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Hankok Medical Science Foundation (since 1971)

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2016
ANNUAL MEETING

KOREAN ASSOCIATION OF ANATOMISTS

제66회
대한해부학회 학술대회
순서 및 초록

2016. 10. 19 ~ 21
양양 오색그린야드호텔

주관
대한해부학회

후원
한국의학학술지원재단
한곡의학장학회

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	17:00 ~ 18:00	Committee activity (각 위원회 활동)	
10. 20 목	08:30 ~ 08:45	개회사, 축사 (2층, 그린야드홀)	
	08:45 ~ 10:30	구연발표 1 (2층, 그린야드홀) 좌장: 정민석(아주대), 박정현(강원대)	구연발표 2 (지하1층, 무궁화홀) 좌장: 유임주(고려대), 노구섭(경상대)
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	10:40 ~ 11:20	Plenary Lecture 1 (2층, 그린야드홀) 좌장: 오창석(성균관대) Of teeth and jaws: adventures in research with stem cells and CT scans 발표자: Beverley Kramer (University of the Witwatersrand, Johannesburg, 세계해부학회장)	
	11:20 ~ 12:20	해부학교육 심포지엄 (2층, 그린야드홀) 좌 장: 허영범(경희대), 조경제(경상대) 발표자: 윤 식(부산대) 조성원(연세대) 이종은(연세대) 이우영(가톨릭대)	
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	14:30 ~ 17:30	심포지엄 1 (2층, 그린야드홀) Future of the Gross Anatomy and the Clinically Orieted Researches 좌 장: 이혜연(연세대), 한후재(이화여대) 발표자: 왕규창(서울대) 윤영은(연세대) 금웅섭(연세대) 박성용(아주대) 박현호(강남세브란스)	심포지엄 2 (지하1층, 무궁화홀) Current Trends in Cancer Stem Cell Research 좌 장: 유영현(동아대), 한장희(강원대) 발표자: 오세옥(부산대) 김형기(고려대) 정재호(연세대) 임대식(KAIST) 오일환(가톨릭대)
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10. 21 금	08:45 ~ 10:30	구연발표 3 (2층, 그린야드홀) 좌장: 이종은(연세대), 한승호(중앙대)	구연발표 4 (지하1층, 무궁화홀) 좌장: 한기환(이화여대), 오세옥(부산대)
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	11:30 ~ 12:20	Plenary Lecture 2 (2층, 그린야드홀) 좌장: 허대영(인제대) NMDA receptor dysfunction in autism spectrum disorders 발표자: 김은준(KAIST)	
	12:20 ~ 13:00	점심	
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	16:30 ~	제66회 정기총회 (지하1층, 컨벤션홀)	

