition, mitochondrial and ER Ca^{2+} uptake sequesters extra-mitochondrial Ca^{2+} to prevent Ca^{2+} cytotoxicity. Upon metabolic stress, however, oxidative stress triggers aberrant ER Ca^{2+} release and thereby depletion of the ER Ca^{2+} store leading to serious ER stress. Simultaneously, store-operated Ca^{2+} entry sustains extracellular Ca^{2+} influx and evokes cytosolic Ca^{2+} overload. Reactive oxygen species (ROS) also induce peri-lysosomal Ca^{2+} dysregulation and defective autophagic flux. Secondary to ER Ca^{2+} release, further increases in cellular Ca^{2+} load aggravates oxidative stress and cytotoxicity eliciting a vicious cycle. These pathogenic changes were attenuated by preventing cellular Ca^{2+} overload, activating autophagic degradation, or scavenging ROS. In this presentation, I would like to introduce the molecular mechanism of inter-organellar microdomain Ca^{2+} regulation in pathophysiologic conditions, which could be an effective therapeutic target for various metabolic and neurodegenerative diseases.

Key Words: Mitochondria, ER, Lysosome, Calcium, Reactive oxygen species

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Oral Presentation

2019년 10월 17일(목) 14:40 ~ 16:00
Oral Presentation Ⅰ (O1~6) 거문도A홀
Oral Presentation Ⅱ (O7~11) 벨라스타홀
Oral Presentation Ⅲ (O12~15) 거문도C홀

2019년 10월 18일(금) 14:30 ~ 15:30
Oral Presentation Ⅳ (O16~21) 거문도A홀
Oral Presentation Ⅴ (O22~25) 벨라스타홀

01~6 Oral Presentation Ⅰ
좌장 이혜연 연세의대 • 박정현 강원의대

07~11 Oral Presentation Ⅱ
좌장 정채용 전남의대 • 허대영 인제의대

012~15 Oral Presentation Ⅲ
좌장 복진웅 연세의대

016~21 Oral Presentation Ⅳ
좌장 송우철 건국의대 • 황영일 서울의대

022~25 Oral Presentation Ⅴ
좌장 노구섭 경상의대

Oral Presentation I (O1~6)

2019년 10월 17일(목) 14:40~16:00, 거문도A홀

좌장: 이혜연(연세의대), 박정현(강원의대)

01 ---------- 62

Perceptions of attractive and healthy-looking lips

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

02 ---------- 62

신경해부학 실습동영상 제작

Dae-Yong Song[1], Kyeung Min Joo[2], Hun-Mu Yang[3], Chan Park[4], Young-il Hwang[5]
[1]Department Anatomy, Eulji University College of Medicine, [2]Department Anatomy, Sungkyunkwan University College of Medicine, [3]Department Anatomy, Yonsei University College of Medicine, [4]Department Anatomy, Kyung Hee University College of Medicine, [5]Department Anatomy, Seoul National University College of Medicine

03 ---------- 63

Retrobulbar filler injection of for orbital volume augmentation: can we define a safety zone?

Shin-Hyo Lee[1], Hyun-Jin Shin[2], Wu-Chul Song[1], Ki Seok Koh[1]
[1]Department of Anatomy, Research Institute of Medical Science, Konkuk University School of Medicine, [2]Department of Ophthalmology, Konkuk University Medical Center, Konkuk University School of Medicine

04 ---------- 63

Anatomical Study for Effective Botulinum Toxin Injection into the Mentalis Muscle

Da-Yae Choi[1], Hyungkyu Bae[2], Jung-Hee Bae[3], Kang-Woo Lee[2], Hee-Jin Kim[2,4], Kyung-Seok Hu[2]
[1]Department of Dental Hygiene, Kwandong University, Gangneung, Korea, [2]Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 PLUS Project, Yonsei University College of Dentistry, Seoul, Korea, [3]Department of Dental Hygiene, Division of Health Science, Dongseo University, Busan, Korea, [4]Department of Materials Science & Engineering, College of Engineering, Yonsei University, Seoul, Korea

05 ---------- 64

Anatomical Continuation between the subSMAS Fat (Innominate Fascia) and ROOF : The True Nature of the ROOF (Retro-Orbicularis Oculi Fat)

Hyosang Ahn[1], Hyoung-Moon Kim[2], Hyung-Jin Lee[1], Ji-Hyun Lee[1], Hee-Jin Kim[1,31]
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06 ---------- 64

Three-dimensional topographic distribution of the superficial temporal artery in the temporal region by MATLAB analysis

Jin-Won Kim[1], Hyungkyu Bae[1], Kang-Woo Lee[1], Kyung-Seok Hu[1], Hee-Jin Kim[1,2]
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Oral Presentation II (O7~11)

2019년 10월 17일(목) 14:40~16:00, 벨라스타홀

좌장: 정채용(전남의대), 허대영(인제의대)

07 ---------- 65

Evolutionary anatomy associated with having a big brain in human

Young Ho Lee
Department of Anatomy, College of Medicine, Chungnam National University

08 ---------- 65

핸드폰에서 발생되는 전자파의 유전적 안정성 연구 (1)

Dae-Kwang Kim
Department of Medical Genetics, School of Medicine Keimyung University

09 ---------- 66

From dead body to birth: The human embryonic lineage tracing by spontaneous early postzygotic variants in dead bodies

Ji Won Oh
Department of Anatomy, School of Medicine, Kyungpook National University. Bio-Medical Research Institute, Kyungpook National University Hospital

010 ---------- 66

Alterations of telomere length and mitochondrial DNA copy number in human blood lymphocyte exposed to moderate hypoxia

Mohammad Rizwan Alam, Dae-Kwang Kim
Department of Medical Genetics, Keimyung University School of Medicine

011 ---------- 67

Elevated GCN5 expression confers tamoxifen resistance by upregulating AIB1 in ER-positive breast cancer

Ji Hoon Oh[1], Ji-Yeon Lee[1], Kwang Hui Kim[2], Clara Yuri Kim[1,3], Da Som Jeong[1,3], Yejin Cho[2], Ki Taek Nam[2,3], Myoung Hee Kim[1,3]
[1]Department of Anatomy, Embryology Laboratory, Yonsei University College of Medicine, Seoul 03722, Korea, [2]Severance Biomedical Science, Yonsei University College of Medicine, Seoul 03722, Korea, [3]Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul 03722, Korea

Oral Presentation Ⅲ (O12~15)

2019년 10월 17일(목) 14:40~16:00, 거문도C홀

좌장: 복진웅(연세의대)

012 ---------- 67

Inhibition of ceramide synthase 2 causes structural abnormalities in the kidney

Sae-Jin Lee[1], Seo Jin Lee[1], Eun-Young Choi[1], Ki-Hwan Han[1], Yael Pewzner-Jung[2], Anthony H. Futerman[2]
[1]Department of Anatomy, College of Medicine, Ewha Womans University, Seoul, [2]Department of Biological Chemistry, Weizmann Institute of Science, Rehovot, Israel

013 ---------- 68

Deep tissue clearing imaging for 3D analysis of the murine vasculature system

Nanda Maya Mali[1,2], Dong-Hwa Choi[3,4], Seock Hwan Choi[5], GilHyun Kim[6], Jung Min Oh[1], Ji Young Park[7], Man-Hoon Han[8], JongHyuk Lee[9], Dong Sun Kim[1], Sungho Maeng[4], Ji Won Oh[1,2,6]
[1]Department of Anatomy, Kyungpook National University, School of Medicine, Daegu, Korea, [2]Department of Biomedical Science, Biomedical Research Institute, Kyungpook National University, Daegu, Korea , [3]Biocenter, Gyeonggido Business & Science Accelerator, Suwon, Gyeonggi, 16229, Korea., [4]Graduate School of East-West Medical Science, Kyung Hee University, Yongin, Gyeonggi, 17104, Korea., [5]Department of Urology, School of Medicine, Kyungpook National University, Daegu, Korea , [6]Binaree, Inc, Daegu, Korea, [7]Department of Pathology, Kyungpook National University Hospital, Chilgok, Daegu, Korea, [8]Department of Pathology, Kyungpook National University Hospital, Daegu, [9]Department of Big Data Engineering, Daegu Catholic University, Gyeongbuk, KoreaMedicine Research Center, College of Medicine, The Catholic University of Korea

014 ---------- 68

The role of lipocalin 2 in skeletal muscle of leptin-deficient ob/ob miceImplication

Eun Bee Choi, Hyeong Seok An, Jong Youl Lee, Kyung-Ah Park, Eun Ae Jeong, Hyun Joo Shin, Kyung Eun Kim, Zhen Jin, Gu Seob Roh
Department of Anatomy and Convergence Medical Science, College of Medicine, Bio Anti-aging Medical Research Center, Institute of Health Sciences, Gyeongsang National University, Jinju, Gyeongnam, Repu

015 ---------- 69

Two-photon microscopy imaging probes based on a highly stable oxazepine core

Yuna Jung[1], Dokyoung Kim[1,2,3]
[1]Department of Biomedical Science, Graduate School, Kyung Hee University, Seoul 02447, Korea., [2]Department of Anatomy and Neurobiology, College of Medicine, Kyung Hee University, Seoul 02447, Korea., [3]Center for Converging Humanities, Kyung Hee University, Seoul 02447, Korea

Oral Presentation Ⅳ (O16~21)

2019년 10월 18일(금) 14:30~15:30, 거문도A홀

좌장: 송우철(건국의대), 황영일(서울의대)

016 ---------- 69

Clinical anatomy of dorsal hand for regional volumetric hand rejuvenation: Dorsal fat compartments

Jung-Ah Park, Ki Seok Koh, Wu-Chul Song
Department of Anatomy, Research Institute of Medical Science, Konkuk University School of Medicine

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Valves in the internal mammary vein cannot disturb retrograde flow in the bi-pedicle breast reconstruction surgery: a cadaveric study

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The anatomical neurovascular study for the procedure targeting chronic osteoarthritis patients with anterior knee pain

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ChungYoh Kim, JinSeo Park
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3차원 머리뼈 CT 영상과 계측학적 분석을 활용한 현대 한국인 눈확지수와 머리뼈지수에 대한 연구

Chang Un Choi[1,2], Won Joon Lee[1], Jeong Hyun Park[2]
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Beom Sun Chung, Min Suk Chung
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Kyung-Ah Park, Hyeong Seok An, Eun Bee Choi, Jong Youl Lee, Eun Ae Jeong, Hyun Joo Shin, Kyung Eun Kim, Zhen Jin, Gyeong Jae Cho, Gu Seob Roh
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Hyeong Seok An, Jong Youl Lee, Eun Bee Choi, Kyung-Ah Park, Eun Ae Jeong, Hyun Joo Shin, Kyung Eun Kim, Zhen Jin, Gu Seob Roh
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Heiyeun Koo[1,2], Min-A Kim[3], Hyehyun Min[1], Jae Yeon Hwang[6], Jeong-Oh Shin[1], Ji-Hyun Ma[1], Harinarayana Ankamreddy[5], Meenakashi Prajapati[4], Martin Matzuk[5], Juw won Park[6], Angelika Doetzlhofer[4], Un-kyung Kim[3], Jinwoong Bok[1,2]
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01

Perceptions of attractive and healthy-looking lips

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The aim of this study was to characterize Koreans' perceptions of attractive and healthy-looking lips. A survey was conducted among 258 women and 72 men who were asked to view illustrations of various examples of the 4 lip-related ratios (lip thickness-to-width ratio [LTW]; upper-to-lower vermillion ratio [ULR]; upper vermillion thickness-to-upper lip height ratio [VUL]; and lip-to-nose width ratio [LNW]) and to choose which they thought were attractive or healthy-looking. The LTW ratios most often identified as attractive were LTW-1/3 (lip thickness is 1/3 of lip width, 40.0%) and LTW-2/5 (47.3%). The LTW value most often identified as healthy-looking was LTW-2/5 (54.3%). The most attractive ULR ratio was ULR-4/5 (upper vermillion thickness is 4/5 of the lower vermillion, 49.4%). The most healthy-looking ULR ratio was ULR-4/5 (47.0%). The most attractive VUL ratio was VUL-1/2 (thickness of the upper vermillion is 1/2 of upper lip height, 60.3%). The most healthy-looking VUL ratio was VUL-1/2 (61.0%). The most attractive LNW ratio was LNW-3/2 (lip width is 3/2 of nose width, 42.1%). LNW-3/2 was also the most preferred in all age groups below 50 years, while those over 50 preferred LNW-4/3 (55.0%). The most healthy-looking LNW ratios were LNW-3/2 (35.2%) and LNW-4/3 (32.1%). LNW-3/2 was the most preferred in all age groups below 50, while those over 50 preferred LNW-4/3 (40.0%). It therefore seems that older people preferred a narrower lip width than younger people. Theresults of this study can be applied in lip augmentations or aesthetic lip surgery.

Keywords: Physical Anthropology, Lip, Patient Preference, Visual Perception, Esthetics

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02

신경해부학 실습동영상 제작

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대한해부학회 교육위원회에서는 2017년 8월, 의과대학생을 비롯한 학습자들의 신경해부실습에 도움을 주고자 '신경해부학 실습동영상' 제작을 결의하였다. 전국 의과대학 및 의학전문대학원의 신경해부학 커리큘럼을 전수조사 하여, 기존 실습서를 활용한 교육의 단점을 극복하고 4K 영상을 통해 뇌의 3차원적 구조를 단계별로 익혀 나갈 수 있도록 구성하였다. 서울대 황영일, 경희대 박찬, 연세대 양헌무, 성균관대 주경민, 을지대 송대용이 TF team을 구성하여 동영상 제작에 참여하였다. 동영상 촬영 및 제작은 ㈜범문에듀케이션이 함께하였고, '7일간의 신경해부학 실습' 교재를 기반으로 하였다. 약 2년간 20여차례의 제작 모임을 통해 동영상을 촬영, 편집, 나래이션 더빙, 수정 과정을 거쳤으며, 지난 2019년 2월, 총 11장으로 구성된 교육 콘텐츠 개발을 완료하였다. 총 런닝타임은 3:06:31 (1. 뇌 척수막과 척수; 00:27:39, 2. 중추신경계 구성/뇌의 개관 및 혈관분포; 00:13:15, 3. 뇌줄기; 00:19:46, 4. 앞뇌의 바깥구조; 00:18:56, 5. 앞뇌의 속구조; 00:21:33, 6. 소뇌와 뇌신경; 00:16:34, 7. 번연계와 후각뇌; 00:13:18, 8. 뇌의 관상단면; 00:14:52, 9. 뇌의 수평단면; 00:08:43, 10. 척수의 단면; 00:14:52, 11. 뇌줄기의 단면; 00:17:03)이며, 사용자의 편의에 따라 자막을 활용할 수 있도록 제작하였다. 현재 www.e-neuroanatomy.or.kr에 동영상을 업로드하여 구독계약을 통해 교육에 활용할 수 있으며, Trial 신청을 통해 콘텐츠를 둘러볼 수 있다. 의과대학생을 비롯한 신경해부를 학습하는 학습자들에게 실질적 도움이 될 수 있기를 희망한다.

Keywords: 신경해부학, 교육콘텐츠, 실습동영상, 인터넷

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03

Retrobulbar filler injection of for orbital volume augmentation: can we define a safety zone?

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Volume enhancement in sighted orbits needs to be safe and easily reversible to minimize the risk of sight loss, diplopia, and significant globe displacement. In the age of nonsurgical facial rejuvenation, fillers are an ideal option for orbital volume enhancement because they are easily performed in the outpatient setting, avoiding general anesthesia. The purpose of the study is to determine the vascular distribution of orbital area and therefore to define a safety zone of retrobulbar filler injection for the orbital volume augmentation. Twenty-seven orbits of 24 formalin-embalmed cadavers were dissected meticulously from ocular skin to the apex of orbits. Connective tissues, extraocular muscles, and nerves were removed to keep arterial branches in the original region. Orbital vasculature of each individual was recorded. A fresh cadaver was investigated to compare a protrusion of the eyeball followed by filler injection in a dose-dependent manner: 1ml of retrobulbar filler injection was performed three times. The anatomy of the orbital vascular bed is highly complex, with tremendous interindividual variations. The analysis showed greater vascular density was in the superomedial quadrant as a result of the superimposition of lined images based on orbital vasculature of each individual. There is less vascularization in the inferolateral quadrant of the orbit than in the other quadrants. In particular, orbital vasculature was scarce at eight o'clock. After filler injection in the fresh cadaver, improvement of enophthalmos was achieved along with a fullness in the upper eyelid and superior sulcus. Hertel exophthalmometry measurement demonstrated 1mm improvement of enophthalmos in every 1ml of retrobulbar filler injection. When applying a retrobulbar injection for orbital volume augmentation with filler, the relative safety could be considered to be located at 8 o'clock of the orbital region. The detailed topographic information about the vascular distribution of orbital area by this study may assist oculofacial surgeons in avoiding

Keywords: Orbital vasculature, Retrobulbar injection, Volume augmentation, Safety zone, Exophthalmometry

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04

Anatomical Study for Effective Botulinum Toxin Injection into the Mentalis Muscle

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The aim of this study was to determine the anatomical morphology and location of the mentalis muscle and thereby provide clinical anatomical information for facilitating procedures for rejuvenating the lower face. Fourty-four adult hemifaces from 5 Thai cadavers and 21 Korean cadavers (18 males and 8 females, mean age 69.5) were used for anatomical study. A detailed dissection was performed to identify the locations of mentalis muscle. Sixty-six hemifaces from thirty-three healthy young Korean subjects were included in ultrasonographic study. The distance from skin, the thickness, the distance from the bone of mentalis muscle were measured by ultrasound imaging. The measurements were made at both points 5mm lateral from the most prominent point of the chin. The mentalis muscle was classified into two types based to its shape: in type A (86.4%, 38 of the 44 cases) the mentalis muscle had a dome shape in three dimensions, while in type B (13.6%) it was flat. Most of the mentalis muscles appear to be located 5 to 10 mm from the facial midsagittal line and 20 to 30 mm from a horizontal line connecting the mouth corners. The average location of mentalis muscle from skin surface was 6.7 to 10.7 mm. This new information may help when determining the location of the mentalis muscle, including to identify effective botulinum toxin injection points and depths during esthetic procedures for weakened facial rhytides on the lower face.

Keywords: Mentalis muscle, Botulinum toxin, Injection point, Anatomical location, Facial rhytides

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05

Anatomical Continuation between the subSMAS Fat (Innominate Fascia) and ROOF : The True Nature of the ROOF (Retro-Orbicularis Oculi Fat)

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In previous studies, the subSMAS fat (named as 'innominate fascia') and the retro-orbicularis oculi fat (ROOF) have been regarded as the different structures without any clear definition. Therefore, this study aims to analyze the anatomical location and continuation between the subSMAS fat and the ROOF by comparing the layered structure between these two deep fat compartments, and thereby to suggest a safe injection guideline for the forehead and temporal augmentation procedures. The ultrasonography scanning was performed from the upper medial eyebrow to the lateral region of superior temporal line from 10 healthy young volunteers to investigate the anatomical location and continuation pattern between the subSMAS fat and ROOF. Four Thai embalmed cadavers were dissected the orbicularis oculi, frontalis muscle, superficial temporal fascia, and SMAS to confirm the location and continuation pattern between the innominate fascia and ROOF. On ultrasound, the frontalis muscle and the superficial temporal fascia were connected each other. And there was hyperechoic connected fat layer underlying those structures from the frontal (submuscular layer) to temporal region (subSMAS fat). When dissecting, the ROOF which located deep to the orbicularis oculi and frontalis muscle continued to the subSMAS fat (innominate fascia) passing through the superior temporal line in the upper temporal region. Based on our results, we confirmed that the subSMAS fat (innominate fascia) is an anatomical fat structure continued from the ROOF. This study may be helpful to suggest the safe injection layer in non-invasive treatment for forehead and temple augmentation procedures.

Keywords: Facial layer, ROOF, subSMAS fat, Innominate fascia, Injection layer

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06

Three-dimensional topographic distribution of the superficial temporal artery in the temporal region by MATLAB analysis

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Temporal region is the target area that frequently performed for the various aesthetic procedures such as thread lifting, filler and botulinum toxin injections. The frontal branch of the superficial temporal artery (STA) is the major vascular branch located at the superficial temporal area. The aim of this study is to analyze the three-dimensional distribution of the STA to provide the safe and efficient procedures. Forty-one embalmed adult Korean and Thai hemifaces (29 Koreans and 12 Thais; 21 males and 20 females; mean age of 78 years) were used. Each hemiface was dissected carefully to trace the STA within the superficial temporal area using a structured-light 3D scanner (Morpheus3D) for the three-dimensional scanning. All the scanned images were aligned based on Frankfort horizontal line. The overall scanned STA distribution imaged were analyzed by MATLAB software. The distribution of the frontal branch of the STA was classified into 3 types (A, B, and C). A 3 by 3 chart was established at the temporal area. The four horizontal lines were placed parallel to Frankfort horizontal line which are passing through lateral canthus, glabella, metopion and half point in between the glabella and the metopion. Two of the vertical lines were aligned evenly between the other two vertical lines passing through the medial margin of the lateral orbital rim and tragus. From this chart, middle vertical column was used to categorize 3 running types of the STA. Type A is upper

temporal middle area (21.95%, 9/41); Type B is middle temporal middle area (51.22%, 21/41); and C is lower temporal middle area (26.83%, 11/41) respectively. Throughout this research, it is observed that there were mainly three morphological distribution types of STA and these finding can be used for clinical procedure guidance.

Keywords: Superficial temporal artery, Three-dimensional scanning system, MATLAB, Aesthetic procedures, Injection site

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07

Evolutionary anatomy associated with having a big brain in human

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The most characteristic feature of Homo sapiens is having a big brain, 3 times larger than other primates. Evolutionary adaptation of human with a big brain, i.e. having high intelligence, is not usual adaptation in mammals. Life of our early ancestors in the eastern Africa may have pressed intelligence development, especially for social cooperation, judgement, and planning. The region of the brain involving these function is anterior part of the brain (prefrontal cortex). Development of the prefrontal cortex had caused displacement of the external occipital protuberance posteriorly, the foramen magnum inferiorly, which helpful to keep erect position. The MYH16 gene (a myosin gene in mastication muscles in our ancestors) mutation had occurred unexpectedly around 2.4 million years ago. This gene mutation had caused dramatic weakness of mastication muscles including Temporalis by decrease of type II muscle myofibers. Weakness and underdevelopment the muscle had allowed enlargement of the skull and consequently enlargement of the brain, larger 50% than before, in our late ancestors, Homo erectus. The brain is the organ have the highest metabolic rate among any tissue or organs in the body. This means human requires more energy compared with other animals. Breast volume development (enlargement) from puberty, aside from lactation, is another special feature of Homo sapiens. Enlargement of the breasts via fat deposition along with development of the buttocks may be considered a good signal for feeding ability and reproductive success, may have become a sexual signal instead of ovulation signaling. The site of male pattern baldness is usually frontal and parietal regions of the scalp. The distinctive feature of the balding scalp is no wrinkles, which are presented in most of human skin. Absence of wrinkles means the scalp is tight by expansion of the scalp from big brain. This suggests that cause of male pattern baldness may be associated with big brain. Another special feature of Homo sapiens is hair pattern of the scalp. The scalp hair consists of follicular units with multi-hairs, and present a whorl pattern, not presented in chimpanzee scalp. Multi-hairs were founded in the rabbit ear, an expanded structure. This suggests that multi-hairs of Homo sapiens is associated with expanded scalp, eventually big brain. Multi-hair pattern have been simulated mathematically with Turing's reaction-diffusion model, and scalp whorl is also could be simulated with other mathematical approach such as vector fields. In summary, big brain of Homo sapiens had caused changes of skull shape and posture, breast and buttock developments, and skin and hair pattern of the scalp.

Keywords: Evolutionary anatomy, Homo sapiens, Big brain, Skull, Breasts, Buttocks, Scalp hair

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08

핸드폰에서 발생되는 전자파의 유전적 안정성 연구(1)

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핸드폰의 사용이 증가하면서 핸드폰에서 발생되는 전자파에 노출될 위험도 증가하고 있다. 그러나 핸드폰 유래 전자파의 유전적 안정성에 대한 연구는 드문 상태이다. 이 연구에서는 말초혈액을 핸드폰 전자파에 노출하여 유전적 안정성을 연구하였다. 30명의 21세의 건장한 남성에서 3 ml의 혈액을 채취하여 대조군은 핸드폰에 노출을 하지 않았고 실험군은 매일 1시간과 3시간으로 노출하였다. 유전적 안정성을 조사하기 위하여 자매염색분체교환(sister chromatid exchange), 텔로미어 길이 그리고 미토콘드리아의 복제수를 측정하기 위해 실시간 PCR을 실시하였다. 자매염색분체교환의 결과는 대조군(6.87±0.45/cell)

에 비해 실험군 모두에서 의미 있게 증가하였다(10.88±0.44/cell for 1hr treatment, 10.89±0.47/cell for 3hr treatment, $p<0.05$). 텔로미어의 상대적 길이는 대조군과 1시간 노출군에서는 차이가 없었으나 3시간 처리군은 의미 있게 텔로미어 길이가 증가하였다(1.41±0.16, $p<0.05$). 미토콘드리아 복제수의 비교에서 대조군과 실험군 사이에는 차이가 없었다. 자매염색분체와 텔로미어 길이에 대해서 핸드폰에서 발생한 전자파가 유전적 불안정을 초래하였지만 미토콘드리아 복제수에서는 유전적 안정성을 보였다. 그러나 장기간에 노출되는 경우에서도 미토콘드리아 복제수의 유전적 안정성이 유지되는지는 계속 연구가 되어야 할 것이다.

Keywords: 핸드폰에서 유래된 전자파, 자매염색분체, 텔로미어 길이, 미토콘드리아 복제수, 유전적 안정성

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09

From dead body to birth: The human embryonic lineage tracing by spontaneous early postzygotic variants in dead bodies

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All the somatic cells in a single human individual developed from a single common ancestor cell, the fertilized egg. During pre-implantation development, the mammalian fertilized egg self-organizes into the blastocyst, which includes the inner-cell mass (ICM), giving rise to all human tissues. The cellular organization is a very complex but tightly controlled process and is fundamental to understanding the formation of human bodies, which consists of 10-100 trillion somatic cells. However, cellular dynamics in early embryogenesis, i.e. tracing cellular lineages and fate decisions, has largely remained unexplored, especially in humans, due to both ethical and technical issues. Here we investigated the developmental cell dynamics early in human embryogenesis by harnessing naturally occurring somatic mutations from the earliest cell divisions in human life. Developmental lineage trees were reconstructed using somatic mutations in ~200 clonal lines established from warm autopsy of many different tissues of human individuals; a clear asymmetric contribution of early embryonic cells to adult human body was found. Our proof-of-principle experiments show that endogenous somatic mutations can be used to advance our understanding of early human development.

Keywords: Somatic mutation, Development, Embryogenesis, Lineage tracing, Blastocyte

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010

Alterations of telomere length and mitochondrial DNA copy number in human blood lymphocyte exposed to moderate hypoxia

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Hypoxia is associated with a wide range of diseases, such as cardiovascular, inflammatory diseases and different form of cancer. Hypoxia results in genetic instability and can induce cell death by pro-apoptotic factors. However, some cells survive by regulating several transcription factors under hypoxic condition. It has been reported that telomere length is related to cell survival. The aim of this study was to investigate the change of relative telomere length and mitochondrial copy number in human blood lymphocyte exposed to moderate hypoxia. For this study blood samples for 34 healthy individuals (only non-smoking males) between ages of 21 and 28 were taken with no history of any disease. In the control groups blood samples were cultured in normoxic conditions, and the moderate hypoxic condition was maintained for 12 and 24 hours in the experimental groups. Relative telomere lengths and mitochondrial DNA copy number were analyzed by quantitative PCR. Triplicate measurements were performed for all samples. We observed a slight increase in relative telomere length was observed in the experimental group for 12 hours (1.26±0.75) but a significant change was observed in the experimental group after 24 hours (1.42±0.70, p

value = 0.015), compared to the controls. There were no significant changes in mitochondrial DNA copy number between the control and two experimental groups. Telomere elongation indicates the compensatory mechanism adopted by the cell to reduce the genotoxic effect of hypoxia. Identifying the exact pathway of telomere elongation may be utilized as therapeutics target.

Keywords: Hypoxia, Telomere length elongation, Mitochondrial DNA copy number, DNA damage

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011

Elevated GCN5 expression confers tamoxifen resistance by upregulating AIB1 in ER-positive breast cancer

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Approximately 70% of breast cancers are estrogen-receptor (ER)-positive and treated with endocrine therapy. A commonly used treatment agent, tamoxifen, shows high efficacy for improving prognosis. However, about one-third of patients treated with tamoxifen develop resistance. We evaluated the function of general control non-derepressible 5 (GCN5) in tamoxifen-resistant breast cancer. Tamoxifen-resistant (TamR) MCF7 cells maintained high GCN5 levels due to its attenuated proteasomal degradation. Highly expressed GCN5 upregulated amplified in breast cancer 1 (AIB1) by binding to its promoter region, leading to decreased p53 stability and tamoxifen resistance. The tamoxifen sensitivity of GCN5-AIB1-overexpressing breast cancer cells was restored by forced p53 expression. An in vivo study demonstrated a positive correlation between GCN5 and AIB1 and their contribution to tamoxifen resistance. We concluded that GCN5 promotes AIB1 expression and tamoxifen resistance in breast cancer by reducing p53 levels, suggesting the utility of GCN5 and its downstream effectors as therapeutic targets.

Keywords: GCN5, AIB1, p53, Tamoxifen resistance, Breast cancer

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012

Inhibition of ceramide synthase 2 causes structural abnormalities in the kidney

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Ceramides, synthesized by a family of six ceramide synthases (CerS1-6), are the major components of mammalian cell membranes. CerS2 is abundantly found in both liver and kidney, and liver cancer develops when CerS2 is genetically ablated. However, no pathological abnormality has been reported in the kidney. The purpose of this study was to examine the effect of CerS2 inhibition in the kidney. Kidney tissues of CerS2 null mice were processed for light and electron microscopy. CerS2 null mice displayed widespread formation of hepatic masses, as previously reported. In the kidney, although gross morphology appeared to be unchanged, histological abnormalities were observed. Kidney tubules, especially the proximal tubules, were enlarged and cell proliferation was frequently observed. Electron microscopy revealed characteristic onion-like lamella inclusions in the cytoplasm. In particular, microvilli were lost to a part of the apical membrane, and the cell surface of the proximal tubule appeared to be smooth. These results suggest that CerS2 may play an important role in maintaining renal cell membranes, and that CerS2 deletion can cause functional disorders in the kidney. This work was supported by funds from the National Research Foundation of Korea (NRF-2017R1D1A1B03030573).

Keywords: Ceramide, CerS2, Kidney, Inclusion body, Cell membrane

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013

Deep tissue clearing imaging for 3D analysis of the murine vasculature system

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Due to the obscuring effects of light scatter and technical limitation of current histochemistry, deep imaging into tissue is problematic though biological interactions are intrinsically three dimensional. The last decade has seen the progress of tissue clearing methods that make large biological samples transparent and allow unprecedented three-dimensional views of a variety of tissues. Especially biological structure of tissue vasculature is highly interconnected in a three-dimensional way within specific organs. However, the three-dimensional view of vasculature systems of each different organ is largely unexplored. Here, we investigated the structure of the vascular system in, liver, spleen, pancreas and kidney using tissue clearing methods. We took more than thousands of still shot pictures of the vasculature system of each organ based on lectin binding images under the light-sheet microscope, requiring three-dimensional reconstruction. Reconstructed images gave us the detailed topological information of the interconnectional status of the vasculature. Tissue clearing methods with reconstructed three-dimensional images allow for quantification of the interconnected status of tissue vasculature as well as spatial insight for the physiological conditions. Furthermore, combined with immune-histochemistry antibody reaction within tissue clearing methods, it can give us topological information of specific cellular populations in the context of the vascular system.

Keywords: Tissue clearing, 3-dimension 3D, Vasculature system, Light Sheet Microscopy Imaging, Analysis

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014

The role of lipocalin 2 in skeletal muscle of leptin-deficient ob/ob mice

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Obesity-induced insulin resistance has been attributed to inflammation, oxidative stress, and impaired muscle contraction. Lipocalin 2 (LCN2) is an iron carrier protein whose circulating level is increased by inflammation in obesity. However, the precise mechanisms of role in skeletal muscle of obese mice remain poorly defined. This study was designed to determine the contribution of LCN2-mediated signaling to muscle remodeling in obese ob/ob mice. Histological analysis showed that there was significant reduction in diameter of muscle fibers in ob/ob mice compared to wild type (WT) mice. Ob/ob mice had upregulation of interleukin-6 (IL-6) and nuclear factor-κB (NF-κB) protein expressions in skeletal muscles. Using RNA-seq analysis, we identified that an iron carrier-associated gene, LCN2, was upregulated in ob/ob mice. Furthermore, we found that transferrin receptor and ferroportin expressions were decreased in ob/ob mice, whereas divalent metal transporter 1, ferritin, and hepcidin expressions were increased in ob/ob. In addition, western blot analysis showed that ob/ob mice had increased expression of nuclear factor erythroid 2-realted factor 2 (Nrf2) and heme oxygenase (HO-1) proteins in skeletal muscles. Our findings suggest that disruption of LCN2-mediated iron regulation may contribute to muscle atrophy, inflammation, and oxidative stress in obese skeletal muscle.