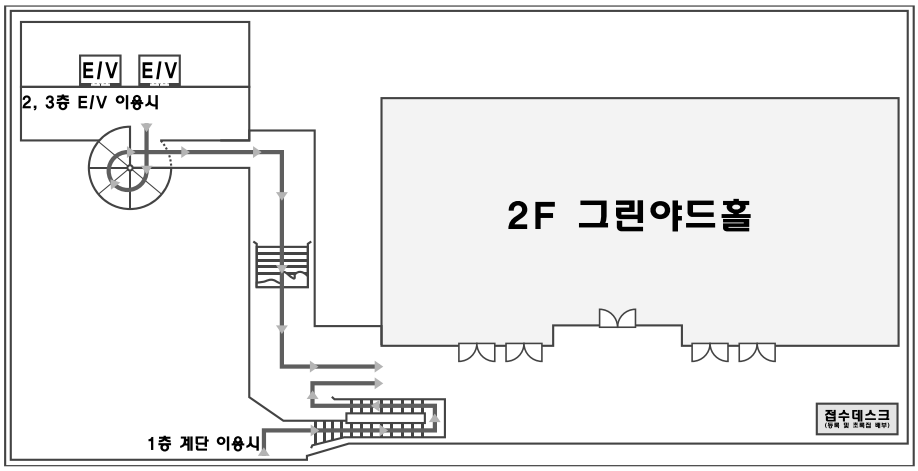
학술대회장 배치도

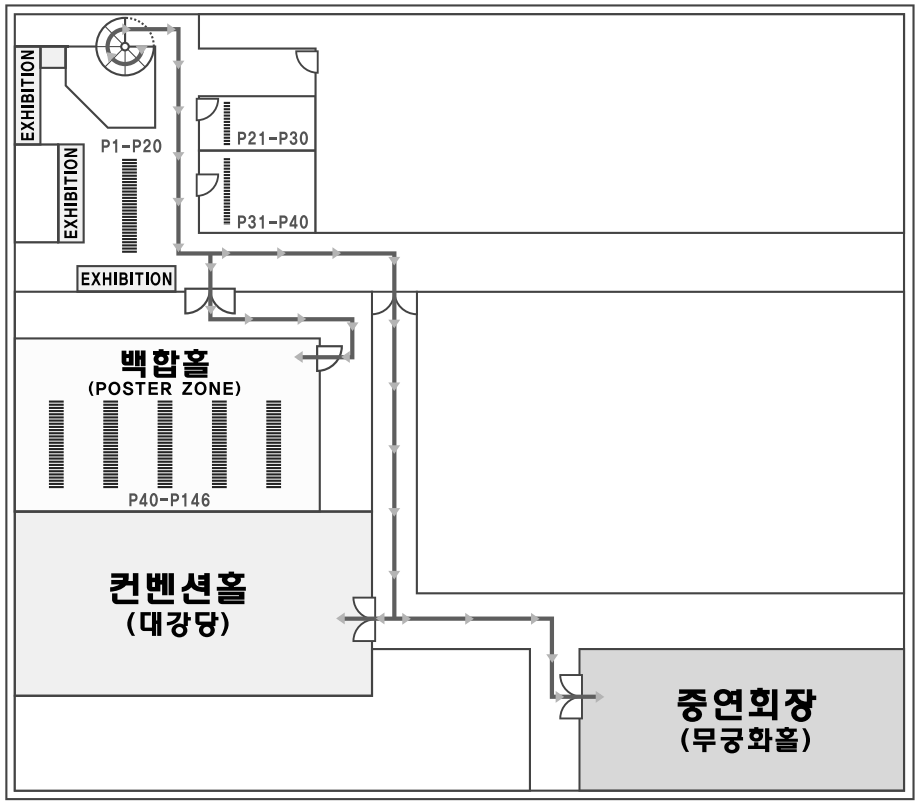
2F 그린야드홀 (등록 및 초록접배부)

1F 호텔안내데스크 (Lobby)

B1 무궁화홀,전시부스, 포스터,Coffee Booth

B2 소연회장(난홀,국홀)





Plenary Lecture-1

2016년 10월 20일(목) 10:40 ~ 11:20
그린야드홀

좌장 오창석 성균관대

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

Of teeth and jaws: adventures in research with stem cells and CT scans

Beverley Kramer • School of Anatomical Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

PL-1

Of teeth and jaws: adventures in research with stem cells and CT scans

Beverley Kramer

School of Anatomical Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

The developing tooth is a fascinating organ, demonstrating reiterating epithelial-mesenchymal interactions that are not unlike those found during the development of other organ systems. However, the resulting tooth is unique in its structure, in its diphyodonty in humans and in its relationship to the developing mandible, itself a dynamic structure. Once the secondary tooth is lost in humans, it cannot currently be replaced, other than by an artificial tooth. In addition, its loss has a marked impact on the bone in which it is housed, with consequences for food intake and mastication. The loss of teeth thus affects the quality of life in humans. Some of our studies have therefore been directed to biological tooth replacement. This overview describes attempts to induce tooth development through the use of mouse stem cells in combination with the ectomesenchyme of the mouse jaw. In addition, we utilized a non-mammalian vertebrate with multiple sets of replacement teeth (polyphyodonty) to provide insight into factors affecting tooth replacement, as a possible mechanism for tooth regeneration in humans in the future. Lastly, utilizing microfocus x-ray computed tomography of human neonatal and postnatal mandibles we explored the role of the developing dentition in the change of the structure of the mandible.