Keywords: Lipocalin 2, Inflammation, Oxidative stress, Skeletal muscle, Obesity

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015

Two-photon microscopy imaging probes based on a highly stable oxazepine core

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Oxazepine, which is comprised of seven membered ring including unsaturated cyclic imine bond and heteroatoms such as nitrogen and oxygen, has biomedical significances. Oxazepine derivatives have been used as an anti-cancer drug, antibiotics for various fungi and bacteria, and pharmacophore. A number of oxazepine derivatives have been introduced and studied since 1965 as it showed great drug potency. However, a new fluorophore containing oxazepine is rarely developed for bioimaging purpose and its related applications due to low stability of imine bond on the oxazepine core backbone within aqueous media [1-2]. In this study, we synthesized a new donor-acceptor (D-A) type of oxazepine fluorophore, named OXN-1. The developed fluorophore exhibited high stability in hydrolytic condition with low cytotoxicity [1]. Photophysical property of OXN-1 was assessed; UV/vis absorption and fluorescence emission change, and LC-MS analysis in various solvents including aqueous media (pH 7, pH 7.4 buffer solution). With the purpose of further biological application, we checked its aptness at bioimaging in cells and tissues by utilizing confocal laser microscope (CLSM) and two-photon excitation microscope (TPM). In conclusion, we designed a stable and biocompatible oxazepine fluorophore, OXN-1, which has a cyclic imine bond, and determined its bioimaging capacity with unusual high stability. These results indicate that OXN-1 can be more adoptable for bioimaging fluorophore or other advanced uses in broad research fields.

Keywords: Fluorophore, Oxazepine, Bio-imaging, Two-photon microscopy, Cellular imaging

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016

Clinical anatomy of dorsal hand for regional volumetric hand rejuvenation: Dorsal fat compartments

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Volumetric rejuvenation of dorsal hand with fat grafting or injectable fillers is gaining popularity in recent years. It is widely accepted that there are three fatty layers existing in the dorsal hand that are dorsal superficial, intermediate and deep lamina. These three fatty layers are known to be separated by two intervening fascia, which are dorsal superficial and intermediate fascia. We performed dissection and histologic analysis in 13 cadaveric hands. Full-thickness samples from the dorsum of the hand overlying the second to forth metacarpals from skin to bone or interosseous muscle were harvested. These samples were fixed in formalin, embedded in paraffin and mounted. Trichrome stains were used for histologic analysis. When performing dissection of the fascial layers of the dorsal hand, we observed a fascia between dorsal superficial and intermediate fascia and this unknown fascia lay between dorsal metacarpal veins and dorsal digital nerves. Histologic analysis of dorsal hand skin samples revealed that there were three fatty layers in dorsal hand: dorsal superficial, intermediate and deep lamina, separated by dorsal superficial and intermediate fascia. In addition, there was unknown additional fascia between the dorsal metacarpal veins and dorsal digital nerves. Knowledge of the dorsal hand anatomy may help to design optimal and safe location for fat grafting or an injectable dermal fillers.

Keywords: Dorsal hand, Fat compartments, Dermal filler injection, Hand rejuvenation, Anatomy

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017

Valves in the internal mammary vein cannot disturb retrograde flow in the bi-pedicle breast reconstruction surgery: a cadaveric study

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When performing the free autologous tissue-based breast reconstruction, the internal mammary artery(IMA) and vein(IMV) are widely used recipient vessels. However, there are few apprehensions about safety of using the opposite side of the IMV as retrograde flow in the surgery. Bilateral IMV from 20 fresh cadavers were used to investigate the number and location of the IMV valves. Additionally, indocyanine green fluorescent angiography was performed to confirm possibility of retrograde blood flow in the IMV. 28 valves were identified in 40 IMVs. 23 (82.1%) valves out of 28 were located above the 2nd intercostal space (ICS). The bifurcation of the IMV commonly occurred at 3rd intercostal space. Communication branches between the medial and lateral IMV were discovered frequently. Large amount drainage of the retrograde flow around IMV was confirmed in the indocyanine green fluorescent angiography. As a conclusion, the opposite site of the IMV can be used for the retrograde flow in the bi-pedicle breast reconstruction, because valve of the IMV are generally located above 2nd intercostal space and there were various retrograde anastomosis.

Keywords: Internal mammary vein, Autologous breast reconstruction, Cadaveric study, Bi-pedicle flap, Retrograde flow

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018

The anatomical neurovascular study for the procedure targeting chronic osteoarthritis patients with anterior knee pain

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Since Choi et al described radiofrequency ablation of articular branch innervating anterior knee capsule, it has been studied as a possible alternative treatment of surgery for degenerative arthritis. During the procedure, precise nerve targeting and avoiding blood vessels are needed to increase effectiveness and reduce complications. However, the neurovascular distribution of the anterior knee capsule is still unclear. A pilot study was conducted using two fresh cadaver donated to our institution. We dissected the region near the landmarks of the conventional procedure to find the nerve and artery. And then, twenty formalin-embalmed cadaveric specimens were used in this study (14 men and 6 women, from 32 to 92 years). We dissected one leg of each specimen. Six nerves and four genicular arteries, known to be responsible for the anterior innervation of the knee (nerve to vastus medialis(NVM), nerve to vastus intermedius(NVI), nerve to vastus lateralis(NVL), infrapatellar branch of saphenous nerve(IPN), lateral retinacular nerve(LRN), recurrent peroneal nerve(RPN); superior medial genicular artery(SMGA), superior lateral genicular artery(SLGA), inferior medial genicular artery(IMGA), inferior lateral genicular artery(ILGA)) were dissected from adductor canal through the distal femur to the knee. After wiring each structure, anteroposterior and lateral view was obtained using C-arm fluoroscopy. The distances between nerve and the conventional ablation points of RFA were measured using 3D reconstruction program. We also measured the probability of genicular arteries being present at the conventional ablation points. Median distance from nerve to the conventional ablation point was 33.5mm[IQR, 23.9-37.4mm], 25.3mm[IQR, 8.5-37.5mm], 33.3mm[IQR, 22.1-37.1mm], 16.7mm[IQR, 12.1-24.9mm], 11.3mm[IQR, 7.8-15.7mm], 6.9mm[IQR, 5.2-11.8mm] for NVM, NVI, NVL, IPN, LRN, RPN, respectively. Results of nerve existence probability at conventional ablation point was as 23.5%, 14.3%, 0%, 16.7%, 33.3% for NVM, NVI, NVL, IPN, LRN, respectively. Whereas the results of genicular artery existence probability at conventional ablation point was as 84.2%, 84.2%, 73.3% for SMGA,

SLGA, IMGA, respectively. According to the result of this study, the existence probability of nerve was low in spite of high presence of genicular arteries at conventional ablation points. Therefore, it would be more appropriate to target more proximal points during the RFA.

Keywords: Osteoarthritis, Radiofrequency ablation, Anterior knee innervation, Genicular nerve, Genicular artery

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019

붉은털 원숭이의 온몸의 실제빛깔 절단 면영상으로 둘러보기 소프트웨어와 3차원영상 만들기

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원숭이는 사람과 유사한 점이 많아서 진화학, 행동학, 의학 등의 연구에 많이 쓰이고 있다. 원숭이를 연구하는 수의사나 연구자들은 기본적으로 원숭이 해부학과 영상의학을 잘 알아야 한다. 그러나 원숭이는 해부하는 것만으로도 힘든데, 해부를 위한 원숭이 구매, 원숭이 보관, 해부윤리 등 선행 필수조건이 많고 까다롭다. 사람의 해부도 마찬가지로 어려워서 요즘은 가상해부 소프트웨어를 많이 쓰고 있다. 그러나 원숭이는 가상해부 소프트웨어뿐 아니라 이러한 소프트웨어를 만드는 데 필요한 2차원영상도 많이 부족하다. 이 연구의 목적은 원숭이 온몸의 단면을 실제빛깔로 둘러볼 수 있는 둘러보기 소프트웨어와 원숭이 구조물의 입체생김새를 깨달을 수 있는 3차원영상을 만들고 퍼뜨려서 수의사, 연구자, 학생들이 원숭이 해부학, 영상의학을 공부하는 데 도움주는 것이다. 이를 위해서 원숭이 온몸을 실제빛깔(48 bits color)과 고해상도(화소크기, 0.024 mm)로 볼 수 있는 절단면영상을 썼다. 포토샵으로 절단면영상에서 보이는 구조물 38개를 구역화하였다. 절단면영상과 구역화영상을 함께 둘러보는 둘러보기 소프트웨어를 만들었다. 이 소프트웨어에서는 영상과 구조물의 이름을 실시간으로 볼 수 있다. 마야 소프트웨어를 써서 구역화영상을 3차원영상으로 만들었다. 3차원영상을 PDF 파일로 만들었다. (본 연구는 산업통상자원부와 한국산업기술진흥원의 "국제공동기술개발사업"의 지원을 받아 수행된 연구결과임(과제 번호: N0002249))

Keywords: 원숭이, 영장류, 절단면영상, 3차원모델, 가상해부 소프트웨어

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020

3차원 머리뼈 CT 영상과 계측학적 분석을 활용한 현대 한국인 눈확지수와 머리뼈지수에 대한 연구

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지금까지의 생물인류학적인 연구에 있어서, 고대와 현대 한국인의 실제 머리뼈를 사용하여 눈확과 머리뼈에 대한 계측학적 연구는 많이 이루어져 왔다. 그러나 현대 한국인들의 3차원 CT영상을 이용한 연구는 드문 실정이다. 본 연구의 목적은 현대 한국인들의 3차원 머리뼈 CT 영상을 활용하여 한국인의 눈확과 머리뼈 형태를 계측학적으로 분석하고, 서로의 연관성 및 시대에 따른 눈확과 머리뼈의 변화 정도를 알아보고자 하였다. 2017년 3월부터 2018년 9월까지 부검을 위해 국립과학수사연구원 서울연구소에 의뢰된 시신 가운데 머리부위에 손상이나 질환이 없는 것으로 확인된 남 · 여 시신 180구를 연구대상으로 선정하였다. 연구대상으로 선정된 시신을 MDCT로 촬영하였고, 촬영된 영상 데이터의 머리뼈 부위를 3차원으로 재구성하여 추출하였다. 눈확의 높이와 너비를 측정하기 위한 표지점 4곳과, 머리뼈의 너비와 길이를 측정하기 위한 표지점 5곳을 선정하였다. 표지점의 식별 및 위치 그리고 표지점 간 거리값의 측정은 3차원 영상분석 프로그램(Materialise Mimics)을 사용하여 시행하였다. 본 연구는 국립과학수사연구원 생명윤리위원회의 허가(승인번호 : 906-190124-HR-006-02)를 받고 진행하였다. 성별에 따른 눈확지수(눈확의 높이/눈확의 너비)의 평균값은 남성에 있어서 오른쪽은 88.95±6.19%, 왼쪽은 89.16±5.81%; 여성에 있어서 오른쪽은 91.23±4.87%, 왼쪽은 91.11±4.43% 이었다. 이 평균 눈확지수 값은 좁은 눈굼형(hypsiconch)에 속하였고, 빈도 또한 좁은 눈굼형(hypsiconch)의 눈확이 가장 높았다. 오른쪽 눈확지수와 왼쪽 눈확지수의 통계적 차이는 없었지만, 남성과 여성

에 있어서는 차이를 보였다($p<0.05$). 머리뼈지수(머리뼈 너비/머리뼈 길이)의 평균값에 있어서 남성은 85.47±4.85%, 여성은 85.06±4.59%으로 통계적으로 남녀간에 유의한 차이는 없었다($p>0.05$). 이번 연구에서 얻은 머리뼈지수의 평균값은 다른 연구와 비슷하게 짧은머리형(brachycranic)에 속했지만, 빈도에 있어서는 꽤 짧은머리형(hyperbrachycranic)이 더 높은 것을 확인할 수 있었다. 본 연구는 현대 한국인 눈확과 머리뼈의 계측학적 특징을 3차원 머리뼈 CT영상과 3차원 영상분석 프로그램을 활용하여 분석하고 그 결과를 얻었다는데 의의가 있었다. 또한 본 연구결과는 생물인류학적 연구에 있어서 한국인 눈확과 머리뼈 형태의 시대적 변화를 관찰하고 눈확지수와 머리뼈지수를 활용한 성별 및 인종 추정 방법 개발에 필요한 기초자료로 활용될 수 있을 것으로 기대한다. 이 연구는 행정안전부 주관 국립과학수사연구원 중장기과학수사감정기법연구개발(R&D)사업의 지원을 받아 수행한 연구임(NFS2017MED05).

Keywords: 눈확지수, 머리뼈지수, 한국인

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021

가상해부학에 이바지하는 Visible Korean의 교육 소프트웨어 네 가지

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최근의 기술 발전 덕분에 가상해부학은 그 교육적 가치로 주목받고 있다. 가상해부학을 더욱 발전시키기 위해서 실제 시신의 영상을 다양하게 처리할 수 있다. 이 연구의 목적은 Visible Korean의 영상을 다양하게 처리하여서, 가상해부학에 이바지하는 것이다. 남성 온몸 시신의 절단면영상으로 교육 소프트웨어 네 가지를 만들었다. 첫째는 절단면영상과 구역화영상을 보여주는 것이다. 둘째는 각 구조물의 표면3차원영상을 보여주는 것이다. 셋째는 부피3차원영상을 피부에서부터 깎아서 보는 것이다. 넷째는 부피3차원영상을 사용자 마음대로 비스듬히 잘라서 보는 것이다. 모든 소프트웨어를 홈페이지 anatomy.co.kr에서 공짜로 내려받을 수 있다. 사용자는 시간과 장소에 제약없이 가상 해부를 할 수 있다. 각 소프트웨어는 서로 다른 장단점이 있으며, 함께 사용하는 것이 바람직하다. 이런 무료 소프트웨어는 상업적으로 판매되는 다른 교육 도구와 서로를 보완한다. 다음 연구에서는 학생들에게 설문조사를 함으로써 이 소프트웨어의 교육 효과를 알아보고자 한다.

Keywords: 절단해부학, 가상해부학, 교육, 시신, 컴퓨터

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022

Neuron-specific Drp1 deletion promotes neurodegeneration in high-fat diet/streptozotocin-induced diabetic mice

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Diabetes-induced cognitive impairment is associated with mitochondrial dysfunction and synaptic injury in the brain. While dynamin-related protein-1 (Drp1)-mediated mitochondrialdysfunction has been implicated in synaptic injury in diabetic brain, its molecular mechanism for this association remains poorly defined. Here, we investigated the effects of Drp1 deficiency on mitochondrial abnormalities, synaptic injury, and autophagy dysfunction in the hippocampus of high-fat diet (HFD)/streptozotocin (STZ)-induced diabetic mice. The experiments wereperformed on male, divided into normal diet (ND)-fed wild type (WT) mice, HFD/STZ-treatedWT mice, ND-fed CaMKIIα-Cre; Drp1lox/lox (Drp1cKO) mice, and HFD/STZ-treated Drp1cKO mice. Compared with ND-fed mice, HFD/STZ-treated diabetic mice showed insulin resistance,macrophage infiltration, and hepatic steatosis. In particular, Golgi staining showed that there were significant reduction of the numbers of dendritic spines within hippocampal CA1 in HFD/STZ-treated Drp1cKO mice compared to HFD/STZ-treated WT mice. Electron microscopy revealed that there were small mitochondria within neurons in the hippocampal CA1 of WT mice by HFD/STZ treatment, whereas HFD/STS-treated Drp1cKO mice showed reduction of the numbers of mitochondria compared to HFD/

STZ-treated WT mice. Additionally, we found that increased accumulation of autophagosomes within neurons in the hippocampal CA1 was characteristic in HFD/STZ-treated Drp1cKO mice. We also found GFAP and Iba1 expressions were significantly increased in HFD/STZ-treated Drp1cKO micerelative to HFD/STZ-treated WT mice. These findings indicated that HFD/STZ induced aberrant mitochondrial abnormality and defective autophagy promote neuroinflammation and neurodegeneration in HFD/STZ-induced diabetic mice

Keywords: Drp1, Mitochondrial fission, Neurodegeneration, Hippocampus, Diabetes

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023

Caloric restriction reverses left ventricular hypertrophy through the regulation ofcardiac iron levels in ob/ob and db/db mice

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High levels in circulating leptin is associated with the development of left ventricular hypertrophy (LVH) in obese patients. However, obese leptin-deficient and leptin–resistant mice also have cardiac hypertrophy. Cardiac iron dysregulation has been recently implicated in cardiomyopathy. Here we investigated the protective effects of caloric restriction on cardiac iron overload in impaired leptin signaling mice. Male ob/ob mice exhibited LVH, cardiac inflammation, and oxidative stress and RNA-seq analysis was performed to assess the differential gene expressions in the heart of wild-type and ob/ob mice. In particular, to investigate the roles of caloric restriction on iron homeostasis-related gene expressions, 10-week-old ob/ob and db/db mice were assigned to ad libitum or calorie-restricted diets for 12 weeks. Using RNA-seq analysis, we identified that an iron uptake-associated gene, transferrin receptor, was upregulated in obese ob/ob mice with LVH. Caloric restriction attenuated myocyte hypertrophy, cardiac inflammation, fibrosis, and oxidative stress in ob/ob and db/db mice. Furthermore, we found that caloric restriction reversed iron homeostasis-related lipocalin 2, divalent metal transporter 1, transferrin receptor, ferritin, hepcidin, and ferroportin expressions in the heart of ob/ob and db/db mice. These findings demonstrate that the cardioprotective effects of caloric restriction result from the cellular regulation of iron homeostasis, thereby decreasing oxidative stress, inflammation, and cardiac remodeling. We suggest that decreasing iron-mediated oxidative stress and inflammation offers new therapeutic approaches for obesity-induced cardiomyopathy.

Keywords: Left ventricular hypertrophy, Iron homeostasis, Caloric restriction, Heart, Leptin

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024

Ultrastructural and molecular characterization of platelet-derived growth factor beta-positive leptomeningeal cells in the adult rat brain

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The leptomeninges, referring to the arachnoid and pia mater and their projections into the perivascular compartments in the central nervous system, actively participate in diverse biological processes including fluid homeostasis, immune cell infiltrations, and neurogenesis, yet their detailed cellular and molecular identities remain elusive. This study aimed to characterize platelet-derived growth factor beta (PDGFR-β)-expressing cells in the leptomeninges in the adult rat brain using light and electron microscopy. PDGFR-β+ cells were observed in the inner arachnoid, arachnoid trabeculae, pia mater, and leptomeningeal sheath of the subarachnoid vessels, thereby forming a cellular network throughout the leptomeninges.

Leptomeningeal PDGFR-β+ cells were commonly characterized by large euchromatic nuclei, thin branching processes forming web-like network, and the expression of the intermediate filaments nestin and vimentin. These cells were typical of active fibroblasts with a well-developed rough endoplasmic reticulum and close spatial correlation with collagen fibrils. Leptomeningeal PDGFR-β+ cells ensheathing the vasculature in the subarachnoid space joined with pial PDGFR-β+ cells upon entering the cortical parenchyma, yet perivascular PDGFR-β+ cells in these penetrating vessels underwent abrupt changes in their morphological and molecular characteristics: they became more flattened with loss of immunoreactivity for nestin and vimentin and deficient collagen deposition, which was indicative of inactive fibroblasts termed fibrocytes. In the cortical parenchyma, PDGFR-β immunoreactivity was almost exclusively localized to larger caliber vessels, and significantly decreased in capillary-like microvessels. Collectively, our data identify PDGFR-β as a novel cellular marker for leptomeningeal fibroblasts comprising the leptomeninges and perivascular adventitial cells of the subarachnoid and penetrating large-sized cortical vasculatures.

Keywords: Platelet-derived growth factor beta, Leptomeninges, Perivascular fibroblast, Leptomeningeal fibroblast, Arachnoid mater, Pia mater.

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025

Follistatin acts as a downstream mediator of sonic hedgehog in establishing the tonotopy of the mammalian cochlea

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The vertebrate cochlea is tonotopically organized, such that hair cells in the base are tuned to high frequency sounds and their counterparts towards the apex progressively tuned to lower frequencies. Recent studies suggest that the tonotopic organization is established by a temporal signaling cascade that is initiated by an increasing base-to-apex gradient of Sonic hedgehog (SHH) signaling both in birds and mammals. In the chicken basilar papilla, Bmp7 is shown to be a key downstream target of SHH in mediating the tonotopic organization. However, the downstream mediators of SHH have been elusive in the mammalian cochlea. It has been shown that expression of Follistatin (Fst), an antagonist for Bmp/TGFβ pathway, is activated by SHH and exhibits a similar graded pattern in the developing mouse cochlea. To test whether Fst plays a role in mediating SHH signaling to facilitate the tonotopic organization of the mammalian cochlea, we analyzed the cochlear structures and function of Fst knockout (KO) and inner ear-specific conditional knockout (Pax2-Cre; Fstlox/lox; cKO) mice. The inner ear morphology of Fst KO embryos was generally normal, yet the cochlear duct was slightly shorter with an extra row of outer hair cells in the apex. Importantly, apical cochlear markers that are positively regulated by SHH and preferentially expressed in the apical cochlea, were specifically abolished or down-regulated in Fst KO cochlea. These abnormal patterning of the apical cochlea did not appear to be due to disrupted SHH signaling. Since Fst KO mutants were embryonic lethal, we generated inner ear-specific Fst cKO mice, which were viable and closely recapitulated the Fst KO phenotypes. Tonotopic characteristics of the hair cells such as gradual changes of stereocilia lengths and angles appeared to be shifted toward the base in 4-week Fst cKO mice. RNA-seq analysis along the cochlear duct suggest that global gene expression profile of the apical cochlea became similar to that of the middle cochlea. Furthermore, Fst cKO mice showed a significant increase in ABR thresholds and decrease in DPOAE amplitudes specifically in the low-frequency range. These results show that morphology, gene expression, and function of the apical cochlea are compromised in the absence of Fst in mice. Taken together, these results suggest that Fst plays an essential role in the tonotopic organization in the mammalian cochlea by promoting the apical cochlear identity. Supported by the BK 21 PLUS Project for Medical Science, Yonsei University

Keywords: Sonic Hedgehog (Shh), Follistatin (Fst), Tonotopy, Tonotopic organization, Hearing loss

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Poster

Poster Presentation Ⅰ (P001-P077)

2019년 10월 17일(목) 12:30 ~ 13:30 에머랄드홀

■육안해부학: P1~P21
■신경과학: P22~P59
■면역 및 종양: P60~P77

Poster Presentation Ⅱ (P078-P131)

2019년 10월 18일(금) 12:30 ~ 13:30 에머랄드홀

■조직 및 발생: P78~P98
■기타: P99~P131

P1

Three-dimensional structure of the middle meningeal vessel in cranial dura mater

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Middle meningeal artery (MMA) in an importer branch which nourishing cranial dura mater and periosteum. The study aimed to describe the microanatomical knowledge on the subject of the middle meningeal vessels. Dura maters adjacent to the MMA were detached carefully with the elevator from the skull base of 3 formalin-embalmed cadavers. Specimens were processed in 10-micron-thick serial sections, underwent Masson's trichrome staining, and subjected 3-dimensional reconstruction. MMAs were enveloped by two layers of dura mater (inner meningeal and external periosteal layers) forming semilunar venous sinus and gives rise accessory meningeal branches before a frontal branch. Meningeal branches of the trigeminal nerve usually supplied both sides of the MMA with some distance and crossed both two layers of dural sheets. Contrary to venous sinuses with blood clots, unidentified structures filled in mucus-like materials occupied some parts of perivascular spaces in a scatted manner. Additional studies identifying this ambiguous structure caught in periosteal and meningeal layers are necessary.

Keywords: Dura mater, Middle meningeal artery, Trigeminal nerve, Venous sinus, Anatomy

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P2

The prediction of the location of the infraorbital foramen using the facial landmarks

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The infraorbital foramen (IOF) is located on the maxilla, about 0.5cm below the middle of the infraorbital margin, which transmits infraorbital vessels and nerve. The infraorbital nerve is the sensory nerve that innervates to the skin in the lower eyelid, nose, nasal septum, anterior part of the cheek and upper lip. Knowledge of the IOF location is important for the anesthesia techniques, infraorbital nerve block, and also the midfacial and oral surgery. Numerous methods have been described regarding the location of IOF under the guidance of the bony or soft tissue landmarks and the teeth. In this study, we tried to find new methods for the prediction of the IOF location using facial tissue landmarks that are more practical and easier to use. In this study, we used 22 hemifaces from 11 embalmed Korean adult cadavers. The IOF was exposed by removing the soft tissue of the infraorbital area while preserving the main soft tissue landmarks. After dissection, the specimens were scanned using a structured-light 3D scanner, and reconstructed using 3D scanner software. On the reconstructed images, the position of the IOF was identified by comparing with the line through the mid-pupillary (MP) and the cheilion (Ch), and the location of the IOF was measured based on the MP-Ch line. Compared to the MP-Ch line, the position of the IOF was observed into three patterns. In 45% of the cases, the IOF was found on the MP-Ch line, and the IOF was found on the medial and lateral side of the MO-Ch line in 32% and 23%, respectively. The average distance of MP-Ch was 80.2 ± 8.4 mm (65.4-93.5 mm). Along the MP-Ch line, the average distance to the IOF from the MP was 27.7 ± 3.4 mm (21.4 – 32.3mm). The vertical distance from to the IFO from the MP-Ch line was 1.1 mm (-3.3-3.6). The location of the IOF can be easily predicted based on the MP-Ch line. The result of the present study can provide new safety guidelines during the various clinical procedures such as the infraorbital nerve block and midfacial surgery.

Keywords: Infraorbital foramen, Infraorbital nerve block, Facial landmark, 3D scanner

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P3

The location of the risorius muscle with references to the facial landmarks

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The risorius muscle (RS), which pulls the mouth corner to the lateral side when smiling, is one of the essential muscles because of the cosmetic and social role of the smile. The damage or paralysis of the RS can occur during the aesthetic procedure, resulting in asymmetric smiles or facial asymmetry. With the increase of the off-label uses of the botulinum toxins, a variety of procedures such as the Nefertiti Lift by the intradermal injection of the botulinum were introduced. During the procedures, the side effects such as asymmetric smile may occur due to injected or diffused of botulinum toxin into the RS. Previous studies have reported on the location of the RS, but the exact pathway of the muscle has not yet been elucidated. In this study, we try to clarify the anatomical information of the RS based on the facial landmarks, which can be easily used during the clinical procedures. Thirty hemifaces from 20 embalmed adult Korean cadavers (8 males and 12 females with a mean age of 75.3 years) were used in this study. The skin and subcutaneous tissues of the lower face were gently dissected to expose the RS. After dissecting, the location of the RS was measured as follows based on the cheilion (Ch) to the otobasion inferius (Oi) line. In most cases, the RS originated near the CH-OI line, then ran under the line in an arch shape. On average, the upper and lower points of the RS were located 49.9 ± 8.6mm, 52.0 ±8.9mm laterally from the Ch, and above 2.9mm, and below 15mm the Ch-Oi line, respectively. The minimum distance from the mandible border to the RS was 12 mm on average. Based on the CH-OI line, the location of the RS can be easily predicted. The detailed information about the location of the RS from the present study can help to provide a safe clinical guideline for the botulinum neurotoxin injection of the lower face.

Keywords: Risorius muscle, Facial landmark, Facial lifting, Botulinum toxin

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P4

Depth of muscular components of midface by ultrasonographic analysis

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Background: Midface area has a crucial clinical importance in facial aging and various clinical procedures. Thus, surgical and non-surgical procedures are performed in this zone. However, there is scarce knowledge about the depth of muscular components. The aim of this study was to describe the depth of the muscle components of midface area in Korean adults. **Materials and Methods:** 12 Facial landmarks (FL) were assessed in midface area of 95 volunteers (53 males; mean age 23.8 years). Ultrasonographic analyses along sagittal (SP) and axial (AP) plane were performed in each FL, location and depth of the muscles were identified and measured using NIH'S imageJ software. Data were analyzed using shapiro-wilk test for normality and student's-t test for comparison by sex. **Results:** Orbicularis oculi was mainly found in FL1 (SP: 98.95%, AP: 95,76%), FL2 (SP: 96.84%; AP: 97.89%), FL3 (SP: 97.89%; AP: 100%) and FL4 (SP: 92.63%; LP: 92.63%), Levator labii superioris alaeque nasi (LLSAN) in FL5 (SP: 90.53%; AP: 95.79%) and FL9 (SP: 82.11%; AP: 74.74%), Levator labii superioris in F6 (SP: 95.79%; AP: 93.86%), Zygomatic minor in FL7 (SP: 94.74%; AP: 96.84%), and FL11 (SP: 63.16%; AP: 54.74%), Zygomaticus major in FL8 (SP: 95.79%; AP: 96.84%). LLSAN's depth was significantly different between sexes in sagittal plane [FL5 (P=0.017), FL9 (P=0.026)] meanwhile zygomaticus major [sagittal plane FL8 (P=0.001), FL12 (P=0.009); axial plane FL8 (P=0.000), FL12 (P=0.001)] and minor [sagittal plane FL7 (P=0.003), FL11 (P=0.007); axial plane FL4 (P=0.000), FL7 (P=0.000), FL11 (P=0.010)] were significantly different in both planes. **Conclusion:** This study contributes to show the importance of knowledge about the position and the depth of midface muscle components. This is quite relevant in clinical areas because in practice, injections in muscles of midface are common. However, there are muscles that must be avoided in these processes, among those LLSAN and zygomatic major and minor are found because the risk of dropped lip or an unnatural smile look, respectively.

Keywords: Ultrasonography, Midface, Facial landmarks, Zygomatic muscle, Levator labii superioris alaeque nasi

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P5

Rphological analysis of palatal bone thickness for mini-implant placement

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The aims of this studyare to measure the palatal bone thickness, to analysis the correlation betweenthe size of the alveolar arch and palatal bone thickness, and to discuss theskeletal structure of the hard palate for mini-implant placement. Twenty-fourdry skulls in Koreans were used. The three different horizontal reference lineswere established at first premolar and second premolar, between second premolarand first molar, and first molar. And then, a total of 12 points were set up inrelation to each horizontal reference line by drawing a vertical reference lineperpendicular to central incisor, between central incisor and lateral incisor,lateral incisor, between lateral incisor and canine. At each point, the palatalbone thickness, the width and length of the alveolar arch, and the width andlength of the incisive foramen were measured directly with the bone caliper andthe digital caliper. The correlation between the width and the length ofalveolar arch and the palatal bone thickness was analyzed. The mean of palatalbone thickness based on the horizontal reference line was 11.4 ± 3.2 mm inbetween first premolar and second premolar, 7.4 ± 2.4 mm in between secondpremolar and first molar, and 5.2 ± 1.5 mm in first molar, decreasedposteriorly with statistically significant difference. The position betweenfirst premolar and second premolar showed a constant thickness, and thickenedlaterally from the median palatal suture due to the alveolar process, but nostatistically significant difference. At the position between second premolarand first molar and the position in first molar, it were also constant, thenbecame significantly thicker toward point between lateral incisor and caninedue to the alveolar process and the palatal spine. The width of the alveolararch was correlated with the length of the alveolar arch and the palatal bonethickness of between first premolar and second premolar, but not with thelength of the alveolar arch and the palatal bone thickness. These results canprovide useful anatomical data on palatal bone thickness including skeletalstructures of hard palate for mini-implant placement.

Keywords: Mini-implant, Palatal bone thickness, Alveolar arch, Incisive foramen, Palatal spine

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P6

왼심방귀의 형태와 동맥분포

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왼심방귀는 왼심방에서 짧은 손가락 형태로 튀어 나와있다. 고령일수록 심장의 부정맥 발생은 증가하며, 왼심방귀에서 발생한 심방세동은 왼심방귀의 수축력을 약화하고, 혈액이 정체되어 색전증이 나타나는 경우가 흔하며 이는 뇌졸중의 원인이 된다. 임상적 진단과 치료방향을 결정하기 위해서 왼심방귀의 형태를 알고 영상의학적으로 잘 분별할 필요가 있다. 한국인 왼심방귀의 형태를 분류하고, 크기를 측정하여 형태적 특성을 밝히고자 이 연구를 진행하였으며, 이곳에 동맥에 대하여 같이 보고하여 임상적 진단에 도움을 주고자 한다. 표본은 27명의 고정한 시신(남 19명, 여8명, 사망나이 67세)에서 적출한 심장을 사용하였다. Epicardium을 조심스럽게 벗겨서 왼심장귀의 형태를 관찰하였고, 분포하는 동맥가지를 해부하여 기록하였다. 왼심방귀를 입구와 가장 긴 길이 및 너비를 측정하였다. 형태는 culiflower, chicken wing, windsock 세 가지로 분류하였으며, culiflower 형태가 가장 많았다(81.5%). 남녀 모두 3/4이상에서 culiflower 형태가 관찰되었으며, chicken wing 형태가 가장 적게 관찰되었다. 입구의 폭은 평균 25.5 ± 6.2 mm, 길이는 34.5 ±9.2 mm, 중간너비는 31.7±7.1 mm 였으며, 여성표본의 크기가 모두 작았다. 입구의 폭은 남성은 windsock 형태인 것이 여성은 chicken wing 형태인 것이 가장 작아 평균크기가 20 mm 이하였다. 왼심방귀에는 왼심장동맥의 가지가 분포하였으며, 주로 왼휘돌이동맥에서 일어났다. 다수의 동맥이 분포하는 것을 관찰하였으며, 동맥이 분지되는 위치는 매우 다양하였다.

Keywords: Left atrial appendage, Auricle, Shape, Demension, Coronary artery

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P7

An extensor digitorum muscle for index finger originated from the extensor carpi radialis brevis

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The anomalous variations in the extensor carpi radialis brevis (ECRB) and extensor digitorum (ED) muscle of the forearm have been previously reported the in the literature. The present article describes an anomalous variations of the ECRB and ED muscle in the forearm. We observed that the accessory muscle originated from the medial aspect of the ECRB muscle inserts into the base of second metacarpal bone and the ED muscle divides into three distinct tendons without tendon of index finger. Knowledge of these variations are important to avoid surgical complications and to prevent diagnostic problems. This case is the first report of the variations of ECRB and ED muscle in the Korean cadaver. The embryological and clinical significance of these variation discussed.

Keywords: Anatomical variations, Accessory muscle, Extensor carpi radialis brevis, Extensor digitorum

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P8

한국인의 긴엄지발가락폄근과 부속힘줄에 대한 형태학적 분류

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긴엄지발가락폄근(extensor hallucis longus)은 앞정강근과 긴발가락폄근 사이의 깊은 층에 있으며, 종아리 중간 부분과 그 근처의 뼈사이막에서 시작되며, 발목관절의 앞쪽에서 힘줄로 바뀌고, 발등으로 들어가서 엄지발가락의 끝마디뼈 바닥에 붙는다. 이 근육은 엄지발가락의 발등굽힘과 발의 안쪽번짐 기능을 한다. 이 근육에서 부속힘줄(accessory tendon) 발생률에 관한 다양한 선행연구들이 있지만, 그들의 기능은 잘 알려져 있지 않다. 본 연구에서는 한국인 시신을 대상으로 긴엄지발가락폄근과 부속힘줄의 발생빈도와 형태학적 분류를 진행하여, 한국인의 긴엄지발가락폄근과 부속힘줄에 대한 체질인류학적 자료를 확보하고자 하였다. 이 연구에는 포르말린으로 고정된 한국인 시신 25구(총 50족-25 우측, 25 좌측)을 사용하였으며, 그 중 3족은 손상과 건조로 인해 총 수에서 제외하였다. 시신의 평균연령은 81.33세(55~89세)였다. 긴엄지발가락폄근과 부속힘줄의 형태학적 분류를 위한 측정은 전자 디지털 캘리퍼를 사용하였고 긴엄지발가락폄근의 닿는곳에 대한 분류는 Samar A-Saggaf (2003년) 분류법을 기준으로 하였다. 유형 1은 16족(32%)으로 한 개의 긴엄지발가락폄근이 엄지발가락 끝마디뼈 바닥으로 닿는 것이다. 유형 2는 30족(60%)으로 한 개의 긴엄지발가락폄근에 부속힘줄 한 개가 더 관찰되었으며 부속힘줄이 더 작았고 안쪽으로 닿아 있었다. 유형 3은 1족(2%)으로 긴엄지발가락폄근에 부속힘줄 두 개가 확인되었으며, 부속힘줄에 추가 부속힘줄이 갈라져 나오는 형태였다. 긴엄지발가락폄근의 닿는곳은 25족(50%)에서 첫째발허리발가락관절주머니이었으며, 7족(14%)에서 엄지발가락 첫마디뼈의 머리, 1족(2%)에서 엄지발가락 첫마디뼈였다. 긴엄지발가락폄근 힘줄의 길이는 38.33cm, 너비는 5.95mm였고, 부속힘줄의 길이는 7.62cm, 너비는 1.68mm였다. 본 연구를 통해, 한국인의 긴엄지발가락폄근의 유형별 발생빈도와 부속힘줄의 부착 패턴이 타 인종의 연구결과와 차이가 있음을 확인하였다. 향후, 한국인의 긴엄지발가락폄근과 부속힘줄에 대한 해부학적 다양성과 인종 특성을 규명하기 위한 추가적인 연구가 필요할 것으로 사료된다.

Keywords: Extensor hullcis longus, EHL, EHC, Extensor hallucis capsulris, Accessory tendon, Variation

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P9

Morphological classification of plantaris tendon ac cording to shape and location of insertion in korean

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The plantaris muscle is a small muscle with a short belly and long thin tendon that forms part of the posterior superficial compartment of the calf. The plantaris tendon(PT) is often used as a donor for grafts in upper and lower extremity surgery. Recent reports have suggested that PT is potentially involved in the tendinopathy of the midportion of the Achilles tendon. The purpose of the study is to examine the insertion type, thickness and width of the PT in the Korean population and provide clinically applicable information to surgeons. The dissection was performed on 61 lower limbs(30 right, 31 left) fixed in formalin mixture. Olewnik et al. classified into 5 types of PT insertion by site and area inserted in calcaneal tuberosity. According to his classification, we confirmed 5 types of the PT insertion in Korean population. Type 1 was characterized by a wide, fan-shaped insertion to the calcaneal tuberosity on the medial side of the Achilles tendon and was present in 23 limbs (37.7%). Type 2 was characterized by insertion to the calcaneal tuberosity, along with the Achilles tendon ; Fan shape is not taken. It was observed in 7 limbs (11.5%). Type 3 was characterized by insertion at the calcaneal bone, anterior to the Achilles tendon and was present in 8 limbs (13.1%). Type 4 was characterized by the insertion not being located on the calcaneal tuberosity but rather in the deep crural fascia. It was observed in 3 limbs (4.9%). Type 5 was characterized by a very wide insertion encircling the posterior and medial surfaces of the Achilles tendon and was detected in 16 limbs (26.2%). The PT was found to be absent in 4 lower limbs (6.6%). Extension point(ExP) is the point at which the distal tendon begins to expand before its insertion. The average(range) thickness and width of PT at ExP were 0.68(0.26~1.81)mm and 2.23(0.82~4.31)mm, respectively. The average(range) distance between calcaneal tuberosity and plantaris tendon ExP was 39.24(18.8~61.2)mm. We found similar pattern and ratio of the PT insertion and slightly lower in measured values of the PT, compared to previous studies. In further study, we have to dissect more limbs of cadavers and evaluate the anatomical diversity and ethnic characteristics of the PT in the Korean population.

Keywords: Plantaris tendon, Insertion type, Tendon thickness, Tendon width

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P10

한국인 뒤정강근힘줄 닿는곳의 해부학적 구조에 따른 형태 분류

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발바닥활에 대한 안정성과 지지력을 제공하는 뒤정강근힘줄의 기능이 저하되면 성인후천성편평발변형(Adult Acquired Flatfoot Deformity, AAFD)이 발생하게 되고, 보존적 치료 혹은 수술적 치료를 시행하게 된다. 본 연구의 목적은 한국인 시신을 대상으로 뒤정강근힘줄 닿는곳을 형태적으로 분류하여, 발바닥활의 안정성에 미치는 뒤정강근힘줄의 역할에 대한 해부학적 기초자료를 확보하는 것이었다. 본 연구에서는 포르말린으로 고정된 한국인 시신 30구(총 57족)를 사용하였다. 시신의 평균 연령은 75.48세(55-89세)였다. 발바닥과 종아리뒤칸의 피부를 절개하고 안쪽복사 뒤쪽 피하조직을 정리하였고, 발바닥 쪽에서 발바닥의 세 층을 차례로 해부하여 뒤정간근힘줄과 발바닥 셋째층의 근육과 다른 힘줄의 융합여부와 뒤정강근힘줄이 닿는곳을 확인하였다. 뒤정강근힘줄의 닿는곳에 대한 분류는 Olewnik(2019) 분류법을 기준으로 하였다. 첫째유형은 힘줄이 한 개이다. 주 힘줄이 발배뼈와 안쪽쐐기뼈에 닿았고, 2개의 다리에서 (3.51%) 관찰되었다. 둘째유형은 힘줄이 두 개이다. 주 힘줄은 첫째유형과 닿는곳이 같았고, 보조힘줄은 가쪽쐐기뼈에 닿았으며, 9개의 다리에서(15.79%) 관찰되었다. 셋째유형은 힘

줄이 세 개이다. 주 힘줄은 첫째유형과 닿는곳이 같았고, 보조힘줄은 닿는 유형에 따라 3개의 하위유형으로 나뉘었다. 13개의 다리에서(22.80%) 관찰되었다. 넷째유형은 힘줄이 네 개이다. 주 힘줄은 첫째유형과 닿는곳이 같았고, 보조힘줄은 닿는 유형에 따라 2개의 하위유형으로 나뉘었다. 33개의 다리에서(57.90%) 관찰되었다. 본 연구를 통해 뒤정강근힘줄 닿는곳 유형의 비율이 한국인과 유럽인 사이에 상당한 인종 차이가 있다고 시사했으며, 또한 성인후천성편평발변형의 발생기전을 밝혀내는 데 기여할 수 있을 것으로 사료된다.

Keywords: 뒤정강근힘줄, 성인후천성편평발변형, 한국인시신, 발바닥활, Olewnik 분류

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P11

한국인 시신에서 발목의 앞목말종아리인대 부착부위의 해부학적 특성

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앞목말종아리인대(Anterior talofibular ligament)는 발목관절의 운동범위를 제한하여 발목염좌(Ankle sprain)를 포함한 발목관절질환으로부터 관절을 안정화시켜주는 역할을 한다. 이에, 본 연구에서는 발목의 가쪽곁인대인 앞목말종아리인대의 부착부위의 형태와 띠의 개수에 따라 분류하고, 발꿈치종아리인대(Calcaneofibular ligament)와 이루는 각도를 측정하여 한국인의 앞목말종아리인대의 해부학적 특성을 밝혀내고자 하였다. 본 연구를 위하여 포르말린으로 고정된 한국인 발 50족을 해부하였다. 발목의 바깥부분의 피부를 절개하여 피부밑물렁조직을 제거하여 앞목말종아리인대 및 발꿈치종아리인대를 노출하였다. 앞목말종아리인대의 띠의 갯수를 확인하였으며, 앞목말종아리인대의 부착부위의 위치는 해부학적 기준점(reference point)을 사용하여 측정하였고. 길이와 너비도 측정하였다. 발목을 중립자세(neutral position)로 위치시킨 후, 앞목말종아리인대의 아랫면과 발꿈치종아리인대의 앞면이 이루는 각도를 측정하였다. 연구 결과, 앞목말종아리인대의 띠의 수는 1개 62%, 2개 38%를 차지하였다. 앞목말종아리인대의 몸쪽 부착부위는 가쪽복사뼈의 앞쪽 가장자리였다. 몸쪽 부착부위 중 종아리뼈 부착부위는 종아리뼈의 앞쪽 거친면에서 평균 20.78mm, 종아리뼈의 끝에서 평균 17.38mm 떨어진 곳이었다. 먼쪽 부착부위는 가쪽복사뼈와 관절하는 목말뼈 관절면의 앞쪽이였다. 먼쪽 부착부위 중 목말뼈 부착부위는 목말뼈 몸통의 위쪽 표면의 앞쪽 모서리에서 14.28mm, 목말뼈 몸통의 아래쪽 모서리에서 16.78mm 떨어진 곳이었다. 앞목말종아리인대의 길이는 20.34mm였고, 너비는 몸쪽 부착부위가 13mm, 인대의 중간부위가 12.26mm, 먼쪽 부착부위가 12.38mm였다. 앞목말종아리인대와 발꿈치종아리인대가 이루는 각도는 평균 114도였다. 띠의 수는 성별에 따라서 차이가 있었으며, 해부학적 기준점을 사용하여 측정한 앞목말종아리인대의 부착점의 위치도 성별에 따른 차이가 있었다. 앞목말종아리인대의 너비는 띠의 수와 관련이 있었다. 앞목말종아리인대의 모든 해부학적 특성은 오른발과 왼발 간의 차이가 없었다. 향후, 앞목말종아리인대에 대한 형태학적 자료를 지속적으로 축적하는 것은 발목의 해부학적 구조를 이해함과 아울러 발목질환의 진단과 치료에 도움이 될 것으로 사료된다.

Keywords: 앞목말종아리인대, 발목염좌, 한국인 시신, 해부학적 기준점, 띠의 수

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엉치엉덩관절 움직임에 대한 고찰 및 실험

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엉치엉덩관절의 비정상적인 움직임은 허리통증의 원인 중 하나로 고려되어왔다. 이러한 허리통증과 엉치엉덩관절의 관계를 이해하기 위해 엉치엉덩관절의 해부학 및 생체역학적 연구가 진행되어왔다. 대부분의 연구에서 엉치엉덩관절은 움직임이 적다고 알려져 있지만, 척추골반지표(spinopelvic parameters)를 이용하여 확인한 결과, 자세에 따른 골반입사각(Pelvic Incidence)의 변화가 언급되었다. 따라서 우리는 엉치엉덩관

절의 움직임에 대한 연구들을 분석하여 엉치엉덩관절의 움직임 범위와 자세 및 동작에 따른 움직임에 대해 확인해보았다. 의학논문검색사이트를 이용하여 엉치엉덩관절 움직임에 대한 논문을 검색하였다. 검색어에는 sacroiliac joint movement, sacroiliac joint biomechanics, spinopelvic parameters, pelvic incidence change가 포함되었다. 엉치엉덩관절의 움직임과 관련된 28건의 논문을 찾고 그 중 21편의 논문을분석하였다. 21편의 논문 중 10편의 논문이 시상면, 가로면, 이마면에 대한 돌림각을 분석하였다. 각 면에 대해 가장 적게 움직인 경우는 각각 0.01°, 0.01°, 0.00° 이었고, 가장 많이 움직인 경우는 2.27°, 1.67°, 1.08°이었다. 나머지 11편의 논문을 통해 척추골반지표를 이용한 자세와 움직임 변화에 따른 골반입사각의 차이를 분석하였다. 그 중 골반입사각의 변화가 가장 큰 경우는 바로선자세와 바로누운자세를 비교하였을 때 9° 차이가 있었고, 가장 차이가 적은 경우는 바로선자세와 앉은자세를 비교한 연구로 변화가 없었다 (0°). 엉치엉덩관절의 움직임은 허리의 통증과 관련하여 임상적으로 관심을 가지는 부분이다. 해부학적으로 엉치엉덩관절의 움직임은 크지 않다고 알려져 있지만, 이전연구들을 살펴본 결과 9° 까지 움직이는 것을 확인 할 수 있었다. 따라서 저자들은 엉치엉덩관절의 움직임에 대한 기능해부학적 연구가 필요하다고 판단하고, 엉치엉덩관절 움직임을 유발할 수 있는 물렁조직과 관절의 움직임에 대한 실험을 진행하고자 해당 장비를 설계하고 있다.

Keywords: Sacroiliac joint, Sacroiliac joint movement, Sacroiliac joint biomechanics, Spinopelvic parameter, Pelvic incidence change

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The enigmatic adductor minimus muscle: topographic study and its clinical significance

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Introduction: The aim of this study is to clarify the morphologic characteristics of the adductor minimus muscle (AMi) and to observe its topographic relationships with respect to the adjacent anatomical structures. **Materials and Methods:** Fifty-eight thighs of 29 Korean cadavers (22 males, 7 females; mean age at death, 71.7 years) were dissected in this study. **Results:** The AMi was a small and flat muscle, and originated from the inferior ramus of the pubis as the anterior-most part of the adductor magnus muscle (AMa), and was inserted posteriorly on the femur from the lesser trochanter to the upper part of the medial lip of the linia aspera. This muscle was observed in 96.6% (n=56) of the specimens. Among these, the case that the AMi was completely separated from the AMa was 72.4% (n=42). The medial femoral circumflex and first perforating arteries were always found superior and inferior to the AMi, respectively. Especially, the AMi was clearly distinguished from the AMa by the first perforating artery. A supernumerary muscle was found with the AMi in 33.3% (n=19) of the specimens. This muscle was located superior to the AMi, inferoanterior to the obturator externus muscle, and anterior to the posterior branch of the obturator nerve. When present, this muscle originated from the inferior ramus of the pubis and inserted to the posterior part of the lesser trochanter. **Conclusion:** The results of this study will help physicians to reduce the confusion about the muscle plane of the upper medial thigh during the ultrasound scan and improve the quality of many diagnoses in this body region.

Keywords: Adductor minimus, Adductor magnus, Obturator nerve, First perforating artery, Variations

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Differences in body composition of upper and lower extremities in elite taekwondo athletes

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Introduction: This study was analyzed the differences in body composition among taekwondo athletes during different stages of their career. **Methods:** Forty taekwondo athletes and 10 non-athletes (20 males and 30 females) with a mean age of 18.2 years (range, 15-23 years), a mean height of 173.4 cm, and a mean body weight of 64.8 kg were studied using dual energy X-ray absorptiometry and Biodex balance system. **Results:** The bone mineral density of upper and lower extremities was higher among university athletes of both sexes than in high school athletes. The lean body mass of male athletes in the university was higher than in high school male athletes. By contrast, in case of females, the opposite results were obtained for the upper and lower extremities. **Discussion:** Elucidation of the body composition according to the career and sex of taekwondo athletes is worthwhile for maximizing the efficiency of taekwondo training.

Keywords: Taekwondo, Body composition, Upper extremity, Lower extremity

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A case report of femoral nerve split with variant iliacus muscle: a potential source of femoral nerve entrapment

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The iliacus muscle is a large flat triangular shaped muscle located in iliac fossa and is one of the muscles comprising iliopsoas muscle complex. Although anatomical variations of iliacus muscles are rare, some variations have clinical importance because of the frequent coexistence of unusual course of the femoral nerve. The femoral nerve is the largest branch of the lumbar plexus and supplies the muscles and skin in front of the thigh. We present a case of a single aberrant slip of the iliacus muscle piercing the femoral nerve in the left iliac fossa of a male cadaver aged 97 years. The femoral nerve was split into two divisions and fused to form a single trunk superior to the inguinal ligament. Further course of the femoral nerve was normal. The potential clinical importance of this variant iliacus muscle accompanied by femoral nerve split would be the femoral neuropathy and possible consequent alterations of sensation in the anteromedial aspect of the thigh or motor deficit on quadriceps muscle.

Keywords: Femoral nerve split, Variant iliacus muscle, Nerve entrapment, Anatomy

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Anatomical study of the deep muscles of the sole

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The plantar muscle layers are arranged in four layers as seen from the plantar side. Due to the lack of studies on their positional relationship, topography and variation in the second layer of the sole, we studied the topography and variation of the structures in the second layer of the sole. In 95 foot of donated cadavers. We are studied the topography and variation of muscular structures in the second layer. According to the pattern of the communication of these muscles, the differences of topography of sole was investigated. The average length of sole was 213.69 + 17.5 mm, as height reference line. Based on this line, Not of Herny was located at 63.57 percentile (140.16 + 14.70 mm) and 56.59 percentile (121.79+ 13.42 mm) from great toe and little toe, respectively. The median of the angle between FDL and FHL was 31.56 + 5.75°. The average width was 79.49 + 6.8 mm, as width reference line. The average width of quadratus plantae was 36.33 + 7.78 percentile (28.92 + 6.58 mm) based on width reference line. The tendon of quadratus plantae was found in 25.3% (24/95) and its presence was associated with longer length of quadratus plantae. And the presence of the communication between FDL and FHL was found in 55.88% (38/68) and it had a relation with longer length of quadratus plantae and increased angle between FDL and FHL. Various patterns and variation at the intersection of the second layer of the plantar are expected to aid in the accurate diagnosis and treatment of the plantar injury.

Keywords: Anatomy, Plantar muscle, Cadaver, Sole, Flexor digitorum longus, Flexor halluces longus

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An anatomical study for uterosacral ligament suspension from female cadavers

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Abstract Introduction Uterosacral ligament suspension (USLS) is a surgical repair post-hysterectomy apical prolapse and involves attachment of the vaginal apex to the uterosacral ligament (USL). USL extends from anterior surface of sacral vertebrae to posterior wall of uterine cervix and is divided into superficial peritoneal and deep neural parts. Postoperative complications of USLS include intraoperative urinary obstruction, neurological pain of hip and thigh, ileus and small bowel obstruction, or stress urinary incontinence. The aim of this study was to identify the relationship of the USL to adjacent anatomy and to suggest the optimal suture site for USLS in order to minimize postoperative complications. Material and Methods The length of USL was measured from its proximal to distal attachment and the midpoint was tied. The origin of hypogastric nerves were identified by dissection and tied to the posterior wall of the pelvis. Four hemisected specimens were prepared and dissected. Straight, metal pins were placed at the midpoint of USL, at the points which were 1cm, 2cm, 3cm-proximally located from the midpoint, and also at the points 1cm, 2cm, 3cm-distally located from the midpoint along the USL. Peritoneum was removed and the relationship of the USL (pins) with adjacent anatomy was identified. Also, minimal distances from seven pinned points (A to G: ordered from most proximal to most distal one) to ureter, pelvic autonomic plexus, and internal iliac vessels and their branches were measured with a string. Results Average length of USL was 7.1 cm (Range 5.0-9.8). Ureter, on its way to bladder from pelvic brim, approached gradually to the USL and was located intimately to it at uterovaginal junction. Pins were observed to perforate the main trunk of hypogastric nerves or inferior hypogastric plexus when peritoneum was removed. All of the average distances from seven points to the closest branch of internal iliac vessels were less than 1 centimeter. At points A-D, internal iliac vein or inferior gluteal vein was the closest. Internal iliac or inferior gluteal artery coursed more laterally to their accompanying veins at these points. At points E-G, vaginal artery (2/4) or middle rectal artery (2/4) were within 1cm from the pinned points. At points D-G, lumbosacral plexus and nerves of it were covered medially by vascular structures in all of our cases. At point A-B which was more proximal, sacral nerve roots were identified within 1cm from pinned points in all cases. At point C, S1 and S2 were identified within 1cm from the pin in 1/4 case. Conclusion Considering all the results, mid-portion of USL is the most optimal site for suture during USLS. Also, sutures placed to the depth of superficial USL are recommended to minimize autonomic nervous injury. This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Education (NRF-2018R1D1A1B07048476).

Keywords: Uterosacral ligament suspension, Nerve-sparing surgery, Uterisacral ligament, Pelvic autonomic plexus, Hypogastric nerves, Inferior hypogastric plexus

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Morphometric study of communicating branch between the musculocutaneous and median nerves

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There are many variations between the musculocutaneous nerve (MCN) and median nerve (MN), and their communicating branch (Com) was extremely frequent. We aimed to establish the prevalence and topography of an anatomical variation between the MCN and MN. 77 upper limbs were dissected and the location of origin of the median nerve and Com were measured. The origin of the median

nerve was located 5.3 ± 17.7 mm from the coracoid process. MN was formed distal to axillary level in 18.2% (14/77). The Com was found in 39.5% (30/76), and it was located 35.69 ± 29.2 mm from the coracoid process. The presence of Com tended to be associated with proximal origin of MN (-0.3 ± 13.3 mm vs. 8.7 ± 19.4 mm, p = 0.066). The small gap between Com and lateral cord was shown as ring shape in 10.5% (8/76). It was renamed as ring form and was also associated with proximal origin of MN (-6.3 ± 13.7 mm vs. 6.4 ± 17.6 mm, p = 0.066). This study provided the morphometric data of the communication between MCN and MN and it will be helpful for surgical approaches and clinical investigation of the upper limb.

Keywords: Musculocutaneous nerve, Median nerve, Anatomical variation, Communicating branch, Morphometric study

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위가슴부위에서 가슴신경사이연결의 해부학적 형태변이

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가슴신경사이연결(intrathoracic anastomosis of Kuntz)은 둘째가슴신경을 첫째가슴신경의 배쪽가지로 연결하는 신경가지를 말한다. 이 가지는 교감신경이 교감신경줄기를 거치지 않고 팔, 머리, 목으로 연결되는 대체경로가 될 수 있으며, 얼굴, 손바닥, 겨드랑 부위의 땀과다증 치료를 위한 교감신경절제술 시 불완전하게 절제될 경우 수술 후 증상이 재발될 수 있다. 이 연구는 첫째에서 셋째갈비사이공간에서 가슴신경사이연결의 형태변이를 밝히고, 가슴신경사이연결 및 교통가지의 형태에 따라 팔신경얼기로 연결될 수 있는 신경연결의 유형을 밝히기 위해 시도하였다. 재료로 한국성인시신(남15, 여11) 가슴교감신경줄기 50쪽을 사용하였다. 먼저 가슴우리의 앞쪽 부분을 젖힌 후 가슴안장기들을 제거하였다. 그 후 첫째에서 셋째갈비사이공간에서 벽쪽가슴막을 제거하면서 가슴신경, 가슴신경사이연결 및 교통가지를 해부하였다. 가슴신경사이연결의 빈도, 가로 및 세로길이, 두께, 교감신경줄기와의 거리를 계측하였으며, 교감신경줄기와의 거리는 가슴신경사이연결의 부위에 따라 크기가 다르기 때문에 가슴신경사이연결의 위쪽끝, 중간, 아래쪽끝에서 모두 계측하였다. 첫째와 둘째가슴신경을 연결하는 첫째가슴신경사이연결은 1개로 74%에서 관찰되었는데, 첫째가슴신경과 가까운 곳에서 두 갈래로 갈라진 후 각각 첫째가슴신경과 갈비사이근으로 연결되는 경우도 10%에서 관찰되었다. 둘째와 셋째가슴신경을 연결하는 둘째가슴신경사이연결은 1개로 6%에서 관찰되었으며, 셋째와 넷째, 넷째와 다섯째가슴신경 사이에서 가슴신경사이연결은 관찰되지 않았다. 첫째가슴신경사이연결의 가로 및 세로길이와 두께의 평균값은 각각 1.2±0.6 mm, 19.2±3.6 mm, 0.4±0.2 mm, 둘째가슴신경사이연결의 경우 각각 0.8±0.5 mm, 19.5±3.5 mm, 0.3 mm였다. 첫째가슴신경사이연결과 교감신경줄기와의 평균거리는 가슴신경사이연결의 위쪽끝, 중간, 아래쪽끝에서 각각 14.1±6.5 mm, 11.1±5.4 mm, 7.4±3.4 mm, 둘째가슴신경사이연결과 교감신경줄기와의 평균거리는 각각 16.2±4.1 mm, 12.7±2.4 mm, 7.6±3.8 mm였다. 교통가지는 교감신경절과 가슴신경과의 연결형태에 따라 세 가지 형태가 관찰되었다. 첫째형태는 교감신경절에서 이에 상응하는 레벨의 가슴신경으로 연결되었고, 둘째 및 셋째형태는 교감신경절에서 이에 상응하는 가슴신경 보다 한 레벨 위와 아래의 가슴신경으로 각각 연결되었다. 첫째에서 셋째가슴신경 사이에서 가슴신경사이연결은 가슴신경사이연결의 유무에 따라 3가지 유형으로 구분되었다. 첫째유형(Type I)은 첫째가슴신경사이연결만 있는 경우로 66%, 둘째유형(Type II)은 첫째와 둘째가슴신경사이연결이 모두 없는 경우로 28%였으며, 셋째유형(Type III)은 첫째와 둘째가슴신경사이연결이 모두 있는 경우로 6%였다. 이들은 교통가지와의 조합에 따라 다시 여덟, 넷, 두 가지 유형으로 각각 구분되었다. 이 연구는 2019년도 강원대학교 대학회계학술연구조성비로 연구하였음

Keywords: 가슴신경사이연결, 교통가지, 갈비사이신경, 손바닥 땀과다증, 교감신경절제술

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P20

Endoscopic fungal ball removal using cotton pledget technique

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Treatment choice for fungal ball is endoscopic endonasal removal. However, frequently it is not easy to remove fungal elements in every corner of maxilla only with endonasal approach. To overcome this difficulty, we introduced cotton pledget technique. In addition, feasibility of cotton pledget technique was evaluated in cadaver, and the efficacy was evaluated in patients. Cadaveric study was performed using ten half heads of seven cadavers. The easiness and safety of cotton pledget technique was compared to previously reported technique. In addition, we performed 52 surgeries with cotton pledget technique and compare their result with that of 36 surgeries with conventional technique. All the study population had impacted fungal materials and underwent surgery in a tertiary hospital. Demographic factors, preoperative Lund-Mackay score, sinonasal outcome test score, surgical morbidity, and incomplete removal rate were analyzed. Cotton pledget technique was easy ($p = 0.011$) and less traumatic ($p=0.068$) than that of previous technique. In addition, clinical evaluation showed that cotton pledget group had significantly lower incomplete removal rate than that of the control group ($p = 0.010$). Cotton pledget technique is easy and safe method. In addition, the cotton pledget technique enables to remove fungal ball more effectively without performing inferior meatal antrostomy or Caldwell-Luc approach. So, when fungal material is impacted to maxillary sinus, we recommend to use the cotton pledget technique at first.

Keywords: Sinusitis, Fungal ball, Endoscopy, Paranasal sinuses, Maxilla, Minimally invasive surgical procedure

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P21

Three-dimensional topography of the human auditory ossicles for effective malleostapedotomy

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Malleostapedotomy for the patients with the otosclerosis is a otologic surgical procedure involving attachment of a prosthesis that grips the malleus handle on one end and passes through the base of the stapes into the vestibule on the other end. The difficulty associated with this procedure is to determine the proper prosthesis sizing and shaping by intersubjective variability. The present study investigated the positional relationship between auditory ossicles and other structures of the middle ear using computer aided 3-D volume rendering with purpose of providing surgical guidelines for the safe and effective mealleostatpedotomy. Fifty-one sides of the temporal bone were scanned by MicroCT and the auditory ossicles and the tympanic membrane were materialized three dimensionally in Mimics software. The mean distances from the grip site of the handle to the umbo, from the umbo to the long crus of the incus, and from the long crus of the incus to the base of the stapes were 3.6, 2.5, and 3.7 mm, respectively. The mean distance from the grip site of the handle to the base of the stapes was 6.5 mm. The mean thickness of the base of the stapes was 0.2 mm. The mean angle between the tympanic membrane and the base of the stapes was 10.7 degrees. The mean angle between the horizontal line of the grip site and the long crus of the incus was 35.4 degrees. The present study has identified the positional relationship between tiny structures involving sound transmission in the middle ear via 3D volume rendering, and has also yielded new navigational guidelines that will facilitate adequate prosthesis sizing and shaping during malleostapedotomy.

Keywords: Auditory ossicles, Otosclerosis, Malleostapedotomy, Prosthesis, MicroCT, 3D

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P22

Glucagon-like peptide 1 improves neural structure by regulating neuroinflammation through neuron-microglia communication

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Glucagon-like peptide 1 (GLP-1) is one of hormones secreted from enteroendocrine L cells. However, it has been reported that GLP-1 is also expressed in the brain. GLP-1 signaling has important roles in regulating neuroinflammation and in enhancing memory function, but it is unknown in which mechanisms are involved in these regulations. Here, we found that GLP-1 enhances neural structure by suppressing LPS-induced inflammation through neuron-microglia communication. Inflammatory secretions of BV-2 microglia by LPS deteriorated mitochondrial function and cell survival, as well as neural structure in Neuro-2a neurons. However, GLP-1 suppressed the secretion of TNFα-associated cytokines and chemokines in BV-2 microglia, resulting in enhanced neural connectivity (neurite length, number of neurites from soma, and secondary branches) in Neuro-2a neurons. We confirmed that GLP-1 enhances neural connectivity, dendritic spine morphogenesis, and spine maturation in TNFα-treated primary cortical neurons, by altering protein levels related to neurite growth and spine morphology. Together with our data that GLP-1 itself improves neural connectivity and spine morphology in neurons, GLP-1 has therapeutic potential in CNS diseases such as neurodegeneration and cognitive deficits.

Keywords: Dendritic spine morphology, Glucagon-like peptide 1 (GLP1), Lipopolysaccharides (LPS), Neuroinflammation, Neurite complexity

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P23

Osteopontin heptamer peptide containing the RGD motif enhances the phagocytic function of microglia

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Osteopontin (OPN) is a phosphorylated glycoprotein expressed in various tissues, including brain, and mediates a wide range of cellular activities. In our previous studies, we reported recombinant OPN and RGD and SLAY-containing OPN-peptide icosamer (OPNpt20) exhibited robust neuroprotective activities in an animal model of transient focal ischemia, and attributed these effects to the anti-inflammatory, pro-angiogenic, and phagocytic functions of OPNpt20. In the present study, we truncated OPNpt20 to an RGD-containing 7 amino acid peptide, which induced phagocytosis in BV2 cells (a microglia cell line). Four OPN peptides containing RGD (R) and/or SLAY (S) motif (OPNpt13RS, OPNpt7R, OPNpt7RS, and OPNpt7S) were synthesized and their cell motility and migration inducing activities were examined in BV2 cells. All four peptides significantly enhanced BV2 cell motility and migration, but OPNpt7R, an RGD-containing 7-amino-acid OPN peptide (VPNGRGD), was found to be most potent. Phagocytic activity and F-actin polymerization were also significantly enhanced in OPNpt7R-treated BV2 cells, and importantly, these effects were RGD-dependent. Furthermore, the Erk and Akt signaling pathways appeared to be involved in the induction of phagocytic activity by OPNpt7R. Co-treating cells with P OPNpt7R and D98059 or wortmannin (pharmacological inhibitors of Erk and Akt, respectively) significantly suppressed OPNpt7R-mediated phagocytosis induction. These results indicate the RGD-containing OPN heptamer OPNpt7R triggers microglial motility, migration, and phagocytic activity and that the RGD motif plays a critical role in these activities.