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Plenary Lecture-2

2016년 10월 21일(금) 11:30 ~ 12:20
그린야드홀

좌장 허대영 인제대

PL-2 **11:30-12:20**
NMDA receptor dysfunction in autism spectrum disorders
김은준 • KAIST 생명과학과, IBS 뇌과학연구단

PL-2

NMDA receptor dysfunction in autism spectrum disorders

Eunjoon Kim

Department of Biological Sciences, KAIST and Center for Synaptic Brain Dysfunctions, IBS, Daejeon 305-701, Korea

A large number of synaptic proteins have recently been associated with diverse neuropsychiatric disorders, including autism spectrum disorders (ASDs), schizophrenia, attention deficit hyperactivity disorder, and mood disorders. ASDs represent a group of neurodevelopmental disorders characterized by impaired social and communication deficits and restricted and repetitive interests, behaviors, and activities. Although a large number of ASD-related genetic variations have been identified, only a small number of them have been verified for their causality by approaches including mouse genetics. In addition, neural mechanisms underlying the development of ASDs remain largely unknown. Synaptic scaffolding proteins at excitatory synapses interact with various other proteins including receptors and signaling molecules in order to couple receptor activation with downstream signaling events. In this presentation, I will discuss how defects in some of the excitatory synaptic scaffolding proteins are associated with NMDA receptor dysfunctions and autistic-like behavioral abnormalities in mice.

References

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2. Lee E, Lee J, and Kim E. (2016). Excitation/inhibition imbalance in animal models of ASDs. Biol Psychiatry, in press.
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4. Lee EJ, Lee H, Huang TNE, Chung C, Shin W, Kim K, Koh JY, Hsueh YP, and Kim E. (2015). Trans-synaptic zinc mobilization improves social interaction in two mouse models of autism through NMDAR activation. Nat Commun 6:7168.
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Special Lecture

2016년 10월 21일(금) 10:40 ~ 11:20
그린야드홀

좌장 황영일 서울대

SL **10:40 ~ 11:20**
STAMP2-mediated alleviation of lipid accumulation and insulin resistance
유영현 • 동아대학교 의과대학 해부학교실

SL

STAMP2-mediated alleviation of lipid ac cumulation and insulin resistance

유영현 /동아대학교 의과대학 해부학교실

My laboratory members have been studying the role of STAMP2 focusing on its lipid accumulation and insulin resistance. Previous studies demonstrated its critical role in metabolism and modulating inflammatory signals. We first studied the hepatic role of STAMP2. I first hypothesized that STAMP2 is involved in non-alcoholic fatty liver disease (NAFLD) pathogenesis. We examined our hypothesis using human NAFLD patient pathology samples and a high-fat diet (HFD)-induced NAFLD mouse model. The molecular mechanism underlying hepatic STAMP2-mediated lipid imbalance was explored using an oleic acid (OA)-induced NAFLD in vitro model. Noticeably, the expression level of STAMP2 protein was reduced in the livers obtained from NAFLD patients and HFD-induced NAFLD mice. In vivo knockdown of hepatic STAMP2 by siRNA accelerated hepatic steatosis and insulin resistance in mice fed a HFD. Conversely, the delivery of adenoviral STAMP2 (Ad-STAMP2) improved hepatic steatosis in HFD-induced NAFLD mice. The expression of lipogenic or adipogenic factors was increased in both in vitro and in vivo NAFLD models but was reversed by Ad-STAMP2. Adenoviral overexpression of STAMP2 improved insulin resistance in the HFD-induced NAFLD mice. *In vivo* and *in vitro* assays demonstrated that STAMP2 modulates insulin sensitivity and glucose metabolism and that STAMP2 counteracts OA-induced insulin resistance by modulating insulin receptor substrate-1 stability. Our findings indicate that STAMP2 may represent a suitable target for interventions targeting NAFLD. We next studied the role of STAMP2 in polychlorinated biphenyls (PCBs)-induced insulin resistance because the mechanism underlying PCBs-induced insulin resistance has remained unsolved. PCBs significantly promoted adipocyte differentiation and increased the LD size in 3T3L1 adipocytes. In mice, PCBs increased adipose mass and adipocyte size. Furthermore, PCBs induced insulin resistance ***in vitro*** and *in vivo*. Expression of fat-specific protein 27 (Fsp27) was increased in PCB-treated 3T3-L1 adipocytes and mice. Depletion of Fsp27 by siRNA resulted in the inhibition of LD enlargement and attenuation of insulin resistance in PCB-treated 3T3-L1 adipocytes. The role of STAMP2 in PCBs exposure-induced lipid accumulation was further investigated. At the end of this special lecture, I am going to briefly introduce our two STAMP2 posters presented at 2016 meeting.