Keywords: Osteopontin heptamer, BV2, RGD, SLAY, Motility, Migration, Phagocytosis

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Chemoattraction from microglia and monocyte which are activated by OGD induces the homing effect of neural stem cell

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After acute ischemic stroke, disruption of blood-brain barrier and the inflammatory response in the brain lesion leads critical disabilities.Recent preclinical studies take notice 'the intravascular homing of neural stem cells (NSC) into the injured brain as a good candidate for therapeutic modalities in the stroke. However, the low cell number of homing into damaged brain parenchyma is main problem. Recently, many studies showed the homing system of NSC was related chemokine. We applied the screening of chemokines secreted from activated J774 (mouse macrophage cell line) and BV2 cells (mouse microglia cell line), which are related with the neuroinflammation and homing system of immune cells. First, these cells were subjected to OGD (oxygen-glucose deprivation) for 4 h and reperfusion up to 20 hr, and the supernatant was harvested as the OGD-conditioned media. We performed to investigate the screening of chemokine and migration of NSC in each OGD-conditioned media of J774 and BV2 cells. OGD-conditioned media of BV2 increased the migration ability of NSC compared to J774. Chemokine screening of OGD-conditioned media of BV2 showed increased signal level of CCL2, CCL6, CCL12, and IL-16. CCL3/4, CCL9/10 and CCL12. In OGD-conditioned media of J774, CCL4/5, CC12, and CCL9/10 were markedly upregulated. Among these ligands of BV2 and J774, CCL6 and CCL9/10 were significantly increased, and these receptors bound CCR1 in common. In NSC, Immunoblot showed the expression of CCR1, and in vitro migration assay indicated the regression effect by using antagonist of CCR1.This result provides that secreted chemokine of immune cells influences the migration of NSC to lesion area after ischemic stroke. Therefore, the all of finding is potentially involved in mechanism to boosting the homing effect of NSC into the lesion and identify CCR1 as a potential target of chemoattraction in NSC migration. This research was supported by grants from the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2016R1D1A1B03933017) to JY Kim, the Brain Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2016M3C7A1905098) to JE Lee

Keywords: Ischemic stroke, NSC, Microglia, Monocyte, Chemokine, Homing effect

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P25

Potentiation of microglia M2 phenotype by agmatine through IRF2 transcription factor

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Microglia, the known residential immune cell in the central nervous system (CNS), shares the similar functional properties of those of macrophages in the periphery. Regarding the functional point of view, resting microglia (M0) can be polarized to different phenotypes such as: M1 phase microglia mostly known for its pro-inflammatory responses and M2 phase microglia which is associated with anti-inflammatory responses. However, the mechanism through which the microglia regulates its phenotypes is not properly known yet. In this study we tried to potentiate the differentiation of M2 phenotype microglia by agmatine treatment in the murine BV2 microglial cell line. Agmatine is a primary amine, which is found to be neuroprotective in different injury mediated inflammatory conditions and also we found that agmatine treatment can increase the differentiation of the M2 phenotype in our previous study. In this study, it was shown that agmatine interacts with IRF2BP2 having high binding affinity through mass protein array analysis. IRF2BP2 is a IRF2 binding protein which has an important role in regulating microglia mediated inflammatory condition via manipulating the expression of the pro- and anti-inflammatory cytokines. We also found that agmatine treatment potentiate the M2 microglia in IL-4 treated BV2 cells than in LPS treated bv2 cells. So we hypothesized that IRF2BP2 may be a key player at the center of this phenotype transition of the microglia induced by agmatine in different inflam-

matory conditions. This study was supported by a national research foundation of Korea (NRF) grant funded by the Korean government (MSIP) (2017R1A2B2005350).

Keywords: Microglia, IRF2BP2, IRF2, KLF2, M1·M2 phenotype

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Chemokine production by microglia mediates blood-derived monocytes trafficking in neuroinflammation

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In CNS inflammation, microglia and recruited macrophages play major roles in neuroinflammation. We explored how these cells affect counterpart's polarization and infiltration and revealed some chemokines and receptors can be important modulators of the interaction. Co-culture of THP-1(monocyte cell line) and BV2(microglia cell line) showed THP-1 polarized into M2 phase, indicates monocytes can be polarized into certain phenotype by microglia. Transwell migration system were used for assessment of THP-1 infiltration and BV2 migration, infiltratory ability of THP-1 were significantly increased when cultured in M2 conditioned media of BV2. We screened chemokines in M2 medium BV2 and performed migration assay of THP-1 when several receptors of chemokines were blocked, the results indicates CCL2, CCL3, CCL4 and CCL5 and their relevant receptor CCR4, CCR5 are the chemokine systems when microglia attracts monocytes. In vivo, CCR2::RFP mice were injected with LPS followed by CCR4, CCR5 antagonists i.c.v injection. The number of CCR2 positive cells in mouse cortex were increased after LPS injection, when CCR4, CCR5 antagonist co-injection could reduce the number of infiltrated CCR2 positive cells. Our study indicates that Chemokine receptors CCR4, CCR5 can be strong candidates of target protein in new therapeutic strategies to acute brain inflammation by modulating the functions of microglia and monocytes. "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: Neuroinflammation, Microglia, Monocytes, Macrophages, Chemokine

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P27

A Dynamic Spectrum of Blood-derived Monocytes in Neuroinflammation Following Ischemic Stroke

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Recently, inflammatory response followed by cerebral ischemia-reperfusion has been a rising issue of stroke outcome. Post-ischemic inflammation of the injured brain is characterized by infiltration of blood immune cells as well as interaction between resident microglia and invaded blood immune cells. Peripheral blood monocytes are endogenously divided into two distinct populations: (1) "pro-inflammatory or classical" monocytes expressing CCR2highCX-3CR1low and circulating in blood. (2) "anti-inflammatory or non-classical" monocytes expressing CCR2lowCX3CR1high and locally patrolling. The former plays pivotal role in homing to inflamed tissue. In addition, the former expresses high levels of lymphocyte antigen 6 complex locus C1 (Ly6C) but low levels of C-X(3)-C motif chemokine receptor 1 (CX3CR1) and also secrete high levels of inflammatory cytokines and chemokines at the inflamed tissue. In contrast, the latter is characterized by high expression of the CX3CR1, but do not express CCR2 and Ly6C. These CCRlowCX-3CR1high monocytes producing anti-inflammatory cytokines such as IL-10 thought to become alternative monocytes. Although many repairing responses related to cerebral inflammation followed by ischemic stroke were reported, less is known about monocytes. In

this study, we performed various experimental techniques including two-photon microscopy to track the two distinct subsets of monocytes and observe the dynamic patterns in time-dependent manners after cerebral ischemia. Here we have identified that CCR2highCX3CR1low monocytes recruited to the injured brain were converted into CCR2lowCX3CR1high monocytes in chemokine/cytokine-dependently. These overall data suggest that (1) regulation of monocytes switching is one of the ultimate reparative strategies in the ischemic stroke. (2) education and adaptation of monocytes in local inflamed milieu are vital to alleviate the ischemic stroke through innate immunity. 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: Ischemic stroke, Neuroinflammation, CCR2 monocyte, CX3CR1 monocyte, Monocyte conversion, Microglia

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P28

Pro-angiogenic functions of Ninjurin 1 N-terminal adhesion motif (N-NAM) in HUVECs and in the postischemic Brain

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Nerve injury-induced protein 1 (ninjurin 1, Ninj1) is a cell adhesion molecule responsible for cell-to-cell interactions between immune cells and endothelial cells. We previously reported Ninj1 plays an important role in neutrophil infiltration in the postischemic brain and that a dodecamer peptide harboring Ninj1 N-terminal adhesion motif (N-NAM, Pro26~Asn37) confers robust neuroprotective and anti-inflammatory effects by inhibiting Ninj1-mediated neutrophil infiltration. In the present study, we investigated the pro-angiogenic effects of N-NAM, in HUVECs (human umbilical vein endothelial cells) and in a rat MCAO (middle cerebral artery occlusion) model of stroke. N-NAM was found to exert robust pro-angiogenic effects in HUVECs by promoting proliferation, migration, and tube formation. Furthermore, knock down of endogenous Ninj1 by Ninj1 siRNA or a N-terminal-specific blocking antibody induced angiogenesis and in these cells, N-NAM did not augment angiogenesis, which suggested the pro-angiogenic effects of N-NAM were derived from the suppression of endogenous Ninj1. In N-NAM-treated HUVEC cultures, AKT and ERK signaling pathways were activated, and more importantly, N-NAM and endogenous Ninj1 were observed to interact, indicating N-NAM stimulates angiogenesis via endogenous Ninj1 and AKT/ERK pathways. Furthermore, intranasal administration of N-NAM from 4 days post-MCAO (1.5 mg daily for 3 days) induced angiogenesis, significantly enhanced total vessel lengths and vessel densities, and induced the expressions of pro-angiogenic markers. Together these results demonstrate the 12-amino acid N-terminal Ninj1 peptide N-NAM, which contains the adhesion motif of Ninj1, exerts pro-angiogenic effects and suggest that these effects contribute to the neuroprotective effects of N-NAM in the postischemic brain.

Keywords: Ninjurin 1, Adhesion motif, Angiogenesis, MCAO, HUVECs

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Effects of high-definition transcranial direct current stimulation on functional improvement in a mouse model of ischemic stroke

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Transcranial direct current stimulation (tDCS) is an adjuvant tool to enhance functional recovery after stroke. Release of growth factors might mediate tDCS effects; thus, we investigated how the mechanism related to growth factors was involved in the therapeutic role

of high-definition tDCS (HD-tDCS) in ischemic mice. Focal cerebral ischemia was induced by middle cerebral artery occlusion for 40 minutes in mice. First, we applied repeated HD-tDCS poststroke to determine the experimental conditions such as the electrode position and polarity. Second, we applied unilateral anodal HD-tDCS over contralateral prefrontal cortex, motor cortex, or parietal cortex to find the effective stimulation site. The effects of HD-tDCS on functional recovery after stroke were confirmed by assessing motor and cognitive function. The expression of growth factor genes was analyzed in the ipsilateral regions after final HD-tDCS, and we confirmed the relationship with growth factors on beneficial effects of HD-tDCS after stroke. Among three different stimulation groups, anodal HD-tDCS over contralateral motor cortex significantly improved motor dysfunction and memory impairment after stroke. The positive changes in six genes (Bmp8b, Gdf5, Il4, Pdgfa, Pgf, and Vegfb) were observed in the HD-tDCS group of ischemic mice, here we highlighted alterations in growth differentiation factor 5 (GDF5) and platelet-derived growth factor subunit A (PDGFA). The expression of GDF5 and PDGFA showed the similar tendency of increase in the ipsilateral and contralateral striatum. Higher expression of GDF5 and PDGFA were observed in the peri-infarct regions of striatum after HD-tDCS, especially PDGFA expression were significant. Moreover, the number of BrdU- or BrdU/Dcx-positive cells in the subventricular zone was higher in the HD-tDCS group than other groups. Anodal HD-tDCS over contralateral motor cortex may support functional recovery through the secretion of GDF5 and PDGFA, it can also lead to adult neurogenesis for behavioral enhancement in ischemic stroke.

Keywords: Anodal stimulation, Growth factors, Motor cortex, Noninvasive brain stimulation, Stroke

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P30

Weisheng-tang ameliorates blood-brain brarrier integrity using ischemic stroke mice model

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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. In this study, we selected two Korean herbal medicine formulas, Weisheng-tang and Togxuewan, from Dongeuibogam through text-mining, and evaluated the protective effect on ischemic stroke using focal cerebral ischemic mouse model. Focal cerebral ischemia was induced by photothrombotic cortical ischemia. Infarct volume, brain edema, neurological deficits, wire-grip and Evans blue leakage were evaluated. Immunofluorescence staining for endothelial cell, tight junction proteins and protease-activated receptor-1 (PAR-1) was performed in brain tissues after ischemic injury. Pretreatment of Weisheng-tang significantly reduced infarct volume and edema and improved neurological and motor functions, but Togxuewan did not. In addition, Weisheng-tang dose-dependently (30, 100, and 300 mg/kg) decreased brain infarct and edema, and recovered neurological and motor deficit. Weisheng-tang pretreatment significantly decreased blood-brain barrier (BBB) breakdown as measured by Evans blue leakage after focal cerebral ischemia. Immunohistochemical analysis reveals that zonula occludens-1 (ZO-1) expression in ipsilateral site was significantly increased in Weisheng-tang pretreated mice. Moreover, high level of PAR-1 was observed in ischemic mice, but PAR-1 immunofluorescence was decreased in Weisheng-tang pretreated mice. These results indicate that Weisheng-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.

Keywords: Stroke, blood-brain barrier, tight junction proteins, PAR-1, Korean medicine

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P31

Spatiotemporal profile of NG2 glia and their association with microglial activation in the CA1 region of the rat hippocampus after transient forebrain ischemia

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We recently demonstrated that NG2 glia, the fourth type of neuroglial cell in the central nervous system, undergo proliferation and morphological changes in the striatum of rats administered the mitochondrial toxin 3-nitropropionic acid. The present study was designed to further substantiate the nature and the time course of reactive NG2 glia in the selectively vulnerable CA1 region of rat hippocampus subjected to transient forebrain ischemia. In control hippocampus, NG2 immunoreactivity was restricted to resting NG2 glia with thin processes, and the density of NG2 glia in the CA1 dendritic subfield, particularly, in the stratum radiatum was higher compared with that in the pyramidal cell layer (somatic region). In the ischemic CA1 hippocampus, the numbers of NG2 glia in both the pyramidal cell layer and the stratum radiatum were significantly increased at 3 days post-lesion, and remained elevated until 28 days, and this increase was due to new cells generated via proliferation. In addition, reactive NG2 glia were localized in association with activated microglia/macrophages expressing NG2. However, morphological features of reactive NG2 glia showed characteristic time- and strata-dependent patterns in the ischemic CA1 hippocampus. The morphologies of reactive NG2 glia in the stratum radiatum were altered with time: the thick and multiple processes of these cells at 3 days were transformed into shorter and highly ramified processes forming a dense network on days 7-14 days, but returned to the morphology of characteristic of NG2 glia observed at 3 days after reperfusion. By contrast, NG2 glia in the CA1 pyramidal cell layer transformed into irregular cell bodies with thick and short processes and this transformation was maintained during the post-ischemic period. These temporal differences of reactive NG2 glia in 2 strata of the CA1 hippocampus, the pyramidal cell layer and the stratum radiatum could be attributed to the degenerating processes that occur in the somata or dendirtes of pyramidal neurons. Thus, our data demonstrated in a rat model of transient forebrain ischemia that NG glia undergo proliferation and dynamic structural changes in the CA1 hippocampus, suggesting that activation of NG2 glia may be involved in the degeneration and subsequent tissue repair and reorganization in the ischemic hippocampus. This research was supported by the National Research Foundation of Korea (NRF) [grant number NRF-2017R1A2B4002922].

Keywords: NG2 glia, Hippocampus, Pyramidal cell layer, Stratum radiatum, Microglia

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P32

Platycarya strobilacea extract ameliorates memory impairment and neuronal death in experimental rat models of dementia

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Dementia is the most common neurodegenerative disorder affecting the elderly with a progressive cognitive decline and memory loss. Given that Alzheimer's dementia (AD) and Vascular dementia (VD), the two most common types of dementia, shares the key pathologies including neuro-inflammation, oral supplement of herbal medicines can provide viable therapies for both types of dementia due to their anti-inflammatory effect. In this study, therapeutic potentials of Platycarya strobilacea Extract (PSE), an oriental drugs showing various health-promoting activities, was tested on experimental rat models of AD and VD. Sprague Dawley rats were orally administered with low (250mg/kg) and high (500mg/kg) doses of PSE for 14 days and subsequently divided for different two paradigms: #1,

experiment for the anti-AD efficacies and #2, for the anti-VD efficacies. While intraperitoneal injection of scopolamine, an anticholinergic drug, and subsequent different behavior tests e.g., novel object recognition-, Y-maze-, and passive avoidance tests, were employed for the experiment #1, 2-vessel occlusion and hypovolemia (2VO/H) operation and postoperative measurement of neuronal viability and the adjacent neuroinflammation were used for the experiment #2. The results of experiment #1 showed that scopolamine triggered the impairment of memory performances under the all tests, which was significantly diminished by PSE supplements. The results of experiment #2 indicated that 2VO/H induced the marked neuronal death in hippocampus and intense microglial activation in the adjacent area, both of which were significantly attenuated by PSE supplements. The aforementioned effects of PSE were partially in a dose-dependent manner. These results provide evidence that PSE supplement can confer the protection against AD-and VD-related deteriorations of memory and histologic structures, suggesting that PSE might be a reliable natural alternative to cope with the two major types of dementia.

Keywords: Alzheimer's dementia, Vascular dementia, Platycarya strobilacea, 2-vessel occlusion and hypovolemia(2VO/H), Hippocampus

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P33

Transcription factor EB activation and neuroprotection by ouabain in Alzheimer's disease models

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Background: The number of neurofibrillary tangles containing abnormal hyper-phosphorylated tau protein correlates with the degree of dementia in Alzheimer's disease (AD). In addition, features of autophagosome accumulation and damage to autophagy, a degradation process of toxic aggregate protein in the cytosol, are also found in the AD brain. These indicate that regulation of the autophagy-lysosome system can be considered a therapeutic strategy for AD. Activation of transcription factor EB (TFEB), a master regulator of autophagy-lysosome system gene transcription, reduces the amount of tau through activation of autophago-lysosomal system in APP mice. Therefore, compounds that activate TFEB can be potential therapeutics for AD. **Method:** To search for therapeutic compounds for AD, we conducted two kinds of high-throughput screenings to determine pharmacologically active compounds which increase 1) neuronal viability in okadaic acid-induced, tau hyperphosphorylation-related neurodegeneration models and 2) the nuclear localization of transcription factor EB (TFEB). **Results:** Ouabain, a cardiac glycoside, was discovered as a common hit compound in both screenings. It also exhibited significant protective effect in tau transgenic fly and mouse models in vivo. Through inhibition of the mTOR pathway and activation of TFEB, ouabain enhances downstream autophagy–lysosomal gene expression and cellular restorative properties and reduces phosphorylated tau in vitro and in vivo. **Conclusion:** These results suggest ouabain as a promising therapeutics to improve the autophagy through the activation of TFEB and reduce the accumulation of abnormal toxic tau.

Keywords: Alzheimer's disease, Okadaic acid, Transcription factor EB, Tau, Ouabain

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P34

Effects of TonEBP deficiency on hippocampal inflammation in oligomeric amyloid β-treated mice

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The development of Alzheimer's disease (AD) has been mainly driven by the amyloid cascade hypothesis. In particular, recent reports indicate that immune system-mediated actions in fact contribute to and drive AD pathogenesis. Neuroinflammation in the hippocampus may contribute to major risk factor of AD. Overexpression of tonicity-responsive enhancer binding protein (TonEBP) is associated with many inflammatory diseases. However, the exact mechanism in neuroinflammation is not fully known. We injected AAV-CaMKII-Cre-eGFP into TonEBPlox/lox mice to selectively delete TonEBP in neurons of hippocampal CA1 region, and infused oligomeric Amyloid β in the hippocampal CA1 region. We found that Amyloid β-treated mice with TonEBP deletion in pyramidal neurons of hippocampus displayed improved memory deficits compared to Amyloid β-treated control mice. Double immunofluorescence study showed that reactive astrocytosis in amyloid β-treated mice was significantly attenuated by TonEBP deletion. Thus, our findings suggest that TonEBP may play an important role in progression of neuroinflammation-related AD pathogenesis.

Keywords: Alzheimer's disease, TonEBP, Amyloid β, Neuroinflammation, Hippocampus

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P35

Electroacupuncture therapy exert protective effects on dopaminergic neurons via upregulation of brain-derived neurotrophic factor and glial cell line-derived neurotrophic factor in MPTP-induced Parkinson's disease mouse model

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Parkinson's disease (PD) is a progressive neurodegenerative condition characterized by motor impairment and loss of dopaminergic neurons in the substantia nigra. However, specific sensory stimulation via electroacupuncture (EA) therapy may attenuate such losses by promoting the expression of endogenous neurotrophic factors, similar to physical therapy. We investigated the potential protective effects of EA on dopaminergic neurons in a mouse model of PD and whether these effects are associated with the promotion of endogenous brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF). Mouse models of PD were generated using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), and EA was stimulated at the Baihui and Dazhui points. Motor performance was assessed using behavioral tests, and Western blot experiments, enzyme-linked immunosorbent assays, and immunohistochemical assays were performed. EA ameliorated motor dysfunction caused by MPTP on rotarod and cat-walk test. MPTP caused a significant loss of dopaminergic neuron by cell death in the striatum and substantia nigra, but EA significantly restored dopaminergic neuron in these regions similar to the effects of levodopa. EA induced upregulation of BDNF and GDNF in the midbrain with increased expression of its receptors, tropomyosin receptor kinase B and GDNF family receptor alpha-1. Furthermore, EA induced activated Akt, cAMP response element binding protein (CREB) and paired-like homeodomain transcription factor 3 (Pitx3) in the substantia nigra. However, levodopa treatment did not induce BDNF/GDNF upregulation. Our results demonstrate that EA therapy may exert protective effects on dopaminergic neurons by upregulating the expression of endogenous BDNF/GDNF, and related signaling factors, thereby improving motor function. Thus, EA therapy offers adjuvant therapy for PD patient to recover motor dysfunction.

Keywords: Parkinson's disease, Electroacupuncture, Brain-derived neurotrophic factor, Glial cell line-derived neurotrophic factor, Dopaminergic neuron

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P36

Expression of Galectin-3 and Activating transcription factor-3 in nigral dopaminergic neurons of 6-hydroxydopamine induced parkinsonian rats

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Parkinson's disease(PD) is a common age-related neurological motor disordermarked 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 often nigrostriatal DA neuron and has been the most widely sued tool for replicating a PD pathology. Galectin-3(Gal-3), a member of the Galectin family of β-galactoside binding lectins. The Galectin-3 plats an important role in the cell adhesion, immune response and sihgnal cascade. Activating Transcription Factor-3 (ATF-3) a member of CREB/ATF family, is induced in wide spectrum of tissues by various types of insults and suggested to be an important immediated early molecules to inhibite 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 ATF-3 expression in 6-OHDA PD animal model. By 6-OHDA DA neuronal cell death occurs it increased time point in the ipsilateral -(injected side) ST, ATF-3 by a 6-OHDA be a retrograde tracer to determine the cell toxicity stress and from degenerating neuron it was confirmed ATF-3 expression also it confirmed the ATF-3 AND Gal-3 in the same cell. ATF-3 and co-expression of Gal-3 is confirmed using the Fluorogold whether due to toxicity of 6-OHDA results by the toxicity of 6-OHDA it was confirmed that the neuron is expression specially these results suggest that Galectin-3 and ATF-3 may be closely participating in 6-OHDA induced neurodegeneration. This is the first in vivo demonstration that DA neurons undergoing neurodegeneration express Galectin-3 and ATF-3.

Keywords: Parkinson's disease(PD), Galectin-3, ATF-3, Dopaminergic neuron, 6-OHDA

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P37

Neuregulin1 attenuates H2O2-induced reductions in EAAC1 protein levels and reduces H2O2-induced oxidative stress

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Neuregulin 1 (NRG1) exhibits potent neuroprotective properties. The aim of the present study was to investigate the antioxidative effects and underlying mechanisms of NRG1 against H2O2-induced oxidative stress in primary rat cortical neurons. The expression level of the excitatory amino acid carrier 1 (EAAC1) protein was measured by Western blotting and immunocytochemistry. The levels of lactate dehydrogenase (LDH) release, reactive oxygen species (ROS) generation, superoxide dismutase (SOD) activity, GPx activity, and mitochondrial membrane potential (Δψm) were determined to examine cell death and the antioxidant properties of NRG1 in primary rat cortical neurons. H2O2 reduced the expression of EAAC1 in a dose-dependent manner. We found that pretreatment with NRG1 attenuated the H2O2-induced reduction in EAAC1 expression. Moreover, NRG1 reduced the cell death and oxidative stress induced by H2O2. In addition, NRG1 attenuated H2O2-induced reductions in antioxidant enzyme activity and Δψm. Our data indicate a role for NRG1 in protecting against oxidative stress via the regulation of EAAC1. These observations may provide novel insights into the mechanisms of NRG1 activity during oxidative stress and may reveal new therapeutic targets for regulating the oxidative stress associated with various neurological diseases.

Keywords: H2O2, Neuregulin 1, EAAC1, Reactive oxygen species, Superoxide dismutase, Glutathione peroxidase

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Neuregulin1 Protects CoCl2-Induced Reactive Oxidative Stress and Overexpression of Excitatory Amino Acid Carrier 1

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Hypoxia-mediated neurotoxicity contributes to various neurodegenerative disorders, including Alzheimer's disease. Neuregulin-1 (NRG1) plays an important role in the development and plasticity of the brain. The aim of the present study was to investigate the antioxidative effects of NRG1 on CoCl2 induced hypoxia. We found that CoCl2 abnormally increased the expression of Excitatory amino acid carrier 1 (EAAC1) in SH-SY5Y cells. The pretreatment with NRG1 rescue CoCl2- induced up regulation of EAAC1 expression and cell death. Moreover, NRG1 reduced the number of CoCl2 induced TUNEL-positive SH-SY5Y cells and the accumulation of reactive oxygen species. NRG1 also induced the upregulation of the expression of the anti-apoptotic protein, Bcl-2, and decreased caspase-3 activation in CoCl2 induced hypoxia.

Keywords: Hypoxia, CoCl2, Neuregulin-1, EAAC1, Oxidative stress

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The involvement of EAAC1 induced depression-like behavior in rat model of early-life stress

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Early life stress (ELS) are relevant to neuropsychiatric disorder in adolescence and adulthood. Neonatal Maternal separation (NMS), as one of the ELS, serves as a risk factor for developing emotional disorders. Glutamate transporters play a crucial role in physiological glutamate homeostasis, neuronal development and plasticity. Neuronal excitatory amino acid carrier1 (EAAC1) is also primary route for uptake of extracellular cysteine for glutathione (GSH) synthesis. However, no previous studies have investigated EAAC1 in relation to ELS-related abnormality. In this research, we examined the expression of EAAC1 and GLAST in hippocampus and cerebral cortex with three length models from postnatal day 1 until day 7, 14 and 21. EAAC1 expression is remarkably reduced in all three length NMS models. We also detected that decreased vigilance and depression-like behaviors following NMS. Moreover, the depression-like behaviors were reversed by pre-administration of acetyl-N-cysteine (NAC). These findings suggest that EAAC1 might be involved in the progress of depression-like behavior in adolescence.

Keywords: Early life stress, EAAC1, Depression, NAC, Adolescence

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P40

Neuregulin1 improves social deficits and anxiety-like behavior induced by CoCl2 microinjection into the mouse ventral hippocampus

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Neuregulin-1 (NRG1) plays an important role in the development and plasticity of the brain. The aim of the present study was to investigate the neuroprotecive effect and underlying mechanisms of NRG1 in Cobalt chloride(CoCl2) microinjection into ventral hippocampus (vHi). CoCl2 microinjection into vHi increased the expression of HIF-1α (Hypoxia Inducible Factor), p53 in a dose and

time-dependent manner. We found that pretreatment with NRG1 rescue CoCl2-induced up regulation of HIF-1α, p53 expression and cell death. Moreover, we report that NRG1 attenuated social deficits and anxiety-like behavior induced by CoCl2 microinjection into the vHi.

Keywords: Neuregulin1, Cobalt chloride, Hypoxia, Behavior, Ventral hippocampus

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P41

Neuregulin 1/ErbB4 signaling attenuates neuronal cell damage under OGD in primary hippocampal neurons

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The hippocampus is one of the most important brain areas of cognition and the region is particularly sensitive to hypoxia an ischemia. Neuregulin-1 (NRG1) was shown to protect against focal cerebral ischemia. The aim of the present study was to investigate the neuroprotective effect and the under mechanism of the NRG1 in primary hippocampal neurons. Our data show that the OGD induced cytotoxicity and change of ErbB4 expression in primary hippocampal neurons. Moreover, we found that pretreatment of NRG1 inhibits the OGD-induced overexpression of ErbB4. In addition, NRG1 significantly attenuates the neurons death induced by OGD. The neuroprotective effect of NRG1 was blocked in ischemic neurons pretreated with AG1478, an inhibitor of ErbB4, but not AG879, an inhibitor of ErbB2. These results indicate an important role of ErbB4 in NRG1-mediated neuroprotection, suggesting that endogenous ErbB4 stands as a valuable therapeutic target for treatment of global cerebral ischemia.

Keywords: Neuregulin 1, OGD, ErbB4

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Carvacrol protects Schwann cell dedifferentiation and proliferation during Wallerian degeneration

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Abnormal neurodegenerative processes induce peripheral neurodegenerative diseases via irreversible nerve damage. Carvacrol possesses various effects on organisms. Here, we investigated the regulatory effect of carvacrol on transient receptor potential (TRP) melastatin M7 (TRPM7)-dependent Schwann cell dedifferentiation and proliferation during Wallerian degeneration An ex vivo peripheral nerve degeneration model was used with a sciatic nerve explant culture. Ex vivo, in vivo sciatic nerves were treated with carvacrol following an assessment of Schwann cell proliferation, and trans-dedifferentiation using morphometric indices. Carvacrol regulated the expression patterns of lysosomal-associated membrane protein-1, p75 neurotrophin receptor, phosphorylated-extracellular signal-regulated kinase, p-cJun, Krox20, and Ki67 in degenerating Schwann cells. These results suggest that carvacrol effectively protects against Schwann cell dedifferentiation and proliferation during Wallerian degeneration.

Keywords: Carvacrol, Transient receptor potential melastatin 7 (TRPM7), Dedifferentiation, Proliferation, Schwann cells

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Inhibition of transient receptor potential melastatin 7 (TRPM7) in Schwann cells effectively protects myelin fragmentation during Wallerian degeneration

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Peripheral neurodegenerative processes are essential for regenerating damaged peripheral nerves mechanically or genetically. Carvacrol, a major component in Origanum vulgare, possesses various effects on organisms, such as antibiotic, anti-inflammatory and cytoprotective effects; although transient receptor potential (TRP) melastatin M7 (TRPM7) is carvacrol-regulated TRPs, however, effect of carvacrol on the peripheral neurodegenerative process, and its underlying mechanism, remain unclear. Here, we investigated the specificity of carvacrol for TRPM7 in Schwann cells and the regulatory effect of carvacrol on TRPM7-dependent neurodegenerative processes. In this study, our results suggest that carvacrol effectively protects against the peripheral neurodegenerative process via TRPM7-dependent regulation in Schwann cells. Thus, pharmacological use of carvacrol or the oil of O. vulgare could be helpful to protect against neurodegeneration that occurs with aging and peripheral neurodegenerative diseases, prophylactically.

Keywords: Carvacrol, Transient receptor potential melastatin 7 (TRPM7), Schwann cells, Demyelination, Axonal degradation

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P44

A 2-min transient ischemia confers cerebral ischemic tolerance in non-obese gerbils, but rather results in neuronal death in obese gerbils by increasing abnormal mTOR activation-mediated oxidative stress and neuroinflammation

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A brief episode of transient ischemia (TI) can confer cerebral ischemic tolerance against a subsequent severer TI in normal condition. The brain under obese condition is more sensitive to ischemic injury. However, impact of a brief episode of TI under obese condition has not been fully addressed yet. Thus, the objective of this study was to determine the effect of a brief TI in the hippocampus of high-fat diet(HFD)-induced obese gerbils and related mechanisms. Gerbils were maintained on HFD or normal diet (ND) for 12 weeks and subjected to a 2 min of TI. HFD gerbils were heavier with higher blood glucose, serum total cholesterol, triglycerides and leptin levels. Massive loss of pyramidal neurons occurred in the hippocampal cornu ammonis 1 (CA1) field of HFD animals at 5 days after 2 min of TI, although 2 min of TI did not elicit death of pyramidal neurons in ND gerbils. The HFD group showed significantly increased levels of oxidative stress indicators (dihydroethidium and 4-hydroxynonenal) and proinflammatory cytokines (tumor necrosis factor-α and interleukin-1β) as well as microglia activation in pre- and/or post-ischemic phases compared to the ND group. Levels of mammalian target of rapamycin (mTOR) and phosphorylated-mTOR in the

CA1 field of the HFD group were also significantly higher than the ND group. On the other hand, inhibition of mTOR activation by rapamycin (an allosteric mTOR inhibitor) significantly attenuated neuronal death induced by HFD, showing reduction of HFD-induced increases of oxidative stress indicators and proinflammatory cytokines as well as microglia activation. Taken together, a brief episode of TI can evoke neuronal death under obese condition. It might be closely associated with abnormal increase of mTOR activation-mediated severe oxidative stress and neuroinflammation in pre- and/or post-ischemic phases.

Keywords: Obesity, Brief transient ischemia,Neuronal death, Oxidative stress, Neuroinflammation, Mammalian target of rapamycin

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P45

Effects of regional body temperature during asphyxial cardiac arrest on mortality and brain damage in rats

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To date, hypothermia has focused on improving rates of resuscitation to increase survival rates in cardiac arrest (CA) patients. For this, it needs to understand what body temperature affects neuronal damage/death in the brain during CA. However, few studies on effects of regional temperature in the body during CA on survival rate and neurological outcomes have been studied. Here, we used adult male rats (12 week-old) which were subjected to 4 conditions as follows: (i) whole body normothermia (37±0.5°C) plus (+) no asphyxial CA, (ii) whole body normothermia+CA, (iii) whole body hypothermia (33±0.5°C)+CA, (iv) body hypothermia/brain normothermia+CA, and (v) brain hypothermia/body normothermia+CA. Survival rate after resuscitation was significantly high in groups of whole body hypothermia+CA and body hypothermia/brain normothermia+CA, but not in groups of whole body normothermia+CA and brain hypothermia/body normothermia+CA. However, the group of hypothermia/brain normothermia+CA exhibited higher neuroprotective effect against asphyxial CA injury: neurological deficit and neuronal death in the hippocampus were improved compared to those in the group of whole body normothermia+CA. In addition, neurological deficit and neuronal death in the group of brain hypothermia/body normothermia+CA were was similar to those in the group of whole body normothermia+CA. In brief, only brain hypothermia during CA did not show effective survival rate, neurological function and neuronal protection compared to those under body (not brain) hypothermia during CA. Our present study suggests that regional temperature in patients during CA can significantly affect outcomes in survival rate and neurological recovery.

Keywords: Asphyxial cardiac arrest and cardiopulmonary resuscitation, Ischemia, Hypothermia, Survival rate, Neurological deficit, Delayed neuronal death

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P46

Bioinformatic analysis of long-range projectome from and to the posterior parietal cortex of the mouse

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The posterior parietal cortex (PPC) is a major multimodal association cortex implicated in a variety of higher-order cognitive functions, such as visuospatial perception, spatial attention, categorization, and decision-making. In corroboration with this notion, inactivation of the PPC both in human and in non-human primate lead to trouble in sensory integration and movement planning without significant deficits in sensory perception per se. As the evidence-related preparatory neural activity was reported in mouse PPC became an attractive model system to study how the neural correlates of evidence were brought about. However, in spite that many recent works have been performed with the mouse as a model system, systematic analysis of long-range connectivity of mouse PPC is still limited and prevents integrative interpretation of the rapidly accumulating functional data. In the present study, we provide quantitative long-range connectivity from- and to PPC by reanalyzing Allen brain connectivity map and consequently confirmed by neurotracers of both directions. Specifically, we conducted a detailed bioinformatic analysis to segregate input/output signal by cortical layers, sub-regions of the PPC, functional/anatomical modalities, or cell-types and experimentally confirmed the major connectivity so as to summarize the organizational principle of the mouse PPC. A comprehensive survey of the reciprocity, topography and bilateral connectivity between the PPC and cortical/subcortical brain areas will provide an important future reference to comprehend the function of the PPC and allow effective paths forward to various studies using mice as a model system. This work will provide a ground truth knowledge on the PPC based on the mouse connectivity data sets, leading to the identification of key input/output regions and organizing principles of the PPC.

Keywords: Cerebral cortex, Posterior parietal cortex, Bioinformatic analysis, Decision-making, Long-range connectivity

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P47

Interaction of high-order thalamic and top-down inputs on distal dendrites of layer 5 pyramidal neurons in somatosensory cortex

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Dendritic integration of motor and sensory inputs formulates a mixed response selectivity in the distal dendrites. However, wiring specificity to produce such feature selectivity is still far from complete understanding. We analyzed relative spatial distribution of representative sensory and motor inputs on distal tuft dendrites of layer 5 (L5) pyramidal neurons in the whisker field of somatosensory cortex (S1BF); paralemniscal inputs from posterior medial thalamic nucleus (POm) and motor inputs from primary motor cortex (M1). Axons both from POm and M1 ramify in layer 1 and make extensive synaptic contacts on distal dendrites of L5 neurons in S1BF. Without regenerative dendritic events, voltage changes occurred in these synapses are significantly diminished along the long dendritic path and subsequently contribute little to the generation of action potential. We hypothesized that synapses on the distal dendrites are wired to evoke an effective regenerative dendritic activity to overcome the passive attenuation. Using in vivo two-photon Ca2+ imaging, we found that indeed dendritic activity can be efficiently induced by electrical stimulation of POm or M1 in the overlapping set of dendritic branches. This result rejects the idea that exclusive origin selective dendritic tropism might account for the efficient dendritic spike generation. Furthermore, we found that coincident activation of POm inputs is suppressive on the M1-driven activity in the majority of the cases. Currently, we are examining the circuit mechanisms by which the high-order thalamic input and top-down input from M1 modulate distal dendritic activity in L5 pyramidal neuron of S1BF. This research was supported by KBRI basic research program through Korea Brain Research Institute funded by Ministry of Science and ICT (19-BR-04-01).

Keywords: Posterior medial thalamic nucleus (POm), Primary motor cortex (M1), Barrel cortex, Dendritic integration, In vivo two-photon Ca2+ imaging, high-order thalamic input, Top-down input

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High-frequency stimulation of cortico-subthalamic projections in the 6-hydroxydopamine model of Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative disorder accompanies clinical deficits in movement initiation and execution caused by the loss of dopaminergic neurons in the basal ganglia. The subthalamic nucleus (STN) is one of the primary input areas of basal ganglia circuitry and often serves as a target of deep brain stimulation for PD therapy. Although the exact mechanism of DBS remains unclear, optogenetic stimulation of motor cortical neurons projecting to STN, the hyper-direct pathway, has been reported to ameliorate the PD-like symptoms in the model mouse. In the present study, we analyze the circuit mechanism of this phenomenon. First we explored the electrophysiological features that can be used for the sign of the symptom from PD model mouse by unilateral nigrostriatal 6-hydroxydopamine (6-OHDA) lesioning. We found that the power of local field potentials (LFP) in both motor cortex (M1) and STN in the beta frequency (12-30 Hz) range and frequency of burst-like firing were significantly enhanced in the dopamine-depleted hemispheres, compared with non-lesioned hemispheres. The exaggerated oscillatory synchronization in the beta (12-30Hz) frequency band has been reported to be associated with the motor symptoms of PD patients. We then tested if high-frequency activity of STN-projecting neurons reduces the beta activity. We used a retrograde adeno associate virus to selectively express channelrhodopsin-2 in the STN-projecting neurons in mice made parkinsonian. We then applied 140 Hz consecutive optogenetic stimulation on the STN projecting neurons. We observed a significant reduction in the beta-band oscillation and the frequency of burst-like firing.
Our findings suggest that elucidation of synaptic properties during M1-STN stimulation could lead to better understanding of DBS mechanism modulating pathological patterns of synchronized oscillations, such as reduction of pathological beta activity in PD.

Keywords: 6-OHDA, Parkinson's disease, M1, STN

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High-definition transcranial direct current stimulation improves cognitive ability through the survival of dopaminergic cells in an animal model of attention-deficit hyperactivity disorder

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Attention-deficit hyperactivity disorder (ADHD) is a cognitive dysfunction characterized by hyperactivity, inattention, working memory deficits and impulsivity. The transcranial direct current stimulation (tDCS) provides to alter brain activity through depolarization of membrane potential in neurons and synaptic plasticity in neurological and psychiatric diseases. In this study, we confirmed the effects of anodal high-definition tDCS (HD-tDCS) improved cognitive behaviors via the survival of dopaminergic neurons caused by the activation of neurotrophic factors (NTFs) in the animal model of ADHD. The HD-tDCS treatment on the prefrontal cortex (PFC) or motor area (M1) (63.7μA/mm2, 20 mins) was progressed to 10 sessions for 2 weeks, and the cathodal was received to the back of the rats using a needle. Positive control for methylphenidate (MPH) was injected once a day for 2 weeks intraperitoneally (i.p). The HD-tDCS treatment alleviates cognitive impairment, such as spontaneous alternation, working memory, and spatial memory. The gene and protein levels of dopamine-related factors and NTFs were significantly changed in HD-tDCS treatment groups at PFC, striatum, hippocampus and substantia nigra/ventral tegmental area. The group of HD-tDCS treatment in PFC was significantly increased dopaminergic neurons (TH) and that significantly reduced the merge cells of TH and dopamine transporter (DAT) immunoreaction compared to sham and MPH groups in the all target region of the dopamine pathway. Activation of mature brain-derived

neurotrophic factor (mBDNF) expression and the merge cells of mBDNF and TrkB receptors were significantly induced in the HD-tDCS group compared to the sham and MPH group. Moreover, we confirmed the neurogenesis through NeuN and BrdU expressions that were significantly improved in the HD-tDCS group compared to the sham group in the hippocampus. These results suggest that HD-tDCS treatment in PFC improves activation of mBDNF and dopamine, which increases dopamine projection through the proliferation and differentiation of neurons. These effects induced cognitive ability and that was explored and provided new options for the clinical treatment of ADHD.

Keywords: Attention-deficit hyperactivity disorder, Anodal transcranial direct current stimulation, Methylphenidate, Dopamine, Neurotrophic factors, Neurogenesis.

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P50

An introduction to using a database of Allen Institute and applying machine learning

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Neuroscience has complex aspects that can be accessed at various levels. Among them, the cellular level approach is labor intensive and requires a significant level of skill. Therefore, there is a limit to the amount of data generated in a single lab, and the quality of data varies from lab to lab, making integrated analysis difficult. Recently, the Allen Institute for Brain Science (AIBS) uses standardized protocols to reveal data from mouse and human brains. This data is suitable for open science. This study introduces how to extract data from AIBS cell databases and use that data. Learn how you can manage and visualize your data in the Jupyter notebook to reproduce your experiment results. Learn how to process the extracted data and apply it to machine learning algorithms. For illustrative purposes, I used data from the electrophysiological recording to form a model that predicts the transgenic marker of recorded neurons. This study shows that you can use public databases to extract meaningful results. We could expect theoretical development of neuroscience to proceed through research using well-maintained open data.

Keywords: Public database, Allen Institute for Brain Science, Data science, Electrophysiology, Jupyter notebook, Python

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Inhibition of AIM2 inflammasome improves post-stroke cognitive impairment

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Stroke survivors follow disability and cognitive deficits. Post stroke cognitive impairment develops up to one third of stroke survivors. Many studies of physical disability were reported, while the post-stroke cognitive impairment (PSCI) and related risk factors are still lacking. Increased activity of inflammation in aging and neurodegenerative diseases plays a harmful role. We assumed that an increase in AIM2 inflammasome after ischemic stroke could lead to PSCI. Behavioral change of PSCI was observed through the elevated plus maze and Morris water maze using 45min MCAO mice model. The overproduction of AIM2 / caspase-1 and pro-inflammatory cytokines, interleukin 1β and 18 were evaluated in the dentate gyrus (DG) and cortex in the subacute phase (day 7) after MCAO. Gasdermin D (GSDMD)-mediated pyroptosis was increased, and neurons were decreased in DG and cortex, also. Interestingly, behavior of PSCI was improved by AIM2 KO mice and treatment of caspase-1 inhibitor (Ac-YVAD-CMK) after MCAO. This study suggests that activation of the AIM2 inflammasome which increases in the subacute phase after MCAO. Inflammasome-mediated pyroptosis and neuron death occurs in the DG and cortex. Based on this result, we propose that the increased of AIM2 inflammasome after stroke plays an important role inducing PSCI.

Keywords: Post-stroke cognitive impairment, Cognitive impairment, AIM2, Inflammasome, Caspase-1, Pyroptosis

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P52

Gintonin, a ginseng-derived ingredient, as a novel therapeutic strategy for Huntington's disease: Activation of the Nrf2 pathway through lysophosphatidic acid receptors

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Gintonin (GT), a ginseng-derived lysophosphatidic acid receptor ligand, regulates various cellular effects and represses inflammation. However, little is known about the potential value of GT regarding inflammation in the neurodegenerative diseases, such as Huntington's disease (HD). In this study, we investigated whether GT could ameliorate the neurological impairment and striatal toxicity in cellular or animal model of HD. Pre-, co-, and onset-treatment with GT (25, 50, or 100 mg/kg/day, p.o.) alleviated the severity of neurological impairment and lethality following 3-nitropropionic acid (3-NPA). Pretreatment with GT also attenuated mitochondrial dysfunction i.e. succinate dehydrogenase and MitoSOX activities, apoptosis, microglial activation, and mRNA expression of inflammatory mediators i.e. IL-1β, IL-6, TNF-α, COX-2, and iNOS in the striatum after 3-NPA-intoxication. Its action mechanism was associated with lysophosphatidic acid receptors (LPARs) and nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway activations and the inhibition of mitogen-activated protein kinases (MAPKs) and nuclear factor-κB (NF-κB) signaling pathways. These beneficial effects of GT were neutralized by pre-inhibiting LPARs with Ki16425 (a LPAR1/3 antagonist). Interestingly, GT reduced cell death and mutant huntingtin (HTT) aggregates in STHdh cells. It also mitigated neurological impairment in mice with adeno-associated viral (AAV) vector serotype DJ-mediated overexpression of N171-82Q-mutant HTT in the striatum. Taken together, our findings firstly suggested that GT has beneficial effects with a wide therapeutic time-window in 3-NPA-induced striatal toxicity by antioxidant and anti-inflammatory activities through LPA. In addition, GT exerts neuroprotective effects in STHdh cells and AAV vector-infected model of HD. Thus GT might be an innovative therapeutic candidate to treat HD-like syndromes. Brain Behav Immun. 2019 Aug;80:146-162. doi: 10.1016/j.bbi.2019.03.001.

Keywords: 3-Nitropropionic acid; Adeno-associated viral vector; Gintonin; Huntington's disease; Lysophosphatidic acid receptor; Nuclear factor erythroid 2-related factor 2

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P53

Synaptic Connectivity of Urinary bladder Afferentsin The Rat Superficial Dorsal Horn and Spinal Parasympathetic Nucleus

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That visceral sensory afferents are functionally distinct from their somatic analogues has been known for a long time but the detailed knowledge of their synaptic connections and neurotransmitters at the 1st relay nucleus in the spinal cord has been limited. To provide information on these topics, we investigated the synapses andneurotransmitters of identified afferents from the urinary bladder to the superficiallaminae of the rat spinal dorsal horn (DH) and the spinal parasympatheticnucleus (SPN) by tracing with horseradish peroxidase, quantitative electronmicroscopical analysis, and immunogold staining for GABA and glycine. In the DH, most bladder afferent boutons formed synapses with 1-2 postsynaptic dendrites, whereas in the SPN, close to a half of them formed synapses with 3-8 postsynapticdendrites. The number of postsynaptic dendrites

and dendritic spines per bladder afferent bouton, both measures of synaptic divergence and of potential for synaptic plasticity at a single bouton level, were significantly higher in the SPN than in the DH. Bladder afferent boutons frequently received inhibitory axoaxonic synapses from presynaptic endings in the DH but rarely in the SPN. The presynaptic endings were GABA- and/or glycine-immunopositive. The bouton volume, mitochondrial volume, and active zone area, all determinants of synaptic strength, of the bladder afferent boutons were positively correlated with the number of postsynaptic dendrites. These findings suggest that visceral sensory information conveyed via the urinary bladder afferents is processed differently in the DH than in the SPN, and differently from the way somatosensory information is processed in the spinal cord.

Keywords: Urinary bladder, Visceral afferent, Synaptic connectivity, Axoaxonic synapse, Spinal cord, Ultrastructure

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P54

Arginase 2 deficiency promotes neuroinflammation and pain behaviors following nerve injury in mice

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Microglia, the resident macrophages, act as the first and main form of active immune defense in the central nervous system. Arginase 2 (Arg2) is an enzyme involved in L-arginine metabolism and is expressed in macrophages and nervous tissue. In this study, we determined whether the absence of Arg2 plays beneficial or detrimental role in the neuroinflammatory process. We then investigated whether loss of Arg2 potentiated microglia activation and pain behaviors following nerve injury-induced neuropathic pain. A spinal nerve transection (SNT) experimental model was used to induce neuropathic pain in mice. As a result of peripheral nerve injury, SNT induced microgliosis and astrogliosis in the spinal cord, and upregulated inflammatory signals in both wild-type (WT) and Arg2 knockout (KO) mice. Notably, inflammation increased significantly in the Arg2 KO group compared to the WT group. We also observed more robust microgliosis and a lower pain threshold in the Arg2 KO group than those in the WT group. Furthermore, our data reveal higher upregulation of M1 pro-inflammatory cytokines, such as interleukin (IL)-1β, and higher downregulation of M2 anti-inflammatory cytokines, including IL4 and IL10, in Arg2 KO mice. Additionally, stronger formation of enzyme inducible nitric oxide synthase, oxidative stress, and decreased expression of CD206 were detected in the Arg2 KO group compared to the WT group. These results suggest that Arg2 deficiency contributes to inflammatory response. The reduction or loss of Arg2 results in stronger neuroinflammation in the spinal dorsal horn, followed by more severe pain behaviors following nerve injury-induced neuropathic pain.

Keywords: Macrophages, Microglia, Neuropathic pain, Neuroinflammation, Arginase 2

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P55

Diesel exhaust particles and urban particulate matters cause oxidative stress-induced death of oligodendrocytes

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Diesel exhaust is a major component of air pollution. The several evidences showed that exposure to air pollution can cause neuro-

inflammation and oxidative stress associated with the disorders in the central nervous system (CNS) including multiple sclerosis. Both oligodendrocyte precursor cells (OPCs) and mature myelinating oligodendrocytes (mOLs) are more susceptible to oxidative stress than any other cell types in the CNS. However, it is not clear whether particulate matters induce oxidative stress in OPCs and mOLs, and affectssurvival of these cells. In this study, we investigated the effects of various concentrations (2, 20, 200 ug/ml) of diesel exhaust particles (DEPs) and urban particulate matters (UPs) on viability measured by Hoechst staining and MTT assay, reactive oxygen species (ROS) generation by DCFH-DA and DHE assays and total antioxidant capacity (TAC) of OPCs, mOLs and astrocytes. In addition, we compared the effect of DEPs and UPs to that of hydrogen peroxide (100 uM/ml), a representative oxidative stress inducer. At 24 hours after exposure to DEPs and UPs, viability and TAC of three cells were decreased in concentration-dependent manner. However, viability and TAC of OPCs and mOLs were significantly lower than those of astrocytes, and those of OPCs were lowest. The amounts of ROS in three cells were increased in concentration-dependent manner of DEPs and UPs. However, the amounts of ROS in OPCs and mOLs was significantly higher than that of astrocytes, and that in OPCs was highest. Interestingly, viability, ROS generation and TAC of three cells in exposure of 200 ug/ml DEPs and UPs were very similar to those in exposure of 100 uM hydrogen peroxide. These results strongly suggest that DEPs and UPs induce oxidative stress-induced death of oligodendrocytes, especially OPCs and are involved in the demyelinating diseases including multiple sclerosis.

Keywords: Diesel exhaust particles, Urban particulate matters, Oligodendrocytes, Oxidative stress, Cell death

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Maternal separation in mice leads to anxiety-like/aggressive behavior and increases immunoreactivity for GAD67 and parvalbumin and GABA level in the adolescence ventral

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Many lines of evidence, including epidemiologic study from human beings and extensive experimental data from various mammalian species, indicate that early life events play a powerful role in influencing later behavioral and emotional responses to stressors. Although the mechanism how the early life stress alters the behavioral and emotional outcome remains unclear, the recent explanation for it is that adverse early life experience can change neural connectivity in the underlying brain networks. 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. 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 (resident-instruder test). To correlate MS behavioral changes with hippocampal changes, EPSc and IPSc were performed. As a result, there was no significant difference in EPSc, and MS was significantly higher in IPSc. To determine the relationship between hippocampal inhibition circuits, glutamic acid decarboxylase-67 (GAD67) and valbumin (PV) immunohistochemistry were performed. The ventral hippocampus was divided into 3 areas (dentate gyrus (DG), conus ammonis (CA) 3 and CA1 the areas were further segmented into 12 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, CA3, CA1. PV positive neurons were also outnumbered in the all layers of DG, CA3. However, there is no significant difference in CA1. As a result of analyzing amino acid in the dorsal hippocampus, Glutamine (GluNH2), glutamate (Glu) and g-ABA were significantly higher in MS group than HD group. 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. This work was partly supported by Institute for Information & communications Technology Promotion (IITP) grant funded by the Korea government (MSIP) (No. B0132151001000303, Next Imaging System XIS) and partly supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (NRF-2015R1D1A3A03020164)

Keywords: Maternal separation, Anxiety, Aggressive, Parvalbumin, Adolescent, Ventral hippocampus

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P57

Differential expression of vascular endothelial growth factor in the cortex and hippocampus upon cerebral hypoperfusion

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Vascular endothelial growth factor (VEGF) provide tolerance againstischemic brain injury. Yet, the pattern of VEGF expression in the neurogenic zonesafter chronic cerebral hypoperfusion has not been studied. Here we evaluated the immunoreactivity of VEGF in a rat model of chronic cerebral hypoperfusion.Chronic hypoperfusion was induced by bilateral common carotid artery ligation in the rats. Immunohistochemistry was performed against hypoxia-inducible factor-1α (HIF-1α) and VEGF on brain sections.The density of HIF1α-positive cells in the hypoxiagroup was increased in the cerebral cortex and hippocampus. Further, the density of VEGF-positive cells was significantly higher in the hypoxia group than in the control group in the cerebral cortex whereas it was similar in the control and hypoxia groups in the subventricular zone, and in the dentate gyrus in the hippocampus. The pattern of VEGF expression varies in different brain regions after chronic cerebral hypoperfusion.

Keywords: Angiogenesis, Bilateral common carotid artery occlusion, Vascular Dementia, Hypoxia, Neurogenesis

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P58

Calpain-2 as a treatment target in prenatal stress-induced epileptic spasms in infant rats

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Stress can induce a serious epileptic encephalopathy that occurs during early infancy. Recent studies have revealed that prenatal stress exposure is a risk factor for the development of infantile spasms. Our previous work demonstrates that prenatal stress with betamethasone-induced alterations to the expression of the K+/Cl– co-transporter (KCC2) in gamma-aminobutyric acid (GABA) interneurons lowers the seizure threshold in exposed animals. Here, we further investigated the mechanisms involved in this KCC2 dysfunction and explored possible treatment options. We stressed Sprague-Dawley rats prenatally and further treated dams with betamethasone on gestational day 15, which increases seizure susceptibility and NMDA (N-Methyl-D-aspartate)-triggered spasms on postnatal day 15. In this animal model, first, we evaluated baseline calpain activity. Second, we examined the cleavage and dephosphorylation of KCC2. Finally, we checked the effect of a calpain inhibitor on seizure occurrence. The phosphorylated-N-methyl-D-aspartate Receptor 2B (NR2B):non-phosphorylated NR2B ratio was found

to be higher in the cortex of the prenatally stressed beta-methasone model. We further found that the betamethasone model exhibited increased phosphorylation of calpain-2 and decreased phosphorylation of KCC2 and Glutamic acid decarboxylase 67 (GAD67). After using a calpain inhibitor in prenatal-stress rats, the seizure frequency decreased, while latency increased. GABAergic depolarization was further normalized in prenatal-stress rats treated with the calpain inhibitor. Our study suggests that calpain-dependent cleavage and dephosphorylation of KCC2 decreased the seizure threshold of rats under prenatal stress. Calpain-2 functions might, thus, be targeted in the future for the development of treatments for epileptic spasms.

Keywords: Epilepsy, Calpain, KCC2, NMDA, Glutamate decarboxylase 67, K+/Cl- co-transporter

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P59

Roles of Shank2, the causative gene of autism spectrum disorder, in cochlear development and function

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Auditory hair cells of the mammalian cochlea have a staircase arrangement of microvilli known as the stereocilia that are filled with actin filament on the apical surface. The stereociliary bundles of inner hair cells are relatively straight, whereas those of outer hair cells were V-shaped with a vertex pointing lateral direction. To form these unique structures, numerous proteins are confined to the restricted domains of the apical surface or the stereociliary bundles of hair cells. Mice harboring mutations in these proteins, such as USH1 proteins, have been shown to have fragmented and disorganized stereociliary bundles. However, the mechanisms of how hair cells form a V-shaped stereociliary bundles in developing cochlea and the effect of disorganized hair bundles on hearing function remain largely unknown. SHANK2 is a multidomain-scaffolding protein implicated in the structural and functional coordination of multiprotein complexes at excitatory postsynaptic density in the brain. Here, we show that Shank2-/- mice suffer from progressive hearing loss especially at mid-high frequencies and have disorganized hair bundles. To analyze the cause of the hearing loss in Shank2 mutant mice, we compared auditory phenotypes of Shank2 knockout (Shank2-/-) with inner ear-specific (Pax2-Cre; Shank2flox/flox) or hair cell-specific (Gfi1-Cre; Shank2flox/flox) conditional knockout mice. Hearing function was assessed by measuring the auditory brainstem response (ABR) threshold indicative of hearing sensitivity and the distortion product otoacoustic emission (DPOAE) threshold reflecting outer hair cell function as a cochlear amplifier. All three types of Shank2 mutants showed progressive hearing loss especially at mid-high frequencies. ABR and DPOAE thresholds were elevated to similar levels in these mutant mice. In addition, the severities of stereocilia bundle defects were also similar in all three types of Shank2 mutant mice. These results suggest that, unlike previously known roles, SHANK2 plays a crucial role in the organization of stereociliary bundles, and hearing loss in Shank2-deficient mice is mainly caused by disorganized stereocilia bundles.

Keywords: Hearing loss, Hair bundle disorganization, Shank2, Hair cell, Spiral ganglion neuron, Autism spectrum disorder

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Development of a risk scoring system for patients with papillary thyroid cancer

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As the importance of personalized therapeutics in aggressive papillary thyroid cancer (PTC) increases, accurate risk stratification is required. To develop a novel prognostic scoring system for patients with PTC (n = 455), we used mRNA expression and clinical data from TheCancer Genome Atlas. We performed variable selection using Network-Regularized high-dimensional Cox-regression with gene network from pathway databases. The risk score was calculated using a linear combination of regression coefficients and mRNA expressions. The risk score and clinical variables were assessed by several survival analyses. The risk score showed high discriminatory power for the prediction of event-free survival as well as the presence of metastasis. In multivariate analysis, the risk score and presence of metastasis were significant risk factors among the clinical variables that were examined together. In the current study, we developed a risk scoring system that will help to identify suitable therapeutic options for PTC.

Keywords: Network-regularized high dimensional cox regression, Papillary thyroid cancer, Pathway databases, Prognosis, TCGA

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P61

UNC13D : a novel biomarker candidate in pancreatic cancer

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UNC13D, Ca2+-dependent Rab binding protein, is known to control granule exocytosis in cytotoxic T lymphocytes and associated with granule maturation and fusion in cells. Mutations in UNC13D are associated with familial hemophagocytic lymphohistiocytosis, a genetically heterogeneous. However, its function related to cancers is rarely understood and its prognostic and diagnostic potential has not been evaluated in cancers. Pancreatic cancer(PC) is one of the deadliest cancers in the world and characterized by poor prognostic and low survival rate. It often spread to other organs such as liver or lung. Although some biomarkers including CA 19-9 have been developed, it is necessary to find new diagnostic, prognostic and therapeutic targets in PC. First, we assessed the prognostic potential of UNC13D in Pancreatic cancer using 4 independent cohorts (TCGA, ICGC, GSE21501, GSE28735). Kaplan-Meier survival analysis showed its overexpression was correlated with poor prognostic of pancreatic cancer with high discriminative ability in cohort studies. We examined the roles of UNC13D in the progress of PC. UNC13D knockdown using siRNA decreased migration rate in AsPC-1, Capan-1, Panc-1 and SNU213. Furthermore, ELISA result showed the release of TGFβ-1, TGFβ-2 and BMP4 in AsPC-1 and Capan-1 was reduced after UNC13D knockdown. These results suggest UNC13D might regulate the migration in pancreatic cancer cells by regulation the release of migration-regulation factors. More studies need to be performed to reveal underlying mechanism of UNC13D.

Keywords: UNC13D, Pancreatic cancer, Exocytosis, TGF beta, BMP4, Migration, Biomarker

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Roles of LTBP1 in The Progression of Solid Cancers

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Latent-transforming growth factor beta-binding protein 1(LTBP1) regulates the secretion and activation of TGF-beta family as a carrier protein. TGF-beta molecules are attracting therapeutic targets in various cancers, because they have been associated with metastasis and migration of cancer cells. Although LTBP1 has been shown to be overexpressed in glioblastoma and ovarian cancer, roles of LTBP1 were poorly characterized in cancer. To find out clinical significance of LTBP1, we extracted the patient data from the TCGA and performed the Kaplan Meier survival analysis. We found the prognostic significance of LTBP1 in various kind of cancers including gastric, breast, liver and pancreatic cancers. To examine the roles of LTBP1

in the progression of solid cancers, we knock-downed LTBP1 using siRNA. Knock down of LTBP1 decreased the proliferation and migration rate of gastric, liver, breast and pancreatic cancer cells. To reveal underlying mechanisms of LTBP1, we examined the secretion of TGFB1, TGFB2, BMP4 using ELISA. The secretion of those EMT-promoting factors was significantly reduced by LTBP1 siRNA. These results suggest LTBP1 can be used as an important prognostic marker in various solid cancers. Further studies are required to identify underlying mechanisms in detail.

Keywords: LTBP1, TGFB, Solid cancer, Mechanisms of LTBP1, Prognostic marker

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Effects of SHIP1 on adipose tissue inflammation and apoptosis in obese mice

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Obesity-induced adipose tissue apoptosis promotes inflammation and insulin resistance. Many factors on apoptosis and inflammation has been previously assessed. According to previous studies, SH2-containing inositol5'-phosphatase-1 (SHIP1) is known to be a key factor of apoptosis and inflammation. However, the role of SHIP1 on adipose tissue apoptosis and inflammation is unclear. We investigated the effects of SHIP1 on inflammation and apoptosis in the epididymal white adipose tissue (WAT) of which wild type (WT) and leptin-deficiency (ob/ob) mice were fed either a normal diet or high-fat diet. The NGS-based RNA-seq analysis showed significant geneexpression alterations related to lipogenesis, apoptosis, and inflammation in obese mice. We performed qRT-PCR to technically validate differential expressed genes. Moreover, western blot analysis showed that SHIP1 in the epididymal WAT of obese model was increased. Immunofluorescence analysis showed that Ly6g (neutrophil marker) or CD11b positive cell (macrophage marker) was localized with SHIP1. In addition, TUNNEL assay showed that SHIP1-positive macrophages were colocalized with apoptotic cells. These findings suggest SHIP1 may be key factor on adipose tissue apoptosis and inflammation in low-grade chronic inflammation.

Keywords: SHIP1, Macrophage, Apoptosis, Inflammation, Obesity

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Activation of orphan G-protein coupled receptor–X (GPR-X) provides neuroprotection against ischemic brain damage

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Stroke is classified as one of the main causes of serious and long-term disability, affecting an estimated 15 million people each year. The only FDA-approved treatment for ischemic stroke is tissue plasminogen activator (tPA), which has a time limit that must be treated within 4.5 hours after occlusion. G-protein coupled receptors (GPCRs) are the most widely expressed proteins responsible for physiological functions. GPR-X is an orphan GPCR that is highly expressed in the striatal medium spiny neurons, and the deletion of GPR-X decreases anxiety-like behavior, increases social interaction and locomotor activity, and impairs motor coordination and motor learning. In this study, we found the reduction of GPR-X expression in focal cerebral ischemic mouse model using western blot and qPCR. In addition, we observed that the expression of GPR-X was high in HT22 neuronal cells among three cell types derived from brain; brain microvascular endothelial cells, microglial cells and neuronal cells, and GPR-X expression was downregulated in HT22 cells under oxygen glucose deprivation (OGD) conditions.

Moreover, injection of GPR-X agonist (10 mg/kg) 30 minutes before ischemic occlusion reduced the cerebral infarction size and restored motor dysfunction. These results suggest that GPR-X is a potential new target for the treatment of CNS diseases including ischemic stroke.

Keywords: Stroke, Cerebral ischemia, GPCR, OGD, HT22

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Establishing patient-derived glioma tumoroid for therapeutic validation

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Glioma is the most lethal and devastating cancer. Their study is limited by the incompleteness of available in vitro models. In this study, we describe a three-dimensional culture system that depends on extracellular matrix providing the required scaffold to support cell attachment and growth, which supports formation of tumoroids derived directly from glioma specimens. Using this model, we performed immunohistochemical reactions for typical glioma markers to analyze if organoids maintain similar characteristics in culture as the tumors they were derived from. In addition, we treated the organoid lines with conventional chemotherapeutic, temozolomide, routinely used in glioma treatment to investigate if glioma tumoroid reflect this divergent response. Our results show potential for the use of organoids as a platform to test human cancer phenotypes that recapitulate key aspects of drug response.

Keywords: Glioma, Tumoroid, Organoid, Temozolomide, Personalized therapy

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Glioblastoma management with platinum-based nanoparticles

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Glioblastoma (GBM), called the most aggressive brain tumor, is represent a grade IV of gliomas that originates in the glial cell of brain [1]. GBM commonly aggressive and serious in older adults, and patients have a clinical surgery to remove the GBM sites with chemo-/radiation-therapy. However, desite of technological advances such as surgical techniques and therapy, the GBM fairly often recur within the site where was excised. Thus, it is important to develop the material which has (i) non toxicity for normal region, (ii) inhibition of recurrence for GBM, and (iii) increased drug sensitivity to overcome drug resistance. Herein, we developed a new nanomaterial that is consist of biocompatible six generation polyamidoamine (PAMAM) dendrimer (G6-NH2 DENs) and platinum nanoparticles, named G6-NH2 DENs (G6 NH2 Pt (200) DENs) [2]. The G6-NH2 DENs showed non-toxicity, recurrence inhibition of GBM, and increment of drug sensitivity. To confirm these abilities, first, we characterized the structure of G6-NH2 Pt (200) DENs by the transmission electron microscopy (TEM) and dynamic light scattering (DLS). Second, we analyzed the cellular ability of G6-NH2 Pt (200) DENs such as cellular uptake, co-localization, migration, invasion, and F-actin staining. Third, we checked the epithelial to mesenchymal transition (EMT) related mRNA expression. Finally, we confirmed the increased drug-sensitivity after treatment of G6-NH2 Pt (200) DENs in drug-resistant GBM cell lines. Overall, we conclude that G6-NH2 Pt (200) DENs can be rising up in clinical application for the GBM therapy, drug delivery, and increment of drug sensitivity in drug-resistant cell lines. We expect our novel materials and new approaches initiate further various applications in biomedical field.

Keywords: Glioblastoma, Dendrimer, Platinum nanoparticle, EMT, Drug-resistance

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Anti-cancer effects of multimineral treatment on non-small cell lung cancer cells

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Lung cancer is frequently diagnosed cancer and the leading cause of death in the world. There are two types of lung cancer, non-small cell lung cancer (NSCLC, 85% of patients) and small cell lung cancer (SCLC, 15% of patients). The most common treatments for lung cancer include surgery, radiation, and chemotherapy. However, many side effects and drug resistance are showing a bad prognosis. Therefore, it is necessary to find a new treatment for the lung cancer. Multimineral compound (K1) is composed of various minerals including sulfur, aluminum and iron. In previous studies, sulfur has been known to have anticancer effects and induce apoptosis in NSCLC. Aluminum is also known to promote inflammation and apoptosis in neuroblastoma cells. In the case of iron, many complexes are known that have anticancer effects. Moreover, iron complexes are known to inhibit glioblastoma growth and induce apoptosis. Based on the anticancer effects of these various minerals, the anticancer effects of K1 were evaluated in this study. The present study, NSCLC cell lines were treated with K1. As a result, K1 inhibits cell proliferation, induces cell cycle arrest and apoptosis. Furthermore, changes in protein markers associated with cell cycle and apoptosis were identified. These results suggest that K1 could be a new treatment for patients with lung cancer.