유영현 | 동아대학교 의과대학 해부학교실 및 미토콘드리아허브제어연구센터 • yhyoo@dau.ac.kr

해부학교육 심포지엄

2016년 10월 20일(목) 11:20 ~ 12:20
그린야드홀

좌장 허영범 경희대 • 조경제 경상대

ES-1 **11:20-11:35**
가상현미경을 이용한 조직학실습 : 7년간의 경험
윤 식 • 부산대학교 의과대학 해부학교실

ES-2 **11:35-11:50**
치과대학 조직학실습에서 조별 oral test의 활용
조성원 • 연세대학교 치과대학 구강생물학교실

ES-3 **11:50-12:05**
조직학 실습에서 현미경 실습과 컴퓨터–기반 실습의 활용:
연세대학교 의과대학 사례
이종은 • 연세대학교 의과대학 해부학교실

ES-4 **12:05-12:20**
기증시신을 이용한 의학과 4학년의 임상술기실습
이우영 • 가톨릭대학교 의과대학 해부학교실 · 가톨릭응용해부연구소

ES-1 가상현미경을 이용한 조직학실습 : 7년간의 경험

윤 식 /부산대학교 의과대학 해부학교실

현재 많은 의과대학에서 현미경을 이용한 전통적인 조직학실습은 가상현미경을 이용한 컴퓨터 시스템 기반의 소프트웨어 교육 도구에 의해 점점 대치되어 가고 있는 추세이다. 본 연구는 그간 부산대학교 의학전문대학원에서 약 7년간 이루어진 가상현미경실습에 대한 경험을 소개한 것이다. 비록 가상현미경을 이용한 조직학실습에 대한 역사는 실제 현미경을 이용한 조직학실습 기간에 비해 훨씬 짧지만 해를 거듭할수록 조직학실습실에서 가상현미경의 중요성이 점점 증가되어 간다는 점은 명확하다고 할 수 있다. 만약 가상현미경을 이용한 조직학실습 추세가 계속되어 간다면, 많은 의과대학에서 더 이상 실제 현미경의 사용 방법에 대해 교육을 하지 않을 수도 있을 것이다. 변화되고 있는 조직학실습 교육 방법에 대한 장단점을 잘 파악함으로서 향후 더욱 효과적인 조직학 교육 시스템을 도입하여야 할 것이다.

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ES-2 치과대학 조직학실습에서 조별 oral test의 활용