Keywords: Non-small cell lung cancer, Multi mineral, Cell proliferation, Cell cycle, Apoptosis

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Decreased phosphorylation of ERK against cell death in 5-fluorouracil resistant colon cancer cells

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We previously demonstrated that yeast extract had anti-tumor effects via activating p38 signal pathway in colon cancer cells, SNU-C5 and 5-fluorouracil resistant SNU-C5 (SNU-C5/5-FUR). But, SNU-C5/5-FUR showed lower rate of apoptosis compared with SNU-C5. Therefore we investigated the possible resistance mechanism of SNU-C5/5-FUR through autophagy related pathways. As a result, SNU-C5/5-FUR showed reduced autophagy after yeast extract treatment via lower level of Atg7 compared with SNU-C5. As the phosphorylation of ERK was differentially regulated after yeast extract treatment, ERK-RSK pathway was also examined. ABCG2 and p90RSK significantly increased in both colon cancer cells after yeast extract treatment: the changes of p90RSK was significant in SNU-C5/5-FUR. The nature of both colon cancer cells was further examined: SNU-C5/5-FUR had higher level of ABCG2, lower level of p90RSK, and lower phosphorylation of ERK when compared with SNU-C5. Taken together, SNU-C5/5-FUR might show the resistance against cell death by decreased phosphorylation of ERK related signaling pathway.

Keywords: ERK, RSK, ABCG2, Resistance, 5-Fluorouracil, Colon cancer

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Chitosan oligosac charide shows anti-proliferative effects on SNU-C5 colorectal cancer cells via activating ERK

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Chitosan oligosaccharide (chitooligosaccharide, COS) is the major degradation product of chitosan via enzymatic degradation involving deacetylation and depolymerization processes. Previous studes have revealed that COS has various promising biomedical implications with complete water solubility, which endowed it with significant biological properties like anti-oxidant, anti-inflammatory, anti-diabetic, and anti-cancer effects. We investigated the anti-tumor effects of COS on colorectal cance since there is a lack of effective therapeutic methods with low side effects. COS was obtained from low molecular weight chitosan by the enzymatic method and the effects were measured by MTT assay, FACScan analysis, and Western blotting. COS suppressed the growth of SNU-C5 compared with HCT116, HT29, and 5-fluorouracil (5-FU) resistant SNU-C5 (SNU-C5/5-FUR), and further inhibited it with the existence of 5-FU. Cell death was not affected with COS, but cell cycle was arrested at G0/G1 phase, which was confimred by the increased level of p21, and the increased activities of anti-oxidant enzymes including catalase, CuZnSOD, and MnSOD. COS increased phosphorylation of ERK with or without 5-FU while 5-FU treatment increassed phosphorylation of p53. Taken together, COS-induced anti-tumor effects were related with cell cycle arrest which might be mediated by activation of ERK.

Keywords: Chitosan oligosaccharide, Colorectal cancer, Cell cycle arrest, ERK, 5-fluorouracil

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HOXB5 regulates tamoxifen resistance in breast cancer cells and promotes tumor aggression and cancer stem-like activity

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Most ER-positive breast cancer patients are treated effectively with tamoxifen; however, long-term treatment ultimately results in the development of resistance in one-thirds of the patients. Although many explanations for acquired tamoxifen resistance such as HOX dysregulation have been put forward, there is yet a clearly defined underlying mechanism. Here, we show evidence of up-regulated HOXB5 gene expression in tamoxifen-resistant MCF7 (TAMR) cells compared to MCF7 cells, thus representing a potential oncogenic and resistance marker. We demonstrate that HOXB5 up-regulation is associated with EGFR signaling pathway activation and enhanced cancer stem cell formation ability. Functional studies revealed that the activated EGFR signaling cascade and the resultant migratory and invasive phenotypes, and importantly, tamoxifen resistance could be reversed with HOXB5 depletion in TAMR cells. Moreover, increased HOXB5 levels also increased expression of stem cell markers such as OCT4 and NANOG in TAMR cells, contributing to their competence in forming mammospheres and growing in anchorage-independent conditions. Gain of HOXB5 in MCF7 cells enabled expansion of cancer stem cell population and growth in suspended state. Taken together, our study suggests an important role of HOXB5 in drug resistance and tumor aggression, and establishes HOXB5 as a promoter of stemness in tamoxifen-resistant breast cancer cells.

Keywords: Breast cancer, Endocrine resistance, HOXB5, EGFR, Cancer stem cell

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LMP2A overexpression is effect of BART17-5p and Prdx1 expressions in NPC cell line C666-1 and HK1 cells

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BACKGROUND: Latent membrane protein 2A (LMP2A) is proteins of the Epstein-Barr virus and these proteins are abundant in NPC cell line, especially C666-1. In Nasopharyngeal carcinoma (NPC), BART miRNAs have been demonstrated, but BART17 is still unclear. Peroxiredoxin 1 (Prdx1) is an antioxidant enzyme and is highly susceptible to oxidative stress. METHODS: To study the roles of BART17-5p and Prdx1 in NPC C666-1 and HK1 cells overexpressed LMP2A, it is transfected to DNA of LMP2A and EBNA1 and then it is measured using RT-PCR for RNA level and western blot for protein level. Moreover, it is compared to the expression of NF-κB in cytosol and nuclear which LMP2A and BART17-5p are overexpressed. To investigate the mechanism of LMP2A, BART17 and Prdx1, it is transfected to siRNA of these genes. RESULTS: The expression of Prdx1 on LMP2A overexpressed C666-1 and HK1 cells are increased. Moreover, the level of Prdx1 expression is reduced by knockdown of BART17 and LMP2A. CONCLUSION: These data suggested that LMP2A is mediated via BART17 and Prdx1 activation.

Keywords: Nasopharyngeal carcinoma, Epstein-Barr virus, MicroRNA, BART17-5, Prdx1

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P72

Xenogeneic immunogenicity of human mesenchymal stem cells in mice

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Mesenchymal stem cells (MSCs) are spotlighted as cell therapeutic agents in regenerative medicine because they can differentiate into several types of cells. For the development of MSCs therapeutics, many animal studies using human MSCs have been performed, and valuable information has been derived from them. However, most of these studies tend to overlook the effects of xenogeneic immune responses on the study results, because these cells are dogmatically mentioned to be immunosuppressive. However, most of the application sites of MSCs in animal disease models are prone to be in an inflammatory environment, where MSCs can activate by pro-inflammatory cytokines, and are provoked to express HLA-DR. This study was performed to evaluate host immune response against exogenously given MSCs. Human adipose tissue-derived MSC and umbilical cord-derived MSC, whether naïve or activated, were injected to Balb/c and C57BL/6 mice twice with a 3-week interval. The mice were sacrificed 10 days after the second injection, and the xenogeneic immune responses were evaluated by immunoglobulin (Ig) titration in the serum, FACS profiling of splenic T cells, germinal center staining in the spleen, and staining of MSCs with immune sera. In Balb/c mice, MSC-injected groups showed significant increases of serum Ig titers, GL7+ germinal center cells, CD62L+ CD44+ memory cells of both CD4 and CD8 T cells, and the formation of germinal centers, compared to the control group. Contrarily, these were not observed in C57BL/6 mice. However, when we stained MSCs with the sera from the MSC-immunized mice, cells were strongly stained, indicating that specific antibodies against injected MSCs had been produced even in C57BL/6 mice, in spite of the absence of phenotypic findings mentioned above. Our results show that human MSCs, even though they are known to be immunosuppressive across species, induced apparent immune responses in both strains of mice, even though phenotypes accompanying the immune response were different in different strains of mice. Attention should be paid in interpreting the results from animal experiments using human MSCs. 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: Human mesenchymal stem cell, Adipose-derived mesenchymal stem cells, Umbilical cord-derived mesenchymal cells, Allogeneic immune response, Xenogeneic immune response

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P73

Clinicopathological and prognostic characteristics of RAD51 in colorectal cancer

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RAD51 plays a central role in the repair of DNA doublestrand breaks performed by homologous recombination. In our study, we analyzed the RAD51 mRNA expression level in CRCs, also evaluated the clinicopathological and prognostic characteristic of the RAD51. We investigated the impact of RAD51 mRNA expression on all 48 cases of CRC. We confirmed that the RAD51 mRNA expression of tumor tissues as compared with that observed in paired adjacent nontumor tissue was upregulated by 2.5 fold. And RAD51 mRNA expression was significantly associated with T stage ($p = 0.027$). According to higher T stage, RAD51 mRNA expression has shown a tendency to increase. We next assessed survival to determine the prognostic significance of RAD51 in CRC. RAD 51 expression was not associated with overall survival ($p = 0.408$) and disease free survival ($p= 0.601$) in CRC. In addition, TCGA big data analysis showed no prognostic value of RAD51 expression in colon and rectal cancers. Our current work suggests that Rad51 may serve as a valuable candidate for developing novel therapies in CRC.

Keywords: RAD51, Colorectal cancer (CRC), TCGA, Prognostic value, Clinicopathological characteristic

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UHRF1-mediated DNA methylation on TXNIP promoter induces carcinogenesis in cervical cancer

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DNA methylation of tumor suppressor genes (TSGs) is considered to be the important epigenetic modulation in the development of cancer. Human oncoviruses including human papillomavirus (HPV) upregulate and augment DNA methyltransferase (DNMT) and histone deacetylase (HDAC) activities which down-regulate TSG expression. UHRF1 (Ubiquitin-like containing PHD and Ring finger domain 1) is an epigenetic regulator in DNA methylation and is overexpressed in cervical cancer which is caused by HPV. To find TSGs regulated by UHRF1in cervical cancer, UHRF1-knockdown cervical cancer HeLa cells were constructed using lenti viral sh-UHRF1 transfections. TXNIP (thioredoxin-interacting protein) known as a TSG was selected by cDNA using microarray method between UHRF1 knockdown and control HeLa cells. Upregulation of UHRF1 expression and decreased expression of TXNIP were found in cervical cancer by western blot and immunohistochemistry. And these expression patterns were confirmed by Illumine infinium Methylation EPIC method and oncomine database analysis in cervical cancer. Chromatin immunoprecipitation assay showed that UHRF1 binding site in TXNIP promoter region was located at position between -780~ -490 which contains inverted CCAAT domain. Then, we found that UHRF1-knockdown inhibits UHRF1 binding to TXNIP promoter and enhanced the TXNIP expression through demethylation of this promoter region. Methylation of CpG site in promoter region of TXNIP was confirmed by pyrosequencing and methylation specific PCR in human cervical cancer. We also found that down-regulation of UHRF1 by siRNA or UHRF1 antagonist, thymoquinone, induced cell cycle arrest and apoptosis. Furthermore, ubiquitin-specific protease 7 (USP7), which is known to stabilize and enhance the function of UHRF1, was increased by HPV viral protein E6/E7. In conclusion, HPV E6/E7-induced carcinogenesis through TXNIP promoter methylation by UHRF1 and demethylation of TXNIP could be a good therapeutic strategy in cervical cancer.

Keywords: Epigenetic modulator, UHRF1, TXNIP, DNA methylation, Cervical cancer

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P75

Gelsolin is epigenetically silenced by UHRF1 in cervical cancer and in E6/E7 transformed HaCaT cells

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Human papillomavirus (HPV) infection is prevalent in cervical cancer. UHRF1(Ubiquitin-like containing PHD and Ring finger domain 1), an epigenetic regulator, is overexpressed in cervical cancer. UHRF1 plays a role in DNA methylation and histone modification and induced silencing of Tumor suppressor genes (TSGs) in tumorigenesis. Gelsolin plays a major role in many physiological processes and changes in gelsolin levels are observed in several diseases including cancer. Of note, gelsolin was down-expressed in cervical cancer tissues compared to normal cervix shown by western blot analysis and immunohistochemistry. 5-Aza2′-deoxycytidine, DNA-hypomethylating agent, treatment enhanced gelsolin expression in E6/E7 transformed HaCaT cells (HEK001). UHRF1 knockdown using si-RNA and thymoquinone (UHRF1 antagonist) increased level of gelsolin and induced cell cycle arrest and apoptosis through the up-regulation of gelsolin in HEK001 cells. These results showed that upregulation of UHRF1 by HPV E6/E7 is caused gelsolin silencing in cervical cancer and cervical cancer cells, suggesting that gelsolin could be a therapeutic target in cervical cancer.

Keywords: Epigenetic,Gelsolin,UHRF1,Cervical cancer, Humam-papiloma virus

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High-intensity ladder-climbing resistance exercise suppresses exacerbation of dermatitis in mice

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Generally, exercise promotes health and inhibits diseases. However, exercise and sweating are the main worsening aspect for the patient with atopic dermatitis (AD). This study was examined the effect of high-intensity ladder-climbing resistance exercise (LREX) on Dermatophagoides farinae extract (DFE; house dust mite extract) and 2,4-dinitrochlorobenzene (DNCB)-induced AD-like skin lesions in BALB/c mice. After 4 weeks of LREX, histopathological examination revealed reduced epidermis/dermis and dermal infiltration of inflammatory cells in the mice ears. In addition, LREX suppressed serum immunoglobulin (Ig) levels and mRNA expression of pathogenic cytokines in the ear tissue and reduced the size, weight of draining lymph node (dLN) and non-dLN (ndLN), and the pathogenic cytokine-related mRNA expression of CD4+T cells from dLNs and ndLNs. In all, we observed a negative correlation between LREX and AD symptoms in mice. This results suggests that positive prospects of high-intensity exercise for patients with AD.

Keywords: Atopic dermatitis, Draining lymph node, Ear thickness, Ladder climbing, Resistance exercise

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P77

Identification of prognostic mRNAs in metastatic cutaneous melanoma

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Cutaneous melanoma is the most common cause of skin cancer related deathsworldwide. There is urgent need for identification of prognostic biomarkers tosupport decision making process in metastatic cutaneous melanoma. Recently,microarray and RNA-seq technology have improved or even changed currentprognostic and therapeutic strategies of several cancers. However, according tocurrent melanoma staging system, prognosis is almost entirely dependent on theclinicopathological features. To identify novel prognostic biomarkers, weinvestigated whole gene expression level and clinical data of patients withcutaneous melanoma from 3 cohorts of The Cancer Genome Atlas and GeneExpression Omnibus. Kaplan–Meier survival analysis using median values of eachgene as cutoff value revealed that 9 genes (ABCC3, CAPS2, CCR6, CDCA8, CLU,DPF1, PTK2B, SATB1, SYNE1) were statistically significant prognostic biomarkers ofmetastatic cutaneous melanoma in all 3 independent cohorts. Low expression of2 genes (CDCA8, DPF1), and high expression of 7 genes (ABCC3, CAPS2, CCR6, CLU,PTK2B, SATB1, SYNE), were significantly associated with good prognosis inmetastatic cutaneous melanoma. Taken together, we suggest 9 novel prognosticbiomarkers for cutaneous metastatic melanoma.

Keywords: Melanoma, Metastatic cutaneous melanoma, Prognostic, Marker, Survival analysis, TCGA,

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Antagonistic Interactions Between Osterix and Pyrophosphate During Cementum Formation

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During cementum formation, the key roles of osterix (Osx) and inorganic pyrophosphate (PPi), mainly controlled by nucleotide pyrophosphatase 1 (Npp1; encoded by the Enpp1 gene) and progressive ankylosis protein (Ank), have been demonstrated by animal models displaying altered cementum formation. In this study, we analyzed the relationship of Osx and local PPi during cementum formation using compound mutant mice with their wildtype and corresponding single gene mutants. Importantly, functional defects in PPi regulation led to the induction of Osx expression at the cervical cementum as demonstrated by Enpp1 mutant mice and cementoblasts with the retroviral transduction of small hairpin RNA for Enpp1 or Ank. Conversely, cementoblasts exposed to inorganic PPi or with the enforced expression of Enpp1 or Ank reduced Osx expression in a concentration dependent manner. Furthermore, the loss of Osx induced the higher expression of Npp1 and Ank at the apical region of the developing tooth root as observed in Osx-deficient mice. The activity of PPi-generating ectoenzymes (nucleoside triphosphate pyrophosphohydrolase, NTPPPHase) and the level of extracellular PPi were significantly increased in Osx-knockdown cementoblasts. However, the formation of ectopic cervical cementum was not completely diminished by inactivation of Osx in Enpp1 mutant mice. In addition, fibroblast growth factor (FGF) receptor 1 (Fgfr1) was strongly localized in cementoblasts lining the acellular cementum and involved in the inhibitory regulation of matrix accumulation and further mineralization by supporting PPi production. Taken together, these results suggest that local PPi suppresses matrix accumulation and further mineralization through an antagonistic interaction with Osx under the synergistic influence ofFGF signaling during cementum formation.

Keywords: Cementogenesis, Cementum, Tooth, Pyrophosphate, Osterix, FGF

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Hedgehog Signaling Is A Negative Regulator For Cementum Apposition

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Hedgehog (Hh) signaling plays a broad role in development of many organs that arise as a result of interactions between the epithelium and underlying mesenchyme, including tooth. It is noted that sustained Hh activity in osteoblasts put a negative regulation for postnatal bone development in mice. Here, to define the roles

of Hh signaling in cementum formation, we analyzed two kinds of transgenic mouse models for Hh signaling activation, which were designed by an inactivation of Suppressor of Fused (Sufu), a negative regulator of Hh signaling, (SufuOC) and a forced endogenous activation of Smo (SmoM2OC) under the control of osteocalcin (OC) promoter-driven Cre recombinase, respectively. Interestingly, cellular cementum apposition was remarkably reduced in both mutants. Consistently, matrix formation and mineralization ability was down-regulated in OCCM-30, a cementoblast cell line, following treatment with a pharmaceutical Smo agonist. In addition, reduction of Osx expression and β-catenin activity, which are critical for cellular cementum formation, were also detected in vitro. Furthermore, double mutation mice designed for stabilization of β-catenin with both Hh-Smo signaling activation in cementoblasts revealed a complete restoration of defective cellular cementum. Besides, Wnt antagonist such as Sostdc1 and Dkk1 were also induced by Smo activation and have a role to reduce Osx expression and β-catenin activity. Collectively, our data demonstrate that Hh signaling negatively regulates cementum apposition in a Wnt/β-catenin/Osx-dependent manner.

Keywords: Cementogenesis, Cementum, Tooth, Hedgehog, Sufu

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P80

HSP70 binds phosphorylated HDAC2 for cardiac hypertrophy

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Previously, we reported that phosphorylation of histone deacetylase 2 (HDAC2) and the resulting activation causes cardiac hypertrophy. Through further study of the specific binding partners of phosphorylated HDAC2 and their mechanism of regulation, we can better understand how cardiac hypertrophy develops. Thus, in the present study, we aimed to elucidate the function of one such binding partner, heat shock protein 70 (HSP70). Primary cultures of rat neonatal ventricular cardiomyocytes and H9c2 cardiomyoblasts were used for in vitro cellular experiments. HSP70 knockout (KO) mice and transgenic (Tg) mice that overexpress HSP70 in the heart were used for in vivo analysis. Peptide-precipitation and immunoprecipitation assay revealed that HSP70 preferentially binds to phosphorylated HDAC2 S394. Forced expression of HSP70 increased phosphorylation of HDAC2 S394 and its activation, but not that of S422/424, whereas knocking down of HSP70 reduced it. However, HSP70 failed to phosphorylate HDAC2 in the cell-free condition. Phosphorylation of HDAC2 S394 by casein kinase 2a1 enhanced the binding of HSP70 to HDAC2, whereas dephosphorylation induced by the catalytic subunit of protein phosphatase 2A (PP2CA) had the opposite effect. HSP70 prevented HDAC2 dephosphorylation by reducing the binding of HDAC2 to PP2CA. HSP70 KO mouse hearts failed to phosphorylate S394 HDAC2 in response to isoproterenol infusion, whereas Tg overexpression of HSP70 increased the phosphorylation and activation of HDAC2. 2-Phenylethynesulfonamide (PES), an HSP70 inhibitor, attenuated cardiac hypertrophy induced either by phenylephrine in neonatal ventricular cardiomyocytes or by aortic banding in mice. PES reduced HDAC2 S394 phosphorylation and its activation by interfering with the binding of HSP70 to HDAC2. These results demonstrate that HSP70 specifically binds to S394-phosphorylated HDAC2 and maintains its phosphorylation status, which results in HDAC2 activation and the development of cardiac hypertrophy. Inhibition of HSP70 has possible application as a therapeutic.

Keywords: HDAC2, HSP70, Hypertrophy, Phosphorylation

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P81

Differential role of primary cilia in cochlear development and hearing establishment

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Dysfunction of primary cilia can cause a range of congenital diseases collectively called ciliopathies, and both biological and clinical studies were performed to elucidate its etiologies. To better understand the hearing loss in ciliopathies and the role of primary cilia in the organ of Corti, three different categories of the ciliary mutant were analyzed for their phenotypes and function in cochlear development. Previously studied inner ear specific Ift88 cKO mouse showed obvious PCP defect of hair cells but the other ciliary mutants including Ick KO and bromi showed only mildly affected PCP in the restrictive region. Rather, well known Shh associated cochlear phenotypes including shorted cochlear duct, reduced hair cell number, premature hair cell differentiation, reversed hair cell differentiation wave and ectopic vestibule like hair cells were found in ciliary mutants. Consistent with that, Shh signaling, the key signaling of developing inner ear was significantly affected in all 3 categories of ciliary mutants with the reduced number of cilia and affected regional identity which is later important for the tonotopic organization before the stage of hair cell differentiation. In a further investigation on hearing function, we could find that auditory dysfunction was more severe in low frequencies in the inner ear specific Ick cKO consistent with the previous reports(Okamoto et al.2017). Our data suggest a new explanation for ciliary phenotypes in mouse cochlear duct and hearing function in the aspect of affected SHH signaling, further implicating the clues on subclinical hearing defects observed in human ciliopathies with affected Shh signaling.

Keywords: Primary cilia, Ciliopathy, Hearing loss, SHH signaling, Cochlear development, Auditory hair cell

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In vivo study of mouse skin pattern development

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Hair follicle is the dynamic mini-organ. Hair Follicles undergo continuous and repetitive cycling between the phases of active growth (anagen), regression (catagen), and relative "quiescence" (telogen). Many authors reported the hair cycle stage in various strains of mouse. Although there is not sufficient knowledge about the hair follicle biology. We studied the skin pattern in C57BL/6 wild type mouse in different time scale. We divided the mouse into two groups; early stage (P0-P65) and late stage (P365 or higher). In this study, we sacrificed the C57BL/6 mouse according to the postnatal date. The skin was observed under microscope and later we performed the histology to confirm the hair stages. We also measured the hair length of different domains of same mouse. Our result showed the skin pattern of mice are variable between mice. The hair growth rate as well as hair length also different in 1st and 2nd hair cycle. There are different factors which directly or indirectly affects the hair follicle biology. Further we need to focus on it. Strategies and concepts of this work will be helpful for future researchers to elaborate the mouse skin biology. Hair follicle is the dynamic mini-organ. Hair Follicles undergo continuous and repetitive cycling between the phases of active growth (anagen), regression (catagen), and relative "quiescence" (telogen). Many authors reported the hair cycle stage in various strains of mouse. Although there is not sufficient knowledge about the hair follicle biology. We studied the skin pattern in C57BL/6 wild type mouse in different time scale. We divided the mouse into two groups; early stage (P0-P65) and late stage (P365 or higher). In this study, we sacrificed the C57BL/6 mouse according to the postnatal date. The skin was observed under microscope and later we performed the histology to confirm the hair stages. We also measured the hair length of different domains of same mouse. Our result showed the skin pattern of mice are variable between mice. The hair growth rate as well as hair length also different in 1st and 2nd hair cycle. There are different factors which directly or indirectly affects the hair follicle biology. Further we need to focus on it. Strategies and concepts of this work will be helpful for future researchers to elaborate the mouse skin biology.

Keywords: Development, Hair cycle, Hair Follicle, Skin biology

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Signature genes in macrodactyly through transcriptome network analysis reveal their association of lipid metabolism

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Macrodactyly is one of the most difficult hand anomalies to treat not only surgically but medically as well. Little is known about the molecular pathways and lipid metabolism of this disease. To elucidate the potential mechanism of macrodactyly progress, we used the bioinformatical analysis including quantile normalization, principal component analysis, heatmap and volcano plot. For the functional bioinformatical study, lipid, lipoprotein and phospholipid metabolism of Kyoto Encyclopedia of Genes and Genomes, Wiki Pathways, and Reactome Pathway were utilized to compare the differentially expressed genes in macrodactyly with control group. We found up-regulation of CDK6 and E2F1, which are associated with the mitotic cell cycle of cancer cells. PIK3CG, associated with cancer and lipid metabolism, was also enriched in macrodactyly. In down-regulated genes, PTEN was highlighted in lipid metabolism, phosphatidylinositol signaling system and insulin signaling. ABCD3, related in peroxisomal import of fatty acids, was also down-regulated. In this study, we predicted the pathogenic candidate genes as well as the potential molecular pathways related to macrodactyly by identifying the signature genes. Signature genes through systems bioinformatical analysis can be utilized to catch the insight of the molecular pathogenesis of macrodactyly.

Keywords: Macrodactyly, Gigantism, Computational biology, Lipid metabolism

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Renal Fibrosis and Oxidative Stress in Ischemia/Reperfusion Injury Model of IL-10 Knockout Mice

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Chronic kidney disease (CKD) is one of the major incurable disease threatening life. Regardless of initial trigger, fibrosis is the common irreversible final pathway to CKD. With regenerative properties, mesenchymal stem cell (MSC) is an attractive source of cells for regenerative medicine as well as for chronic degenerative disease. IL-10 is an immuno-modulative cytokine decreasing inflammation but our previous study showed that IL-10 itself may also decrease oxidative stress directly. In this study, We compared influence of IL-10 and MSC in progress of CKD, as one part of a study for decreasing fibrosis in CKD. Progressive renal damage was achieved by bilateral ischemia in IL-10 knockout mice and C57BL/6 mice for 30 min and followed by immediate reperfusion. After 24 hr, 5×105 human bone marrow derived MSCs were injected via tail vein and gave another booster with 48 hr interval for MSC group. Same dose of saline was given for CON group. Parallel Normal group were provided by sham operation with C57BL/6 mice. Animals were sacrificed after 1 week and the level of oxidative stress and renal damage were evaluated. Oxidative stress as well as fibrotic change and BUN/creatinine level were more accelerated IL-10 knockout mice whereas mitigating effect of MSC for I/R injury reduced in IL-10 knockout mice. This result provided some evidence that IL-10 may reduce renal fibrosis beside immunomodulation pathway.

Keywords: IL-10, Oxidative stress, Renal fibrosis, Mesenchymal stem cell, Ischemia referfusion injury

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P85

Expression of RhBG in the pig kidney

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Rh B glycoprotein (RhBG) is expressed in the human kidney and plays an important role in urinary ammonia excretion. Pig kidneys share many similarities with humans. The purpose of this study was to investigate the expression of RhBG in the pig kidney. Kidney tissues from pigs were processed for light and electron microscope immunohistochemistry, and immunoblot analysis. In pig kidneys, specific protein bands were detected at ~50 kDa. RhBG immunoreactivity was localized to the basolateral membrane in the connecting segment (CNT), cortical collecting duct (CCD), and outer medullary collecting duct (OMCD). Double immunolabeling revealed that RhBG was mainly expressed in H+-ATPase-positive cells but is rarely expressed in AQP2-positive cells in the CNT, CCD, and OMCD. These results suggest that the RhBG is expressed in the basolateral membrane of acid-secreting cells and may be involved in urinary ammonia excretion in the pig. This work was supported by funds from the National Research Foundation of Korea (NRF-2017R1D1A1B03030573).

Keywords: Ammonia, Excretion, RhBG, Pig, Kidney

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p16INK4a siRNA encapsulated PLGA nanoparticles attenuates pain and cartilage degradation in osteoarthritis

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Osteoarthritis (OA) is a chronic joint disease caused mostly by aging and appears in the elderly. In OA, chondrocytes in cartilage undergo phenotypic changes and senescence, restricting cartilage regeneration and favouring disease progression. The senescence biomarker p16INK4a expression is known to induce aging by stopping cell cycles. In this study, we aimed to reduce cartilage damage and alleviate pain by using nanoparticle p16INK4a in OA. We confirmed the increased expression of p16INK4a in tissues and chondrocytes isolated from OA patients. The destabilization of the medial meniscus (DMM) model was used as OA animal model. OA progression was confirmed by safranin O staining and pain behavior in cartilage. p16INK4a siRNA was encapsulated into nanoparticles using PLGA, and then intra-articular injection into the DMM model. The p16INK4a siRNA loaded NPs alleviated pain for one month and reduced cartilage damage. In vitro, in OA modeling on human chondrocytes with IL-1b treatment, p16INKA4a NPs reduced the cytokine (TNF-a, IL-1b, IL-6) and MMPs (MMP3, MMP13). Taken together, these findings establish that the reduction of p16INK4a by RNAi contributed to the recovery of osteoarthritic cartilage and pain, suggesting that p16INK4a may be a viable future therapeutic candidate.

Keywords: Osteoarthritis, Senescence, Pain, p16INK4a, Pain

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P87

A potential role for placental genes in cancer

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There are many common features between the processes of establishment of a successful pregnancy and the development of cancer growth. During placenta development, trophoblasts invade the adjacent tissue (uterus) and avoid the host (maternal) immune system. Abnormal proliferation and infiltration of trophoblast cells during placental development negatively affects implantation or pregnancy and leads to pathological conditions. Similarly, cancer cells grow and metastasize through cell proliferation, angiogenesis, and invasion, but exhibit uncontrolled abilities that disrupt normal cell-to cell

communication. Based on it, this study aimed to identify common biomarkers that are important for both development and cancer. Since many components and signaling pathways crucial to tumor cell migration and invasion are shared by trophoblast, trophoblastic cell lines are good model system for the study of tumor-like cellular process. Basically, the mouse model was used to select placental coding and noncoding genes differentially expressed in stressed conditions that induce placental inflammation. The biological roles of human homologs for the selected genes were investigated in human trophoblast cell lines and cancer cells. Particular attention is paid to the study of the roles and mechanisms of long noncoding RNAs (lncRNAs) and epigenetic modifiers that can act as gene expression regulators.

Keywords: Placenta, Cancer, Trophoblast, LncRNAs, Biomarkers

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P88

Elucidation of the junctional zone in neural development of chick embryo

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Neural tube defect (NTD), which results from disturbances in neurulation, is the most common congenital anomaly in newborns. An ambivalent clinical case of NTD suggesting a new phenotype has been reported. Since it encompasses traits from both open (primary) and closed (secondary) phenotypes, we hypothesized that it may be due to defects during junctional neurulation that takes place between primary and secondary neurulation. In present study, we investigated the spatiotemporal change in the development of the junctional neural tube throughout developmental stages of the chick embryo. To locate a potential position of the junction, we scanned the morphology of the chick tail bud when primary neural tube, which forms from rolling and folding of the neural plate, is near complete and during the onset of secondary neural tube formation, which begins from a dispersed mesenchyme. Since it involves both mesenchymal and neural stem cell character, we additionally investigated the role of neuromesenchymal progenitor cells in junctional neurulation.

Keywords: Neural tube defect, Junctional zone, Chick embryo, Neurulation, Caudal cell mass

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P89

Pregnancy-specific glycoproteins regulate trophoblast cell proliferation, invasion, and migration

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The pregnancy-specific glycoproteins (PSGs), members of the immunoglobulin (Ig) superfamily, are the most abundant fetal proteins produced by placenta during pregnancy and have possible roles in immune tolerance to fetus. Decreased PSG levels in human maternal serum are associated with adverse pregnancy outcomes including intrauterine growth retardation, preterm labor and pre-eclampsia (PE). There is accumulating evidence that prenatal stress or maternal infection induces placental inflammation and causes abnormal pregnancy outcomes. Interestingly, our previous work showed that many immune-related genes including Psg genes were dysregulated by administration of synthetic glucocorticoid, dexamethasone, on pregnant mice. RNA-seq analysis of the pregnant mice after the administration of lipopolysaccharide (LPS) also showed that multiple Psg genes were downregulated under placental inflammation condition. To investigate the biological roles of human homologs for mouse placental Psg genes, functional assay for PSG were performed in human first-trimester trophoblast cells (Sw.71, trophoblast cell line). In this study, we demonstrate that simultaneous silencing of multiple PSG genes (PSG1-9, -11) significantly suppress trophoblast cell invasion and migration. In addition, PSG knockdown slightly inhibited trophoblast cell proliferation. The mechanism of action associated with this phenomenon will be further examined. Placental dysfunction caused by pathologic conditions greatly affects the

normal development of the fetus, and thus elucidating the mechanism by which placental genes regulate trophoblast cell function is necessary for the development of diagnostics and therapeutics for placental disease.

Keywords: Pregnancy-specific glycoproteins (PSGs), Lipopolysaccharide (LPS), Placental inflammation, Trophoblast cell line (Sw.71), Placental development

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P90

Inflammatory esponses in the aging mouse retina is associated with caveolin-2

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Aging is a multifactorial process that affects the entire organism. Chronic inflammation is one of a key factor in age-related retinal disease, such as age-related macular degeneration and glaucoma. However, the relationship between aging and neuroinflammation is not clearly determined. Caveolin-2(cav-2) is known to have multiple activities in the regulation of cellular processes, including adhesion and transmigration. The aim of this study is to determine whether cav-2 promotes microglial infiltration into aging retina. Immunohistochemistry and western blot for cav-2 and Ionized calcium-binding adapter molecule-1(Iba-1) was conducted in the normal and cav-2 knockout mouse retina obtained at 3 month (young) and 15 month (old). In the normal mouse retina, cav-2 is seen in blood vessels and the amount of cav-2 protein is more in the old retina than young retina. As cav-2 is increased with aging retina, Iba-1 positive microglia also increased in retina. In addition, microglia is mainly seen in IPL (inner plexiform layer) and OPL (outer plexiform layer) of the young mouse retina, while the retina of old mouse model is also observed in GCL (ganglion cell layer). However, cav-2 knockout mouse model has been shown to reduce the number of microglia. This suggests that cav-2 plays an important role in induced inflammatory cell in the aging retina.