조성원 /연세대학교 치과대학 구강생물학교실

연세대학교 치과대학 조직학은 크게 (일반)조직학과 구강조직학으로 나누어진다. 조직학은 본과 1학년 1~2 쿼터동안 진행되고, 구강조직학은 치과대학의 여러 과목에 포함되어 있으며, 1학년 3쿼터와 2학년 1쿼터 때 진행된다. 이중 조직학은 강의, 실습 강의, 실습 순으로 진행된다. 실습은 조 단위로 진행한다. 한 조는 다섯 명으로 구성된다. 한 조는 광학현미경 3대와 가상현미경 2대를 공유한다. 가상현미경 용 이미지 파일은 원래 보유 중이던 슬라이드를 스캔하여 제작하였다.
조직학 실습의 목적을 다음과 같이 설정하였다. 모든 학생은 현미경이나 가상현미경에서 특정 구조를 찾을 수 있어야 한다. 모든 학생은 특정 구조에 대해 의학용어 및 조직학적 용어를 이용하여 다른 사람에게 잘 설명할 수 있어야 한다. 모든 학생은 현미경을 보지 않더라도 설명만 듣고도 구조의 명칭을 말할 수 있어야 한다.
이러한 목적을 달성하기 위해서 우리대학에서는 2013년부터 실습시간에 oral test를 실시하고 있다. oral test는 다음과 같은 형식으로 진행하였다. 먼저 oral test 진행자 (조교 또는 교수)는 그 조의 모든 학생에게 문제를 제시한다. 진행자는 각 조의 첫 번째 학생에게만 답(특정 구조의 명칭)을 보여준다. 첫 번째 학생은 현미경 또는 가상현미경에서 그 구조를 찾는다. 첫 번째 학생이 현미경 또는 가상현미경에서 찾은 구조를 두 번째, 세 번째, 네 번째 학생은 보고, 그 구조에 대해서 의학용어를 사용하여 다섯 번째 학생에게 순서대로 설명해 준다. 다섯 번째 학생은 세 학생의 설명을 듣고, 답을 말한다. 현미경에서 정확한 구조를 찾았고, 구조에 대한 설명이 정확하며, 최종 답이 정확한 경우 그 문제를 맞는 것으로 간주한다. 매 실습시간 마다 문제 수는 총 4문제이며, 새로운 문제마다 학생의 역할을 바꾸어 진행한다. 예를 들어, 다음 문제에서는 두 번째 학생이 현미경을 맞추고, 세 번째, 네 번째, 다섯 번째 학생이 설명을 하며, 첫 번째 학생이 답을 말하도록 한다.
우리 대학 본과 1학년 학생의 정원은 매년 평균 65명 정도이며, 13개의 조로 편성하였다. oral test 진행자는 가급적 세 명이상으로 배정하였으며, 모든 진행자는 문제, 슬라이드 번호, 힌트, 답이 적혀있는 실습 가이드에 따라 동일한 문제를 제시하고, 동일한 기준으로 진행하려고 노력하였다. oral test를 시행한 결과 학생들의 실습에 대한 자세는 적극적으로 바뀌었고, 실습시간 내내 조별 학습이 활성화되었으며, 실습 내용뿐만 아니라 강의 내용도 숙지하게 되는 등 학습 효과가 높게 나타났다.
우선은 각 대학의 기존 실습 진행방식에 oral test를 부분적으로 적용하실 것을 제안한다. 각 대학의 상황에 맞게 조별 학생 수, 문제 수, 문제 당 시간 등을 변형시키면서 최적화 조건을 찾으신다면, oral test가 매우 효과적인 실습 방법으로 쓰일 것으로 생각된다.

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ES-3 조직학 실습에서 현미경 실습과 컴퓨터-기반 실습의 활용: 연세대학교 의과대학 사례

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의과대학에서의 해부학교육은 전체 의과대학 교육 방향의 전환에 맞춰 최근 몇 년 동안 많은 변화가 있었다. 대한기초의학협의회에서 제시하고 있는 의학교육의 목표는 학생들에게 미래 사회가 요구하는 의료인의 기본자질과 덕목이 무엇인지를 알려주고, 이들이 의과대학 교육기간 중에 이런 기본자질과 덕목을 성공적으로 터득하는 데에 필요한 교육여건과 교육과정을 마련하는 데에 중점을 두고 있다. 따라서 의과대학에서의 교육의 방향은 지식전수에서 지식창출로, 그리고 평생교육과 자기주도 학습으로 변화되고 있다. 이와 같은 의학교육 방향의 변화를 위해 과목 내에서는 통합교육을 통한 연계성을 추구하고, 문제중심학습(problem-based learning) 과 같은 교육과정의 다양화를 통해 학생들에게 더 많은 자율성을 제공함으로써 학생중심의 교육을 제공하고 있다. 연세대학교 의과대학에서도 의학교육 방향의 변화에 맞춰 CDP2013 교육과정을 통해 학생중심(student-oriented learning), 통합교육(integrated learning), 성과중심(outcome-based learning) 및 연구중심교육(research-oriented learning)을 추구하고 있다. 이와 같은 의학교육과정의 변화로 조직학 교육과정은 이전 교육과정에서의 조직학 총론에 해당하던 부분들은 '세포구조와 기능'이라는 과목으로 조직학과 생리학이 통합되어 진행되고 있고, 조직학 각론 부분의 수업은 순환기계통, 호흡기계통, 소화기계통, 비뇨생식기계통 및 내분비계통의 통합과목 내에서 이루어지고 있다. 한편 이와 같은 통합 교육과정 내에서 조직학 수업 시간이 감소 되었고, 실습시간 역시 일부 감소되었다. 조직학 실습의 효율성과 내실화를 위하여 연세대학교 의과대학에서는 조직학 실습과정을 현미경실습과 컴퓨터 실습을 병행하여 진행하고 있다. 조직학 실습과정은 조직학의 지식 전수뿐 아니라, 의학교육 내에서 현미경을 다루는 방법 및 조직의 구성을 단계적으로 접근하는 방법 등을 교육하는 것도 중요하다. 따라서 총론을 공부하는 시기에는 현미경실습을 통해 학생들에게 조직을 이루고 있는 기본 구조들이 어떻게 구성되어 있는 지를 단계적으로 찾아가며 학습하도록 하고 있고, 총론으로 들어가면서는 각 장기나 조직의 구조들을 좀 더 넓은 시야에서 다양하게 관찰할 수 있도록 조직 슬라이드를 스캔 한 자료들을 가지고 컴퓨터기반으로 실습할 수 있는 환경을 제공하고 있다. 조직학 실습 시간 중 이러한 두 가지 실습 방법을 통해 학생들에게 조직학의 기본 구조에 대한 지식뿐 아니라, 실습을 통한 의학적 교육 성과를 성취할 수 있는 다양한 학습의 기회를 제공할 수 있기를 기대해 본다.