Keywords: Aging, Inflammatory response, Retina, Caveolin-2, Microglia

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P91

PARP-1 inhibition in dental pulp stem cells enhances white matter regeneration in the mouse model of periventricular leukomalacia

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Periventricular leukomalacia (PVL) is a severe type of white matter damage characterized by hypomyelination and pre-myelinating oligodendrocyte death in premature infants and the most common cause to lead to cerebral palsy. A promising attempt to regenerate white matter involves the cell-based therapy that can differentiate to neuroglial cells and/or secrete trophic factors to promote axon remyelination and regeneration. There is increasing evidence that exogenous transplanted cells promote neonatal white matter regeneration. The proposed project adopts an innovative and alternative approach to white matter regenerative sciences by leveraging the neurotrophic features of microenvironmentally engineered dental pulp stem cells (DPSCs). Our data demonstrate that DPSCs stimulate oligodendrocyte differentiation and PARP-1 inhibition under hypoxia during DPSC differentiation shows a significant increase in cell proliferation and brain-derived neurotrophic factor secretion compared to mesenchymal stem cell-derived cells. Further, we identified that erythropoietin (EPO) is a key factor in remyelination and modified DPSCs demonstrate an enhanced EPO production. Transplanted DPSCs were able to regenerate white matter in the mouse PVL model and in vitro myelination is dependent on p38 pathway. Taken together, our data provide mechanistic and molecular understanding for microenvironmentally modified DPSC-based cell

therapy in white matter regeneration and create future targets for therapeutic tools. Acknowledgment: This research was supported by Korea Research Foundation (NRF-2017R1D1A3B040348). *Corresponding author: Nam-Seob Lee (nslee@konyang.ac.kr) & Seung H Chung (chungsh@uic.edu)

Keywords: DPSCs, PVL, Hypoxia, PARP-1, EPO

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Regenerating inferior alveolar nerve using microenvironmentally engineered dental pulp stem cell

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Inferior alveolar nerve (IAN) regeneration is essential for proper nerve sensation as well as maintaining tooth integrity and function. A promising attempt to regenerate peripheral nerve involves the cell-based therapy that can differentiate to neurons and/or secrete trophic factors to promote nerve regeneration. There is increasing evidence that transplanted stem cells promote peripheral nerve regeneration and restore some degree of motor function in human clinical trials, but the overall outcomes are inconsistent and not completely satisfactory. This study adopts an innovative and alternative approach to IAN regenerative sciences by leveraging the neurotrophic features of microenvironmentally engineered dental pulp stem cells (DPSCs). Our data demonstrate that adjusting the microenvironments during DPSC differentiation by hypoxia, cell-to-cell contact and modification of the receptor/intracellular signaling significantly enhanced the neurotrophic capacity of the differentiated cells. Our DPSC-derived cells by the nuclear enzyme, PARP-1 inhibition and complement C5a receptor (C5aR) blocking under hypoxia show significantly enhanced brain-derived neurotrophic factor (BDNF) and erythropoietin (EPO) secretion as well as enhanced proliferation capacity. As several previous and our studies demonstrate that BDNF and EPO are critical factors governing nerve growth and myelination, we next applied these engineered DPSCs into our mouse IAN regeneration model. Our data confirm that the transplanted DPSCs can regenerate the dissected IAN in our mouse IAN model, and p38 is activated and required at the regenerating IAN, and this is BDNF dependent. Taken together, our data provide a fundamental understanding and strategy for the DPSC-based stem cell therapy in IAN regeneration. Acknowledgment: This research was supported by Korea Research Foundation (NRF-2017R1D1A3B040348).

Keywords: DPSCs, IAN, Hypoxia, BDNF, EPO

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The effect of host age on the proliferative capacity of the human periodontal ligament stem cells (PDLSC)

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The use of MSC as a means of cell therapy in many diseases is being considered. To be used as a therapeutic agent, enough number of cells must be obtained in vitro. Thus, the in vitro proliferative capacity of MSC is one of the most important features. MSCs derived from patients with chronic diseases are known to have the poor proliferative capacity. Also, considering the nature of the stem cells, MSCs derived from older individuals may be less proliferative than those derived from young individuals. In this study, we compared the characteristics of MSCs including proliferative capacity in deciduous and permanent teeth-derived PDLSCs. Human periodontal ligament stem cells were extracted from deciduous (d-PDLSCs) and permanent teeth (p-PDLSCs), and their characteristics were evaluated for the proliferative capacity with the doubling time, the differentiation capacity, and the immunophenotyping. We obtained extracted teeth; five clones of d-PDLSC from children with average age of 11.2 1.3, and five adult clones from three men and two women with

average age of 24.2 2.0. Experiments were performed with cells of passages 8 ~ 14. As a result, both kinds of PDLSCs differentiated into the osteoblasts, adipocytes, and chondroblasts under appropriate culture conditions, without any differences between them. Also, both kinds of cells were positive for surface markers including CD73, CD90, CD105, HLA-ABC, and negative for CD34, CD40, CD45, CD80, CD86, CD154, HLA-DR, with no differences between them. However, the doubling time of the d-PDLSC was 23 hours, faster than that of the p-PDLSC, which was 30 hours. Furthermore, when we evaluated the in vitro immunosuppressive capacity of each kind of MSCs, d-PDLSC showed more effective suppression of the proliferation of the activated lymphocytes. In summary, the d-PDLSC showed more proliferative capacity and a more immunosuppressive effect than the p-PDLSC, with no difference in phenotypes and differentiation capacity. It can be suggested that the d-PDLSCs could be a source of autologous MSC which can be obtained in a healthy state and stored for future usage. 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: Human periodontal ligament stem cell, Deciduous teeth, Permanent teeth, Cell proliferation, Immunosuppressive effect

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P94

Alu digital PCR-based quantification of human umbilical cord-mesenchymal stem cells (UC-MSCs) among rat tissues

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Because it is difficult to sequentially demonstrate the absorption, distribution, metabolism, and the excretion of cells used for therapy, the bio-distribution test to track the residual cells is used instead, for the evaluation of the bio-dynamics of the administered cells at a non-clinical level. The Alu-qPCR (quantitative polymerase chain reaction) is especially wildly used, because it is a highly sensitive method at its cost. However, method validation should be done using standard material because the copy number of the Alu elements is over one million per person with individual variation. Also, even though its detection is very specific because of its small size (300 nucleotides), being one of the primate-specific short interspersed elements (SINEs), the same reason makes the detection difficult when the Alu elements are mixed with genomic DNA from other species. That is due to the increased background noise, and decreased confidence interval (CI) and the limit of detection (LoD). Meanwhile, digital PCR (dPCR) can quantify the low amount of DNA directly without external calibration. However, there had been no attempt to try to apply dPCR for the bio-distribution test. The purpose of this study was to compare the efficiency of the qPCR and dPCR methods in detecting the Alu elements of UC-MSC, which was mixed with rat genomic DNA. For the qPCR, Applied Biosystems™ QuantStudio™ 6 Flex Real-Time PCR System was used. Ten-fold serial dilution of the DNA samples were carried out up to from 1 ng to 1 pg, and the linearity, CI, and the LoD was determined. For the dPCR, QuantStudio 3D Digital PCR System was used. The copy number of the Alu element was counted with dilution-limited DNA into ~120,000 wells of ~865 pL. As a result, both PCRs detected as little as 1 fg of DNA when human UC-MSC DNA was used singly. In the case of qPCR, the linear range of the standard curve extended over five orders of magnitude, with a correlation coefficient (R2) of 0.991. However, when the human DNA was mixed with the rodent DNA, the detection limit was 10 fg in the case of the qPCR while that of the dPCR was still 1 fg. From these results, we concluded that the dPCR is superior to the dPCR in that it maintains its sensitivity to permit the detection of rare events in the xenogeneically mixed genomic DNA regardless of the high background signal shown in the qPCR. 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, Digital PCR, Human umbilical cord-derived mesenchymal cells, Alu element, Stem cell

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Bio-distribution and survival of the intra-tendinous injected human umbilical cord-mesenchymal stem cells

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Allogeneic mesenchymal stem cells (MSC) are considered for use in many diseases in place of autologous ones. For this, safety is one of the major issues. If administered allogeneic MSC persist longer time than expected in the body, they could cause unpredicted problems. Thus, Government Guideline recommends following up on the administered cells in experimental animals as a prerequisite for the development of the cell therapy module. Factors such as the type of the cells, the administration route, and the number of cells can influence the survival of the cells. As a treatment module for damaged rotator cuff muscle tendons, the usage of allogeneic MSC is under investigation. In this study, we evaluated the distribution and survival of intra-tendinous injected human umbilical cord-derived MSCs (hUC-MSC) in immune-compromised nude rats (Crl:NIH-Foxn1rnu). hUC-MSC, 106 cells in 10 μL PBS were injected into the tendon of the supraspinatus muscle. Animals were sacrificed on days 1, 2, 7, 14, 28, and 42 after injection. Each group consisted of three males and three females. Twelve organs (blood, pancreas, spleen, kidney, liver, testes/ovary, lung, heart, lymph node, tendon, brain, and bone marrow) were obtained, and genomic DNA of each sample was extracted, which were subjected to quantitative analysis for the Alu gene by real-time qPCR, as a maker for the human-derived cells. As a result, the Alu gene was detected in the tendon for about one week. Other than the tendon, the liver was the major site where the gene was detected. In there, the gene persisted until 28 days after injection. Besides, the gene was sporadically detected in the kidney until 7 days, in the pancreas until 14 days, and in the lung until 28 days. At 42 days, no Alu gene was detected in all samples. In summary, hUC-MSC stayed at the site of administration, the tendon, for one week. The cells were re-distributed in organs outside the site such as the liver, lung, pancreas, and the kidney. Within 6 weeks after administration, UC-MSC disappeared in all organs. 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, Rotator cuff syndrome, Human umbilical cord-derived mesenchymal cells, Real-time qPCR, Tendon

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P96

Chorion-derived mesenchymal stem cell is a preferential option for stem cell therapy for ischemic heart disease

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Stem cell therapy for ischemic heart disease has emerged as a new treatment method to reduce progression of the heart failure, after myocardial infraction (Ml). However, the effect of stem cell therapy is still controversial, and needs further optimization. In our previous report (Kwon et al. (2016) Sci Rep 6:23544), chorion-derived MSCs (C-MSCs), and umbilical cord-derived MSCs (UC-MSCs) of 3 different perinatal MSCs showed a more pronounced ability in vitro to differentiate into cardiomyocyte and neural cells, respectively. Thus, this study was designed to test whether the specific differentiation potency of C-MSCs produces more effective outcome in in vivo ischemic heart disease model than ones with UC-MSCs besides BM-MSCs. We applied C-MSC, UC-MSCs, and BM-MSCs in a rat ischemic heart injury model and compared their effects. 8-week-old Fischer 344 rats were anesthetized with 2% inhaled isoflurane and intubated via the trachea for mechanical ventilation. Left ventricle was visualized through the left thoracotomy, and then left anterior descending (LAD) artery was permanently ligated to induce myocardial infarction. Cells were labeled by Dil and injected in to the border zone of the infarcted myocardium right after ligation with PBS. Echocardiogram was performed at 1, 2, 4, 8, and 12 weeks after LAD artery ligation and measured left ventricle ejection fraction (LVEF) and fraction shortening (FS). Hearts were perfused with PBS for 15 min, and fixed in 4% paraformaldehyde overnight. Tis-

sues were embedded in paraffin and sectioned in 4 μm thickness. Three different cardiac markers, anti-human alpha-sarcomeric actin (α-SA), cardiac troponin-T (cTnT) and connexin 43 (CX43) were immunostained to evaluate degrees of differentiation into cardiomyocyte. In functional assessment, echocardiograms showed no differences in LVEF and FS among control injured group and all MSC-injected groups by 4 weeks after LAD ligation (ANOVA, $p>0.05$). In 8 and 12 weeks groups, however, both LVEF and FS were significantly increased in C-MSC injected group ($p<0.05$), compared to control and UC-MSC and BM-MSC injected groups. In tissue sections containing Dil-labled MSCs were apparently observed. Although in all MSC injected groups, Dil-labeld MSCs expressing α-SA, cTnT and CX43 immunoreactivities were observed, number of C-MSCs showing cardiomyocyte differentiation markers were statistically more than those of UC-MSCs and BM-MSCs ($p<0.05$). These functional and histological results suggest that C-MSC could be better candidate for stem cell therapy for ischemic heart disease than other MSCs including BM-MSCs.

Keywords: Mesenchymal stem cell, Myocardial infarction, Differentiation, Cardiac markers, Echocardiogram

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Akt1 decreases Gcn5 protein stability through regulating the ubiquitin-proteasome pathway in MEFs

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General control non-derepressible 5 (Gcn5) is known to play key roles during embryogenesis as well as in the development of various human cancers. We previously reported that Gcn5 protein level is negatively regulated by Akt1, consequently down-regulating Hoxc11, a downstream target gene of Gcn5 in mouse embryonic fibroblasts (MEFs). However, detailed mechanisms of how Gcn5 expression is synchronized have not yet been defined. In this study, we demonstrate that Gcn5 is negatively regulated by Akt1 at the post-translational level through a protein stability chase assay in MEFs. When Akt1 is depleted in wild-type MEFs, Gcn5 protein status is recovered, similar to that of Akt1-null MEFs. We also reveal that the competitive binding between Gcn5 and Akt1-regulated And-1 and/or Cul4a-Ddb1 complex modulates the protein stability of Gcn5. Taken together, our study reveals that Akt1 negatively controls Gcn5 via the proteasomal degradation pathway, suggesting a potential mechanism for the regulation of Hox genes in MEFs.

Keywords: Gcn5, Akt1, Ubiquitin-proteasome, MEFs

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P98

Adult human multipotent neural cells (ahMNCs) could be distinguished from other cell-types by pro-angiogenic paracrine effects via MCP-1 and GRO

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Adult human multipotent neural cells (ahMNCs) are unique cells derived from adult human temporal lobes. They show multipotent differentiation potentials into neurons and astrocytes. In addition, they possess pro-angiogenic capacities. The objective of this study was to characterize ahMNCs in terms of expression of cell-type specific markers, in vitro differentiation potentials, and paracrine factors compared with several other cell-types including fetal neural stem cells (fNSCs) to provide detailed molecular and functional features of ahMNCs. Interestingly, expression of cell-type specific markers of ahMNCs could not be differentiated from those of pericytes, mesenchymal stem cells (MSCs), or fNSCs. In contrast, differentiation potentials of ahMNCs and fNSCs into neural cells were higher than

those of other cell-types. Compared with MSCs, ahMNCs showed lower differentiation capacities into osteogenic- and adipogenic-cells. Moreover, ahMNCs uniquely expressed higher levels of MCP-1 and GRO family paracrine factors than fNSCs and MSCs. These high levels of MCP-1 and GRO family mediated in vivo pro-angiogenic effects of ahMNCs. These results indicate that ahMNCs have their own distinct characteristics that could distinguish ahMNCs from other cell-types. Characteristics of ahMNCs could be utilized further in preclinical and clinical development of ahMNCs for regenerative medicine. They could also be used as experimental references for other cell-types including fNSCs.

Keywords: Adult human multipotent neural cells (ahMNCs), Neural stem cells (NSCs), Cell-type specific marker, Differentiation potential, Pro-angiogenic capacity, MCP-1, GRO

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P99

Caffeine alleviates inflammation in an OVA-induced allergic rhinitis mouse model by regulating Th1/Th2 cytokines imbalance

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Caffeine (1,3,7-tri-methylxanthine) is one of the most widely consumed pharmacological active products in the world. The main source of caffeine in daily life is coffee or other caffeinated beverages such as energy drinks, tea, and carbonated soft drinks. Caffeine has wide-ranging pharmacological activities including effects on the central nervous, cardiovascular and respiratory systems. Although caffeine has been shown to have the anti-inflammatory effect, however, to the best of our knowledge, there has been no study about the anti-inflammatory activities of caffeine on allergic rhinitis (AR). Therefore, the purpose of this study is to investigate the anti-allergic effect of caffeine on the ovalbumin (OVA)-induced AR murine model. The AR mouse model was initiated in BALB/C mice by sensitized with OVA emulsified in aluminum on days 1, 8, and 15, then nasal installation challenged with OVA from days 22 to 28. From days 16 to 28, caffeine (5, 10, 20 mg/kg) and dexamethasone (Dex, 2.5 mg/kg) groups were administrated 20 μL per nasal cavity on OVA immunized mice, and from days 22 to 28, mice were received caffeine or Dex treatment 1 hour before OVA challenge. Mice of the control group were treated with saline and without sensitization and challenge. In this study, caffeine attenuated the nasal symptoms include rubbing and sneezing, reduced the thickness of nasal mucosa and alleviated goblet cell hyperplasia in the nasal mucosa, ameliorated the inflammation in the lung tissue, decreased the levels of OVA-specific IgE and OVA-specific IgG1 but up-regulated the level of OVA-specific IgG2a in serum. Furthermore, caffeine suppressed the secretion of Th2 (IL-4, IL-5, IL-13) and Th17 (IL-17) cytokines in nasal lavage fluid (NALF), and increased the production of Th1 (IL-12, IFN-γ) cytokines in NALF. Taken together, we suggest that caffeine may have the therapeutic effect on AR.

Keywords: Caffeine, Allergic rhinitis, Th1 cytokines, Th2 cytokines, Anti-inflammation

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Molecular insights for HPV-induced head and neck squamous cell carcinoma

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Head and neck squamous cell carcinoma (HNSCC) is the sixth most common malignant tumor in the worldwide and a deadly disease, with a poor rate of survival. The major carcinogens of HNSCC are known to be smoking, alcohol abuse, and human papillomavirus (HPV) infection. Compared with smoking-related HNSCC, the incidence of HPV-associated HNSCC has increased recently, but there are not enough studies on that. The purpose of this study was to identify the differentially expressed genes (DEGs) and related pathways between HPV-positive and HPV-negative HNSCCs.

Downloading three independent cohorts from Gene Expression Omnibus (GSE65858, n = 270; GSE39366, n = 138) and The Cancer Genome Atlas (TCGA, n = 528). We divided the cohorts into two groups, HPV (+) (GSE65858, n = 73; GSE39366, n = 14; TCGA, n= 99) and HPV (-) groups (GSE65858, n = 196; GSE39366, n = 82; TCGA, n= 427), according to the HPV status. To screen out DEGs, we performed the Significance Analysis of Microarray using R software and obtained 13 upregulated genes (C18orf55, CHAF1B, CREB3L4, FANCG, LIG1, MCM5, MCM6, MGA, MTMR14, NASP, NUSAP1, PPM1M, SLFN13; FDR = 0.01). Then, we performed pathway enrichment analysis of the DEGs and obtained Metabolic pathways (MGA, and MTMR14), Cell cycle (MCM5, and MCM6) and DNA replication (MCM5, MCM6, and MGA). In conclusion, we suggest that these pathways will contribute to understand HPV-induced HNSCC.

Keywords: Head and neck squamous cell carcinomas, Human papillomavirus, Differentially expressed genes

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P101

Involvement of phosphatidylserine and its receptors in cell fusion duringosteoclstogenesis

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Fusion of preosteoclasts is essential for the effective bone resorptive activity of osteoclasts. In this study, we investigated the externalization of phosphatidylserine (PS), expression of its receptors, and their biological functions for the fusion of preosteoclasts during osteoclastogenesis. Firstly, we showed that strong immunoreactivities for PS receptors such as Tim4, Bai1, and Stab2 was detected in TRAP-positive multinucleated cells in the alveolar bone of the head tissue of rats, and their expression was increased significantly during MCSF/RANKL-induced in vitro osteoclastogenesis. Moreover, PS externalization in preosteoclasts was increased on day 4 after treatment of M-CSF/RANKL of bone marrow-derived cells. Multinucleation of preosteoclasts was inhibited markedly by specific antibodies against PS and its receptors. Next, we found that CD47 and CD31 were increased or sustained in the early phase of osteoclastogenesis, besides Annexin1 and MFG-E8 were increased in the late phase of it. In addition, Z-VAD-FMK, a pan caspase inhibitor, had no effect on the fusion of preosteoclasts in the early phase of osteoclastogenesis, and apoptosis of osteoclasts during the late phase of osteoclastogenesis was decreased by specific Abs against PS, Tim4, and Bai1. These imply that externalized PS during early and late phase of osteoclastogenesis would be essential in M-CSF/RANKL-induced cellular fusion of preosteoclasts and apoptosis, respectively. Floppases such as Abcb4, Abcc5, and Abcg1 were increased, besides flippase Atp11c was decreased in the early phase of osteoclastogenesis, and preosteoclasts fusion was blocked markedly by an ATPase inhibitor, Na3VO4 and specific siRNAs against Abcc5 and Abcg1, revealing the importance of PS externalization in the fusion of osteoclast. These results suggest that flopping of PS and its receptors such as Stab2, Bai1, and Tim4 are essential in cell fusion during the early phase of osteoclastogenesis. Therefore, modulation of PS and its receptors could be a useful strategy for regulating bone resorption.

Keywords: Osteoclasts, Phosphatidylserine, Cell fusion, ATP-dependent transporter, Apoptosis

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P102

Foundation Research For Building Dental Simulation Model By Merging CBCT Data And CAD System

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Currently, the CAD system is widely used in dental treatment. The prosthesis manufacturing method, which has been mostly done by

hand in the past, has been pointed out the disadvantages such as error, manpower, and time wasted even if the individual differences of workers or the same person made. However, the CAD technology that can compensate for these shortcomings is being studied in various areas. In this study, we intend to build a dental treatment simulation model through the merging of CAD system using the CBCT data. The process is as follows. In order to extract patient data in 3D using CBCT data, 3D data is extracted after reconstruction using mimics program of the patient's CBCT. Patient data extracted in 3D was imported into the CAD system and the upper and lower first molar, the criteria for malocclusion, were checked to determine the treatment area and occlusion of the patient. The occlusal of the buccal and lingual mesial distal cusps of the maxillary and mandibular first molars were set to one axis, respectively, and the patient's occlusion was judged by four axes. Then check for differences between occlusion of the patient's gypsum model and the fabricated simulation. After all the processes, we analyze the occlusal point of the patient and decide whether to produce the prosthesis for dental treatment on the CAD system. The dental simulation model produced through the above process did not show any difference from the existing gypsum model, and it is expected to suggest a new paradigm of the advanced dental industry for patient-specific dental treatment in the future.

Keywords: 3D, CBCT, CAD, CAD System, Dental treatment

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P103

Medical and dental education in Korea-Massive Open Online Course

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The aims of this study were to analyze the current status and the instructional design strategies of the medical and dental courses in Korea-Massive Open Online Course (K-MOOC), and to present a practical direction for application in future dental education. Three courses were selected for this study among 30 courses categorized as medical education in K-MOOC as of December 2018. The courses were analyzed based on the proposed instructional design strategies for facilitating online interaction among participants-instructors, teaching assistants, and learners. In addition, this study reviewed the current status of free online dentistry courses in MOOC including K-MOOC. While the number of basic medical science courses was five in total, the dentistry courses in K-MOOC was not offered yet. Regarding the format of the medical courses was similar to a lecture-based traditional classroom which was characterized with one-way content delivery style. However, the current courses were appropriately designed with the proposed instructional design strategies for facilitating online interaction. And, there were 11 dentistry courses on MOOC platforms in 2018, but most of them have started to operate the courses recently. The results of this study denote current scarcity of dental MOOCs that could have educational potential benefits from well-structured courses with rich media delivered online and encourage dental educators to consider MOOCs as alternative educational opportunities. In addition, it provides the instructional design strategies that should be considered in designing new MOOCs. It would also provide a practical direction for the development of personalized learning dentistry courses in K-MOOC.

Keywords: Dental education, K-MOOC, e-learning, Instructional design strategies

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P104

3D evaluation of maxillary sinus volume in different gender groups using CBCT

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Anatomical knowledge of the maxillary sinus is valuable to prevent possible complications in maxillofacial surgery. Many studies have been used in literature to measure the maxillary sinus volume such as radiographs, computed tomography, magnetic resonance imaging. The aim of this study is to evaluate the maxillary sinus volume according to gender with three dimensional(3D) models. This study included 57 patients of Dankook university dental hospital. Cone-

beam computed tomography data images were imported and reconstructed into 3D models by an interative medical image control system, Mimics 17.0 software (Materialise, Leuven, Belgium). We compared the differences in the measured maxillary sinus volume among these gender group. There was no difference in the right and left maxillary sinus volume according to the findings obtained from our study (p=0.686), and the left and right maxillary sinus volume in males was found to be significantly bigger than that of females (left p=0.001, right p=0.002). With the results in our study, we expectation that elaboration of the studies related to maxillary sinus volume in the future by using 3D programs will contribute to the scientific literature. NRF-2016R1D1A1B01008853

Keywords: CBCT, Mimics, 3D, Sinus, Gender

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P105

DNA Polymerase Performance On The Degraded Human DNA Samples

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Human DNA from tombs, soil, or ancient burials are highly degraded. Especially very old and severely fragmented human DNA samples are common in the forensic studies. Despite many various methods and efforts to identify the DNA status, it is often found out to be unsuccessful due to the poor quality and quantity of the DNA samples. We have extensively evaluated the most used DNA polymerase for the successful pcr of severely fragmented human DNA samples. We have tried to study various DNA polymerases. We found DNA polymerases in the market, which included enzymes that are reportedly effective for pcr-inhibitory samples. We could give comments that the several DNA polymerases are more efficient for higher probability of success pcr that could give the desired results from highly degraded human DNA samples.

Keywords: DNA Polymerase Degraded Human DNA

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P106

Gender Typing Of Highly Fragmented Human DNA Samples

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The determination of human gender with fresh human DNA is very easy and rarely difficulty to do with it But it has been well known to be very difficult to confirm the gender of severely degraded human DNA The dropout of some alleles due to different amount in fragmented and severely degraded small quantity DNA seems to be very serious problem to type the gender To rule out the genotyping errors, many studies require pcr amplification to solve this replication correctly Usually the limiting factors are small amount and degraded level of human DNA samples Here we want to report our study to verify the gender type with a real time pcr based amelogenin y amely We introduced an allele dropout estimation model in an amel based gender typing The gender of all the degraded human DNA samples was confirmed by sex determination region y marker amplification We also suggest this model as a securing amely allele dropout safe method from degraded inhibitory DNA samples

Keywords: Gender Fragmented Human DNA

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Gene expression profiling and gene network analysis in EGFL8 overexpressed/silenced mouse thymic epithelial cells

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A genome-wide expression profiling was analyzed in EGFL8-overexpressed or silenced 427.1 thymic epithelial cells (TECs). Microarray analysis revealed that a total of 458 genes exhibited more than 2 fold changes in expression level in EGFL8-overexpressed versus silenced 427.1 TECs. Several genes involved in a number of molecular signaling pathways such as cell cycle, proliferation, growth, migration, and differentiation as well as apoptosis, ROS generation, chemotaxis, and immune responses were differentially expressed in the EGFL8-overexpressed or silenced 427.1 TECs. Of importance, the gene network analysis revealed that EGFL8 can have negative effects on vascular endothelial growth factor-A (VEGF-A) gene expression. It is concluded that altered expression of several genes associated with manipulation of EGFL8 expression in TECs highlights important physiological processes in which EGFL8 is involved, and provides insight into biological functions of EGFL8.

Keywords: Gene network analysis, Epidermal growth factor-like domain 8, Thymic epithelial cells, Molecular signaling pathways, Vascular endothelial growth factor-A

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P108

Microarray analysis of global gene expression in EGFL8-overexpressed and EGFL8-knockdown mouse thymic epithelial cells

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Epidermal growth factor-like domain 8 (EGFL8) has recently been discovered to have some negative regulatory roles in mouse thymic epithelial cells (TECs) and thymocytes. However, little is currently known about the mechanism by which EGFL8 exerts its effects on these cells. To understand the pathways and networks that may involve EGFL8 function, microarray analysis was performed to examine global gene expression in EGFL8 overexpressed or silenced TECs. WST-1 analysis showed that overexpression of EGFL8 inhibited TEC proliferation. To investigate the underlying mechanism of EGFL8 in the regulation of TEC function, we selected some genes functionally related with essential cellular functions such as CD74, FasL, CXCL10, CXCL16, CCL20, CXCL5, Angptl1, VEGF-A, NRP-1, Sema3D, Sema7A, IRF-7, IGFBP-4 and NF-κB2. The RT-PCR analysis revealed that overexpression of EGFL8 downregulated the expression of CD74, FasL, CXCL10, CXCL16, CCL20, CXCL5, Angptl1, VEGF-A, IRF-7, IGFBP-4 and NF-κB2, while induced upregulated expression of NRP-1, Sema3D and Sema7A genes. In addition, EGFL8 overexpression inhibited anti-apoptotic molecules such as Bcl-2 and Bcl-xL as well as the cell cycle regulating molecules such as CDK1, CKD4, CDK6 and cyclin D1. Taken together, these results shed new light on the functional role of EGFL8 in mouse TECs.

Keywords: EGFL8, TECs, Proliferation, Anti-apoptotic, Cell cycle regulating

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P109

MicroRNA regulates messenger RNA affecting multifocality in BRAF-positive papillary thyroid cancer

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The most common form of thyroid neoplasm is papillary thyroid cancer (PTC), which accounts for 80~85% of all cases. Multifocal PTC appears in the rate of 18~87%, but the characteristics of their molecular and histopathologic features are not clear. Previous studies have identified 145 messenger RNAs (mRNAs) that are overexpressed in multifocal BRAF-positive PTCs. The mRNAs are associated with 13 pathways consisting of Axon guidance, Breast cancer, Ectoderm differentiation, Gastric cancer, Hippo signaling pathway, Neural crest differentiation, O-linked glycosylation, Phospholipase D signaling pathway, Rap1 signaling pathway, Signaling by WNT, Signaling pathways regulating pluripotency of stem cells, TCF dependent signaling in response to WNT, Wnt signaling pathway and pluripotency. In this study, we identified the correlation between microRNAs (miRNAs) and the mRNAs in BRAF-positive PTC. Clinical and genomic data were downloaded from The Can-

cer Genome Atlas. Of the 237 BRAF-positive PTC patients, 110 patients were multifocal PTC and 127 of BRAF-positive patients were unifocal PTC. To find out the relationship between the 145 mRNAs and miRNAs, we used spearman correlation method. There were 13 miRNAs in Axon guidance, 15 miRNAs in Breast cancer, 29 miRNAs in Ectoderm differentiation, 20 miRNAs in Gastric cancer, 5 miRNAs in Hippo signaling pathway, 15 miRNAs in Neural crest differentiation, 31 miRNAs in O-linked glycosylation, 5 miRNAs in Phospholipase D signaling pathway, 8 miRNAs in Rap1 signaling pathway, 16 miRNAs in signaling by WNT, 11 miRNAs in signaling pathways regulating pluripotency of stem cells, 16 miRNAs in TCF dependent signaling in response to WNT, 12 miRNAs in Wnt signaling pathway and pluripotency. In conclusion, although additional experiments are required, we found potential miRNAs that regulate mRNAs affecting multifocality in BRAF-positive PTC.

Keywords: Micro RNA, Messenger RNA, Correlation, Multifocality, Tyroid cancer

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P110

Kidney ischemia reperfusion induces lung cilia fragmention and its release to bronchoalveolar lavage fluid

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Background: Acute kidney injury (AKI) commonly causes lung failure. However, its molecular mechanisms and early and rapid diagnosis tool remain to be defined. Primary cilium, a rod-like organelle, plays an important role to sense and transmit signals in various types of cells. Recent studies have demonstrated that cilia shortening is associated with the progression of kidney injury and that change could be an indicator of kidney injury. Therefore, we investigated whether AKI-induced lung injury is associated with cilia length alteration and this alteration can be an indicator of lung injury. **Methods:** Mice were subjected to 35mins of bilateral renal ischemia. Brochoalveolar lavage fluid (BALF) Lung and kidney morphology and kidney function were evaluated by PAS staining and measurements of creatinine BUN, respectively. Cell number and protein concentration in BALF were determined. Expression of acetylated α tubulin (ac-α tubulin), ADP-ribosylation factor-like protein 13B (ARL 13b) and 4-hydroxy-2-nonenal (4-HNE) were evaluated by western blot and immunofluorescence staining. **Results:** The reduction of alveolar size, expansion of interstitial tissue, infiltration of immune cells in interstitial tissue, and increase of DNA oxidation were observed in the lung after kidney ischemia reperfusion (IR). ARL13b positive signals were reduced in the lung of mice which was subjected to kidney IR when compared with sham-operated mice. ARL13b-positive signal was observed in BALF smeared slide and this signal was greater in BALF harvested from IR mice than sham-operated mice. 4-HNE, ac-α tubulin, and ARL13b expressions were greater in BALF of IR mice when compared with those in sham-operated mice. **Conclusion:** Data indicate that kidney ischemia reperfusion induced fragmentation of cilia of lung and this fragmented cilia was released into the BALF, suggesting that kidney IR-induced lung damage is associated with cilia injury and that ciliary protein in BALF could be an indicator of lung injury.

Keywords: Acute kidney injury, Ischemia Reperfusion, Lung injury, Bronchoalveolar lavage fluid, Cilia

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Water restriction shortens primary cilia length in the kidney tubular cells

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The primary cilium, a microtubule-based cellular organelle, plays a crucial role for maintenance of cellular homeostasis. In kidney, primary cilium links to the number of diseases which are associated with fluid flow and composition. Here, we investigate the relationship between water restriction and the primary cilium length in kidney tubular epithelial cells. In this study, water restriction increased urine osmolality and shortened primary cilia in mouse kidney tu-

bular cells. Water restriction decreased the expression of acetylated-α-tubulin (ac-α-tubulin), α-tubulin transferase (α-TAT), and sec10, a component of exocyst complex, in the kidneys. Tubastatin A (an inhibitor of histone deacetylase 6, HDAC6), treatment prevented those water restriction-induced increase of urine osmolality and shortening of primary cilia and expression of ac-α-tubulin, α-TAT, and sec10. These findings demonstrate that the length of primary cilium in kidney tubule cells is associated with water supply and urine osmolality, suggesting that primary cilia play important role in the regulation of body water homeostasis and urine osmolality.

Keywords: Osmolality, Water restriction, Primary cilia, HDAC6, Tubastatin A

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The effect of high fat diet intake on cisplatin-induced nephrotoxicity

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The use of cis-diamminedichloroplatinum (II) (cisplatin), an effective chemotherapeutic agent, is limited by its side effects including nephrotoxicity. Cisplatin nephrotoxicity is associated with the increase of reactive oxygen species (ROS). Over-providing of nutrient affects cellular redox balance. Therefore, in this study, we investigate whether high-fat intake affects cisplatin nephrotoxicity, and if so, its mechanisms. C57BL/6 male mice were administered with either cisplatin (20 mg/kg B.W.) or saline. Some mice were fed with high-fat diet (HFD) for 7 days before cisplatin injection. Cisplatin injection induced the disruption of kidney tubular cells and also increased BUN and PCr concentration. These increases were greater in the HFD feeding mice than the normal diet ND feeding mice. Levels of hydrogen peroxide and DNA oxidation increased in the kidney after cisplatin injection and these increase were also greater in the kidney of HFD feeding mice than ND feeding mice. When the mitochondrial morphology of the kidney proximal tubule cell was observed under TEM, mitochondrial damage was observed in the proximal tubule cells after cisplatin injection and this mitochondria damage was more severe in the kidney of HFD feeding mice than ND feeding mice. The level of peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC-1α), a member of a family of transcription coactivators, was lowered in the kidney after cisplatin injection and this lowing was greater in the HFD mice kidneys than ND mice. This result indicates that high-fat diet worsens cisplatin-induced nephrotoxicity along with increased oxidative stress and mitochondrial damage. This suggests that energy metabolism is associated with cisplatin nephrotoxicity and cisplatin nephrotoxicity may be controlled by food supply.

Keywords: Cisplatin nephrotoxicity, Mitochondria, ROS, PGC-1a, High-fat-diet

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P113

VSIG4 induces fibrosis of kidney cells with high-glucose

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Kidney damage from diabetes with high blood glucoseor sugar can make diabetic nephropathy. Damaged kidney needs renal fibrosis asa repair mechanism, however, it is a process that is important the progressionof chronic kidney disease to end-stage renal failure. This study investigatedmolecular mechanism underlying fibrosis marker genes in kidney cells at high-glucoseconcentration. Previously, we evaluated that EBV-encoded LMP1 regulates EMT through the NF-kB-VSIG4 (V-set and Igdomain-containing 4) axis in both HK-2 cells and MDCK cells and VSIG4 havedetermined an important molecule in the pathogenic process of renal tubularinterstitial injury. We revealed that VSIG4 expression was increased withhigh-glucose in both HK-2 cells and MDCK cells, kidney tubular epithelialcells. In addition, the expression of fibrosis marker genes, E-cadherin, N-cadherin,MMP-9, MMP-2 and vimentin has been regulated. The absence of VSIG4 rendered therelation with NF-kB signaling. These data suggest that VSIG4 could be an indicatoror regulator at kidney fibrosis in high-glucose condition.

Keywords: Kidney, High-glucose, VSIG4, Fibrosis, NF-kB

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P114

Morphological and functional evaluation of a mouse retinal detachment model

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Retinal detachment (RD) is a sight-threatening condition or complication common in many highly prevalent retinal disorders. RD rapidly leads to photoreceptor cell death and sustained RD leads to significant and permanent loss of vision. Although several animal models to study pathogenesis of RD have been introduced, they have not been characterized. Thus, there is little established animal model for RD. This study was designed to characterize a mouse retinal detachment model induced by subretinal injection of phosphate buffered saline (PBS). C57BL/6 mice were used. To examine retinal functions, electroretinography (ERG) was performed at the 1, 3, 5, 7, and 14 days after detachment. Eyes were enucleated after ERG and fixed in 4% paraformaldehyde. Eyecups were frozen in OCT compound and cryo-sectioned. Hematoxylin and eosin (H&E) staining were conducted to screen the morphological changes in the retina after detachment. Retinal cell death was evaluated by terminal deoxynucleotidyltransferase dUTP nick end labeling (TUNEL) assay. To evaluate glial reaction, immunohistochemistry with anti-glial fibraillary acidic protein (GFAP) as a Müller glial cell marker, anti-ionized calcium binding adaptor molecule 1 (Iba-1), as a microglial cell marker, and anti-osteopontin (OPN) as an inflammation marker were performed. In the scotopic ERG, a- and b-wave were significantly reduced ($p<0.05$), as time passed. In H&E staining, thickness of the outer nuclear layer (ONL) where photoreceptors reside was significantly decreased ($p<0.05$). TUNEL-positive cells that are mostly observed in the ONL of the detached retina were significantly increased by 5 days after RD ($p<0.05$) and thereafter, decreased by 14 days. The expression of GFAP increased in a time-dependent manner. Iba-1 and OPN immunoreactivities became stronger by 5 days after RD at detached region, but not in the attached region. Some microglial cells expressed both Iba-1 and OPN, but others did not. These results clearly demonstrate morphological and functional changes in a mouse RD model induced by PBS subretinal injection. This RD model might be useful to study pathogenesis of RD and mechanism of photoreceptor cell death in RD.

Keywords: Retinal detachment, Animal model, Electroretinography, Immunohistochemistry

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The histomorphometric analysis and immunohistochemical study of new bone formation using concentrated growth factors (CGF) in maxillary sinus bone grafting in rabbits

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The aim of this animal study is to evaluate, by histomorphometric analysis and immunohistochemical study, new bone formation in rabbit maxillary sinuses with Bio-Oss and Bio-Oss plus concentrated growth factors (CGF). Bilateral sinus augmentation procedures were performed in 16 adult male rabbits. Replaceable bony windows were made with a piezoelectric surgical device with a saw insert on lateral wall of nasal cavity. In control group, deproteinized anorganic bovine graft (Bio-Oss®) was grafted in the new compartment of the maxillary sinus after elevation of the sinus membrane. In experimental group, Bio-Oss plus CGF was grafted in the sinus. The replaceable bony window was repositioned over bone graft in both groups. The rabbits were sacrificed at 1, 2, 4, and 8 weeks postoperatively. The augmented sinuses were evaluated by histomorphometric analysis using hematoxylin-eosin and Masson's trichrome stains and immunohistochemical study of bromodeoxyuridine (BrdU), proliferating cell nuclear antigen (PCNA), CD34, stromal precursor

antigen-1 (STRO-1), type I collagen, osteopontin, and osteocalcin content. Histologically, new bone was revealed along the elevated sinus membrane and both bone graft. The area of newly formed bone increased significantly in the experimental group from 1 week to 4 weeks, compared with the control group ($P < 0.05$). The area of bone marrow increased significantly in the experimental group at 8 weeks. The number of BrdU labeled cells at 1 week in the experimental group was significantly greater than in the control group ($P < 0.05$). Immunoreactivity of PCNA increased in the experimental group at 1 week compared with the control group. Immunoreactivities of CD34 and STRO-1 increased in the experimental group from 1 week to 4 weeks, compared with the control group. Immunoreactivity of type I collagen at 1 week in the experimental group was greater than in the control group. Immunoreactivities of osteopontin and osteocalcin increased in the experimental group from 1 week to 2 weeks, compared with the control group. New bone formation of Bio-Oss plus CGF groups began more rapidly than Bio-Oss only groups, and CGF was more effective in bone formation in rabbit maxillary sinuses.

Keywords: Maxillary sinus augmentation, Concentrated growth factor, Bio-Oss, Replaceable bony window, Histomorphometric analysis, Immunohistochemical study

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PCB 126-induced disruption of hepatic iron homeostasis through downregulation of hepatic STAMP2 causes NAFLD

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Polychlorinated biphenyls (PCBs), with 209 congeners, are a large family of persistent organic pollutants (POPs) and have been associated with neurotoxicity, hepatoxicity, oncogenicity, and endocrine-disrupting effects. Although epidemiological and experimental studies demonstrated that PCBs lead to non-alcoholic fatty liver disease (NAFLD), the underlying mechanism has remained unsolved. In this study, we examined in vivo and in vitro effects of dioxin-like PCB 126 on liver. For in vivo studies, 8-weeks-old C57BL/6 mice were fed either a standard diet (SD) or a high fat diet (HFD) for 4 weeks and then were administered vehicle (corn oil), PCB 126 (1 or 5 mg/kg) by intraperitoneal injection for a total of four injections (2, 3, 4 and 5 weeks) during the 6-week study duration. The detailed molecular mechanism was investigated by using HepG2 hepatocytes. PCB 126 significantly promoted hepatic fat accumulation in HepG2 cells treated with oleic acid. In mice, PCB 126 induced hepatic steatosis, inflammation and fibrosis. Because our previous study suggested that STAMP2 may be a suitable target for treating NAFLD, we examined whether hepatic STAMP2 involves in PCB 126-induced NAFLD. Expression of hepatic STAMP2 was decreased in PCB 126 treated HepG2 cells and C57BL/6 mice. Overexpression of hepatic STAMP2 using adenoviral delivery resulted in attenuation of hepatic fat accumulation in HepG2 cells treated with oleic acid. Recent studies demonstrated that exposure to environmental pollutants could lead to disruption of the hepcidin–ferroportin axis along with disordered systemic iron homeostasis and diseases. Also, STAMP2 protein has been identified as ferrireductases responsible for the reduction of Fe3+. Thus, we next investigated the effects of PCBs exposure on hepatic iron homeostasis. We observed that exposure to PCB 126 significantly induced hepatic iron overload in vivo and in vitro. Noticeably, overexpression of hepatic STAMP2 attenuated effects of PCB 126-induced hepatic iron overload in HepG2 cells. This study suggests that PCB 126 disrupts hepatic iron homeostasis by downregulation of hepatic STAMP2 expression, resulting in induces NAFLD. Our findings indicate that enhancing STAMP2 expression represents a potential therapeutic avenue for treatment of PCB 126-induced NAFLD.

Keywords: PCBs, STAMP2, Iron homeostasis, Hepatic iron overload, NAFLD

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The mechanistic insights into the therapeutic effect of recombinant FGF21 on NAFLD: Including supplementary data obtained for the last year corroborating the involvement of hepatic STAMP2-mediated increase in FPN expression

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We previously demonstrated that hepatic six transmembrane protein of prostate 2 (STAMP2) may represent a suitable therapeutic intervention target for non-alcoholic fatty liver disease (NAFLD). Despite the pleiotropic metabolic effects of FGF21, the mechanisms underlying the metabolic actions of FGF21 remain unknown. We undertook this study to identify the mechanism underlying the therapeutic effect of recombinant FGF21 on NAFLD, focusing on the involvement of STAMP2. In this study, we used human non-alcoholic steatosis (NAS) patient pathology samples, a HFD-induced in vivo NAFLD model and an oleic acid (OA)-induced in vitro NAFLD model. Mice fed a standard diet or high-fat diet (HFD) were treated with vehicle or recombinant murine FGF21 (rmFGF21) (1 mg/kg/day) for 10 days. Recombinant FGF21 treatment improved HFD-induced hepatic steatosis and insulin resistance in C57BL/6 mice and significantly increased the expression level of STAMP2 in vivo and in vitro. Importantly, we observed hepatic iron overload (HIO) and reduced iron exporter ferroportin (FPN) expression in the liver samples obtained from NAS patients and HFD-induced NAFLD mice and in OA-treated HepG2 cells. Additionally, we found that recombinant FGF21 improves HIO through the hepatic STAMP2-mediated upregulation of FPN expression. Notably, the in vivo knockdown of hepatic STAMP2 undermined the effects of rmFGF21 in the HFD-induced NAFLD model. In conclusion, recombinant FGF21 attenuates hepatic iron overload by upregulating the expression of FPN via hepatic STAMP2, resulting in the amelioration of HFD-induced NAFLD. Our findings present a new perspective on iron homeostasis in the mechanism by which recombinant FGF21 ameliorates NAFLD.

Keywords: FGF21, STAMP2, Ferroportin, Hepatic iron overload, NAFLD

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Nicotine receptors induce breast cancer cells proliferation, invasion and migration through targeting EBV encoded LMP1

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Nicotine, the main addictive component of tobaccosmoke, has been shown to promote cell proliferation, angiogenesis, andepithelial-mesenchymal transition (EMT), leading to enhanced lung, head and neck tumors growthand metastasis. Recently, evidencefor an increasing breast cancer riskassociated with tobacco smoke exposure hasbeen emerging. The effects of nicotine are usually mediated through thenicotinic acetylcholine receptors (nAChRs) that are expressed on a variety ofneuronal and non-neuronal cells. In breast cancer cells, at least fourdifferent subunits (α5, α7, α9, and β4) of nAChRs are known, but nicotineexposure increases mostly the expression of α9nAChR and α7nAChR. LMP1 isconsidered the major EBV-encoded oncogenic protein, as promoting cell growth,protecting cells from apoptosis, enhancing cell motility, promoting angiogenesisand frequently expressed in EBV-associated human cancer cell lines. Here, weestablished EBV infected or LMP1 transfected breast cancer cell lines. LMP1induces α9-nAChR and α7-nAChR expression in transfected MDAMB231 and MCF-7 cells respectively. Theexpression of nicotine receptor was upregulated in transfected or EBV infectedcells. In addition, we confirmedexpression of nicotine receptor in response to increase in EBV-transformedbreast cancer cells. Inconclusion, our study demonstrates that Nicotine promotes proliferation ofEBV-transformed cells through the EBV-related proteins LMP1 which act as apotential molecular target for breast cancer.

Keywords: Breast cancer, EBV, LMP1, Nicotine, Nicotine receptors

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P119

p66shc targeted PLGA nanoparticels alleviate brain damage from photothrombotic ischemic stroke

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Growing evidence showed an association between ischemic stroke and increased systemic and local production of ROS. The p66Shc adaptor protein regulates oxidative stress, inflammation, apoptosis via ROS signaling. Here, we show the effect of inhibition of p66Shc on brain damages by siRNA encapsulated PLGA nanoparticles (NPs) in Rose Bengal induced photothrombotic stroke mice model. Two days before exposure photo-light at intact skulls, p66Shc siRNA NPs were administered to mice with through intrathecal administration. We observed that p66Shc siRNA NP treated group preserved blood–brain barrier integrity that resulted in improved stroke outcome, as identified by smaller lesion volumes, decreased neurological deficits, and increased survival. Also, we showed that decreased of microglia / astrocyte activation by p66Shc siRNA NP treated in stroke induced mice through tissue staining. The mRNA expression of inflammatory mediators such as Il-1β, Il-6, iNos, and Cox-2 was more attenuated in p66Shc siRNA NP treated group than in vehicle-treated group. Furthermore, the levels of p-p38MAPK and p-ERK known to be activated in microglia and p-JNK known to be activated in astrocyte were significantly decreased by p66Shc siRNA. These results suggest that inhibition of p66Shc attenuate Rose bengal-induced ischemia damage by inhibiting microglia and astrocyte activation followed inflammation. Therefore, targeting the activity of p66Shc might be an interesting strategy to treat ischemia damage induced inflammation.

Keywords: Rose-bengal photothrombosis, p66shc, Nanoparticle, Stroke, siRNA

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P120

Regulation AMPK isoform expression by Epigenetic modification on the glucose metabolisms in skeletal muscle cells

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The AMP-activated protein kinase (AMPK) is a potential therapeutic target for diabetes mellitus based on its reported actions. AMPK activation reduces glucose levels in animal models of diabetes and obesity by increasing glucose uptake in skeletal muscle cells. However, the effects of AMPK expression on the glucose metabolisms and the regulation mechanisms of AMPK expression by DNA methylation is unclear. The aim of this study was to identify the relationship between expression and DNA methylation of AMPK isoforms by hyperglycemia and maintaining glucose metabolisms through recovered its expression in skeletal muscle cells. In result, expression of AMPK isoforms by hyperglycemia is decreased in mouse skeletal muscle C2C12 cells, and rat skeletal muscle L6 cells. The both cells were observed to recover the expression of AMPK isoforms when treated with demethylating reagent, 5-aza-2'-deoxycytidine (5-aza). In addition, the promoter activities of AMPK isoforms were decreased after treatment with high concentration of glucose, whereas it was observed that the promoter activity was increased after treatment with 5-aza in C2C12 and L6 cells. The methylated AMPK isoform promoter was significantly reduced the activity compared with normal AMPK isoform promoter. In conclusion, AMPK isoforms may be a potential therapeutic target for glucose metabolism disease through epigenetic regulation in skeletal muscle.

Keywords: AMPK, Epigenetic, Diabetes, Hyperglycemia, Skeletal muscle

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P121

Fish collagen peptides protect HaCaT cells against CoCl2- and TNF-α-induced cytotoxicity and inflammation via suppressing ROS/MAPK/NF-κB pathway

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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, ROS pathway, MAPK pathway, NF-κB pathway

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P122

Anti-inflammatory effect of organic Germanium extracted from Oenanthe javanica in osteoclast differentiation

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Despite serious safety concerns, Germanium is used for osteoarthritis, rheumatoid arthritis, and osteoporosis because Germanium (Ge) might act against inflammation and oxidative stress. However inorganic germanium makes the renal function deteriorated with no proteinuria or hematuria. Therefore there have been several attempts to make an organic Ge, and poly-trans-[(2-carboxyethyl) germasesquioxane] (Ge-132) is the most common synthetic organic Ge compound currently. But there has no attempt to make natural origin Ge from plants. To make natural organic Ge, we cultured Oenanthe javanica in hydroponics containing high Ge water (GOJ), dried its stem and leaves, and made it powder. Oenanthe javanica in hydroponics only (OJ) was used for control material. Each 100 mg powder was dissolved in 100% ethanol, and filtered using a RC syringes system to obtain the organic Ge. We compared cell viability and the toxicity of Ge by MTT assay, measured anti-inflammatory cytokine by ELISA, osteoclast differentiation by TRAP staining, cell cycle by PI staining, and NF-κB expression by immune-blotting/ As a result, organic Ge was not influenced in cell viability and in cell cycle even though high dose was treated. Anti-inflammatory cytokine such as IL-10 was more increased in GOJ extract than in OJ one, but osteoclast was less differentiated after GOJ addition than after OJ one. Finally both phospho-IκB and phospho-NF-κB was decreased dramatically in GOJ group by dose-dependent manners, which mean organic Ge could be inhibited NF-κB signal network. These results indicate that the organic Ge extracted from Oenanthe javanica has an anti-inflammatory effect during osteoclast differentiation by preventing pro-inflammatory signal network.

Keywords: Oenanthe javanica, Organic Germanium, Osteoclast, Inflammation, Cell cycle

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P123

Mercaptoethanol protects oxidative stress and inflammation induced by unilateral ureteral obstruction

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Mercaptoethanol acts as an antioxidant by scavenging hydroxyl radicals, while it is considered toxic. However, a role of mercaptoethanol in kidney tubulointerstitial fibrosis remains to be defined. We have demonstrated that unilateral ureteral obstruction (UUO) decreased the expression of SLC7A11, a known ferrotosis-related glutamate/cysteine transporter. Otherwise, treatment with mercaptoethanol significantly suppressed UUO-induced decrease of SLC7A11 expression. Furthermore, UUO kidneys a time-dependent decreased the ratio of GSH to GSSG, but treatment with mercaptoethanol significantly increased ratio of GSH to GSSG. During UUO, glutathione peroxidase 4 (GPX4) and other antioxidant enzymes including copper/zinc superoxide dismutase (CuZnSOD) and manganese superoxide dismutase (MnSOD) were downregulated, but treatment with mercaptoethanol markedly reduced their downregulations at 10 days after UUO. Furthermore, expression of intercellular adhesion molecule (ICAM-1) and interleukin-6 (IL-6) among pro-inflammatory proteins were increased during UUO, but treatment with mercaptoethanol significantly reduced their increases at 10 days after UUO. Moreover, infiltration of polymorphonuclear neutrophil (PMN)-positive neutrophils occurred in UUO kidneys, whereas treatment with mercaptoethanol significantly reduced UUO-induced increase interstitial PMN-positive neutrophils. However, UUO-induced upregulation of profibrotic proteins including α-smooth muscle actin (α-SMA) in kidney was not significantly alters by any dose of mercaptoetanol. These data suggest that a pharmacological inhibition through promoting SLC7A11 glutamate/cysteine transporter protects kidneys against oxidative stress and inflammation during unilateral ureteral obstruction. (NRF-2016R1C1B2012080 and NRF-2019R1F1A1041410)

Keywords: Ferrotosis, Mercaptoethanol, Unilateral ureateral obstruction (UUO), SLC7A11, Oxidative stress, Inflammation

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Arctii lappa Fructus Extract Induces Lipogenesis Through SREBP-1 Activation

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Arctii Lappa Fructus has the numerous health benefits, including antioxidant, anti-inflammatory, and anti-carcinogenic properties. Skin lipids are one of several factors that maintain epidermal barrier function. This study was to explore the lipogenic effect by ethanol extract of Arctii Lappa Fructus (EAF) in sebocytes. First, it was confirmed that EAF exhibited high antioxidant activity and collagenase activity inhibition. We found that cholesterol and triglyceride levels of cells by EAF were increased significantly in a dose-dependent manner. Moreover, EAF increased the expression of transcription factor sterol regulatory element-binding protein-1 (SREBP-1) in the cells. These results suggest that EAF induces lipogenesis in cells through the activation of SREBP-1.

Keywords: Arctii Lappa Fructus, Cholesterol, Triglyceride, SREBP-1, Sebocyte

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Korean Red Ginseng Extract prevents dehydroepiandrosterone-induced polycystic ovarian syndrome in rats via inhibiting NF-kB pathway and stimulating Nrf2 pathway

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Role of Korean red ginseng (KRG) on polycystic ovarian syndrome (PCOS) remains unclear. We investigated pre-treatment (daily from 2 hours before PCOS induction) with KRG extract in water (KRGE; 75 and 150 mg/kg/day, p.o.) could exert a favorable effect in a DHEA-induced PCOS rat model. Pre-treatment with KRGE significantly inhibited the elevation of body and ovary weights, the increase in number and size of ovarian cysts, and the elevation of serum testosterone and estradiol levels induced by DHEA. Pre-treatment with KRGE also inhibited macrophage infiltration and enhanced mRNA expression levels of chemokines [interleukin (IL)-8, monocyte chemoattractant protein-1), pro-inflammatory cytokines (IL-1β, IL-6), and inducible nitric oxide synthase in ovaries induced by DHEA. It also prevented the reduction in mRNA expression of growth factors (EGF, TGF-β) related to inhibition of the nuclear factor kappa-light-chain-enhancer of activated B (NF-kB) cell pathway and stimulation of the nuclear factor erythroid-derived 2-related factor 2 (Nrf2) pathway. Interestingly, KRGE or representative ginsenosides (Rb1, Rg1, and Rg3(s)) inhibited the activity of inflammatory enzymes COX-2 and iNOS, cytosolic p-IkB, and nuclear p-NF-kB in lipopolysaccharide-induced RAW264.7 cells, whereas they increased Nrf2 nuclear translocation. These results provide that KRGE could prevent DHEA-induced PCOS via anti-inflammatory and anti-oxidant activities. Thus, KRGE may be used in preventive and therapeutic strategies for PCOS-like symptoms.

Keywords: Korean red ginseng extract; Dehydroepiandrosterone; Polycystic ovarian syndrome

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Icariin Promotes Melanin Synthesis

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We investigated the effects of major constituents of Epimedium koreanum Nakai (Icariin, epimedium A, epimedium B, and epimedium C) on melanin synthesis. Among them, icariin enhanced tyrosinase activity and melanin content. We confirmed that Epimedium koreanum Nakai augmented melanin synthesis via cAMP/PKA. Icariin-induced tyrosinase activity and melanin content were attenuated by PKA inhibitor H89, while melanogenic effect of icariin was further augmented by cAMP analog, dbc AMP. But icariin did not affect the expression of Rab27a involved in melanosome transport. These results suggest that icariin promotes melanogenesis through PKA.

Keywords: Icariin, Epimedium koreanum Nakai, Tyrosinase, PKA, Rab27a

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P127

Novel prognostic factor for uveal melanoma: bioinformatics analysis of three independent cohorts

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Uveal melanoma (UVM) is rare cancer of the eye developing the choroid, ciliary body or iris in the United States, Nonetheless, It has steadily diagnosed about 1000 people every year in the USA. Even though the size, thickness, and metastasis are used as an important

factor in predicting patients' prognosis, they are insufficient. The present study identified significant genes of UVM for prognostic markers using independent three cohorts. Gene expression profiles are obtained from The Cancer Genome Atlas and Gene Expression Omnibus that can download gene expression data and clinical information. To identify prognostic genes, we performed survival analyses in three independent cohorts (Log-rank test, Kaplan-Meier survival curve, and cox proportional hazard regression analysis). Thereafter, we selected hub genes by protein-protein interaction (String, Cytoscope). As a result, we identified a set of genes that are statistically significant (Oncogenic like genes, 37; Tumor suppressive like genes, 14). Furthermore, NDUFV2, NDUFB9, CYC1, and CTNN1 showed strong network connections as hub genes. In conclusion, although the additional experiments are required, the genes would be playing the role of prognosis factor.

Keywords: Uveal melanoma, Gene expression, Survival analysis, Protein-protein interaction, Hub gene

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Prognostic role of high cathepsin d expression in breast cancer: a systematic review and meta-analysis

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Background: High CTSD is known to be associated with a poor prognosis in breast cancer, but the results of many studies are controversial. We assessed the associations between high CTSD expression and worse prognosis by conducting a meta-analysis. **Methods:** A comprehensive search strategy was used to search relevant literature in PUBMED, EMBASE in September 2018. This meta-analysis was carried out using Review Manager 5.3 and hazard ratios (HRs) with 95% confidence intervals (CI) was applied to perform a quantitative meta-analysis. **Results:** A total 15,355 breast cancer patients from 26 eligible studies were included in this meta-analysis. Significant associations between elevated CTSD protein expression and poor overall survival (OS) (HR = 1.61, 95% CI: 1.35-1.92, P < 0.0001) and disease-free survival (DFS) (HR = 1.52, 95 % CI:1.31-2.18, P < 0.001) were observed. In subgroup analysis for DFS, high CTSD was significantly associated with poor prognosis in node positive (HR = 1.38, 95% CI: 1.25-1.71, P < 0.00001), node negative group (HR = 1.78, 95% CI:1.39-2.27, P < 0.0001), early stage (HR = 1.73, 95% CI:1.34-2.23, P < 0.0001), adjuvant chemotherapy (HR = 1.60, 95% CI:1.21-2.12, P < 0.001) patients. One of the interesting results in our subgroup analysis is the tamoxifen drug response. The patients with high CTSD had a low risk of relapse (HR = 0.71, 95% CI:0.52-0.98, P = 0.04) through treatment with tamoxifen, in contract, the patients with low CTSD had a high risk of relapse (HR = 1.50, 95% CI:1.22-1.85, P = 0.0001) through treatment with tamoxifen. **Conclusions:** Our meta-analysis suggests that high expression levels of CTSD are associated with a poor prognosis in breast cancer. Based on our subgroup analyses, we believe that high CTSD expression can help clinicians to develop therapeutic strategies.

Keywords: Cathepsin D, Breast cancer, Disease-free survival, Overall survival, Meta-analysis, Systematic review

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P129

Three dimensional cell culture using a decellularized porcine liver extracellular matrix derived hydrogel scaffold

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One of the most crucial problems of the generally used two-dimensional (2D) cell culture method is that it does not accurately depict the three-dimensional biological environment. To solve this problem, it is essential to fabricate three-dimensional (3D) cell culture techniques which not only support long term stable culture of cells but also maintain greater cellular activity of the cultured cells than do 2D cell culture techniques. In the present study, a composite

hydrogel containing decellularized PLE-1-1 and MF-1-1 was constructed for use in 3D culture of thymic epithelial cells (TEC). The cytotoxicity and cell proliferation was evaluated by WST-1 assay. The efficiency of spheroid formation was assessed by phase contrast microscopy and confocal microscopy. The gene expressions associated with activity of TECs was examined by RT-PCR. It was found that the PLE-1-1 and MF-1-1 composite hydrogels not only facilitated the proliferation and spheroid formation of TECs, but also stimulated the expression of genes involved in TEC activity compared to the PLE-1-1 alone or MF-1-1 alone hydrogel. Thus, these results suggest that PLE-1-1 and MF-1-1 composite hydrogel will be a useful model of 3D cell culture for TECs and may have wide applicability for 3D culture of various cell types.

Keywords: 3D cell culture, Hydrogel, Spheroid, Decellularized, Extracellular matrix

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P130

Construction of 3D-rendering imaging of rat brain with ischemia model using planar FMMD technique

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The occlusion of the major cerebral artery usually results in brain hypoxic-ischemic injury which evokes neuroinflammation and microglial activation. Activated microglia are considered as one of the sources of multiple neurotoxic factors, such as reactive oxygen species (ROS), in the central nervous system (CNS). We present a 3D-rendering brain imaging technique for an experimental rodent model of cerebral ischemia, based on 2D magnetic images of superparamagnetic iron oxide nanoparticles (SPIONs) using the planar frequency mixing magnetic detection (p-FMMD) technique. A rat model of cerebral ischemia was established by unilateral middle cerebral artery occlusion with reperfusion (MCAO/R) injury. 2,3,5-triphenyltetrazolium chloride (TTC) staining was performed to demonstrate irreversibly damaged ischemic brain tissues, and double immunofluorescent labeling of OX6 (activated microglial marker) and ethidium (ROS marker) was conducted to confirm ROS generation in the activated microglia in the infarcted brain region. The ischemic brain sections treated with OX6-conjugated SPIONs were scanned using our p-FMMD system, yielding 2D images on the basis of nonlinear magnetic characteristics inherent in SPIONs. The p-FMMD signal images show a remarkable coincidence with the TTC staining and the double immunofluorescent labeling. Furthermore, we developed a 3D-rendering brain imaging process based on the 2D p-FMMD signal images. The 3D reconstructed model was compared with that of magnetic resonance imaging (MRI), showing a spatial coincidence of the ischemic regions between p-FMMD and MRI model. In this study, we have successfully conducted a feasibility test on whether our p-FMMD technology, a technique for signaling and imaging based on the non-linearity of SPIONs, can be used to mediately visualize the ischemic brain region by detecting the activated microglia in MCAO/R animal model. Therefore, our method might allow better analysis of the pathophysiology of ischemic stroke through molecular imaging. Furthermore, we propose that this magnetic particle imaging (MPI) technique detecting the nonlinear magnetization properties of SPIONs could be applied not only to a stroke model but also various types of pathophysiological studies as a new bio-imaging tool.

Keywords: ROS, p-FMMD, Microglia, MCAo, SPION

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합동시신추모식 참석 여부가 의과대학생들의 해부실습에 미치는 영향

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해부학은 임상의학의 기초가 되는 학문이기 때문에 해부실습은 의과대학학생들이 꼭 참석해야 하는 실습 중에 하나이다. 대부분의 의과대학에서는 모든 해부실습이 종료되고 난 후 합동 시

신 추모식을 진행하여 학생들이 고인에 대한 명복을 기리도록 한다. 따라서 해부실습과 합동 시신 추모식은 밀접한 연관이 있을 것으로 보인다. 하지만 해부실습을 진행하기 전 합동 시신 추모식을 참석하는 것이 학생들의 해부실습에 어떤 영향을 미치는 지에 대한 연구가 없다. 본 연구에서는 합동 시신추모식에 참석하고 난 후 실습과정 중 학생들이 겪는 정서적, 감정적 경험에 대해 파악하고 합동 시신추모식 참석 여부에 따라 학생들에게 어떤 영향을 미치는 지 확인한다. 2018학년도 해부학교육을 참여한 예과2학년 학생 69명을 대상으로 자유형식의 보고서를 받아서 이를 3명의 검토자가 확인하여 눈 통증, 코 통증, 두통, 식욕부진, 정서불안(땀), 역함(메스꺼움) 등의 신체적인 증상이나 무서움, 징그러움, 두려움, 슬픔 혹은 미안함 등의 감정, 또는 감사함(존경심), 직업사명감, 학습의욕, 협동심 등의 긍정적 영향들의 여부에 따라 분석하였다. 그 결과, 해부학실습에 대한 긍정적인 영향으로 전체참여 인원 69명 중, 학습의욕 32명(46.4%), 감사함 혹은 존경 30명(43.5%), 사명감 9명(13.0%), 협동심 8명(11.6%)등을 보였다. 합동 시신추모식에 참석한 학생 37명 중 34명(91.9%), 참석하지 않은 학생 32명 중 22명(68.8%)이 긍정적인 영향을 받았다. 합동 시신추모식에 참석한 경우 긍정적인 영향을 받는 비율이 높았고, 통계적으로도 유의하였다(pvalue<0.05). 이러한 연구 결과를 바탕으로 합동 시신추모식에 참석하여 긍정적인 영향을 유도하고 인간의 존엄성과, 생명윤리 등에 대한 인식을 유도하는 것이 필요하고 해부실습 전에 추모식 참석을 권장하는 것이 좋을 것으로 사료된다. 이에 따라 본 연구는 의과대학생들이 해부실습에 참여 하기 전 합동 시신 추모식에 참석하여 실습참여 후 나타날 수 있는 여러 영향에 대해 파악함으로써 효과적인 해부실습교육의 방향을 모색하기 위하여 필요한 기초자료를 제공할 수 있다.

Keywords: Anatomy, Cadaver, Memorial service, Cadaver dissection, Medical students

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