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ES-4 기증시신을 이용한 의학과 4학년의 임상술기실습

이우영 /가톨릭대학교 의과대학 해부학교실 · 가톨릭응용해부연구소

가톨릭대학교 의과대학은 기초의학과 임상의학에 대한 모든 강의와 임상실습을 마친 의학과 4학년 학생들이 의료 현장에 나가기 전에 본인의 의료 술기와 해부학 지식을 보다 발전시키고 의사로서의 역량과 합리적 사고 능력 함양하기 위해 기증시신을 이용한 임상술기실습 과정을 2014년에 개설하였다. 이번 심포지움에서는 이렇게 개설된 '응용해부술기실습'과정이 현재까지 수행한 내용과 결과를 소개하고자 한다.

응용해부술기실습은 총 3일의 강의 및 실습 과정과 1회의 시험으로 이루어진다. 1일차에는 영상의학교실에서 중요 계통 별 영상의학 지식을 강의하고 아울러 참여 임상의학교실에서 2, 3일차에 수행할 술기에 대한 간단한 지식을 강의한다. 2일차에는 기증시신 한 구 당 약 12명의 학생이 한 조를 이루고 8 종류의 임상술기를 담당하는 임상교수가 각 조를 1시간씩 돌면서 학생들은 각 술기를 실습한다. 3일차 오전에는 참여를 신청한 임상과의 수술 방법을 기증시신을 이용하여 시연하고 학생들은 자유롭게 참관한다. 3일차 오후에는 신경외과학교실에서 개두술을 시연하고 성형외과학교실의 감독 하에 학생들이 직접 기증시신에 개방되어 있는 모든 부위를 봉합하는 실습을 한다. 시험은 영상의학과 술기 내용 중 중요한 지식을 확인 수준에서 총 48문항에 대해 CBT 방식으로 치른다.

지난 3년간 응용해부술기실습에 대한 학생들의 설문 결과를 보면 전반적인 과정에 대한 만족도는 77 - 81 %이었다. 자유의견에서 주목할 만한 내용은 실습과정의 시행 시기였다. 현재 과정은 임상실습이 끝난 8월말에 시행하고 있어 국가고시를 앞둔 의학과 4학년들에게 부담으로 작용하고 있다. 그 외 짧은 실습 기간과 실습을 제외한 강의와 시험의 필요성에 대해 의문을 제기하는 의견이 있었다.

응용해부술기실습 과정은 각 임상교실에게 수련의의 실습 참여 기회를 제공하고 있어 특히 3일차 수술 시연 시 다수의 수련의 교육을 실시할 수 있어 임상교실로부터 좋은 호응을 얻고 있다. 다만 한정된 시신 수와 기간으로 수련의 참여 기회를 제한될 수밖에 없는 한계성이 존재한다.

개설된 이후 3년간 응용해부술기실습 과정은 해부학교실과 임상교실의 적극적인 참여와 배려, 학교와 병원의 제도적 지원을 통해 원활히 시행할 수 있었다. 향후 가톨릭대학교 의과대학은 시신 이용이 적합한 필수 술기의 종류 선정 및 확대, 참여 임상교실의 확대, 시행 시기와 기간, 수련의 교육 확대 등의 문제점 보완하여 응용해부술기실습이 양질의 임상술기실습이 되도록 노력하고 있다.

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심포지엄-1

2016년 10월 20일(목) 14:30 ~ 17:30
그린야드홀

Future of the Gross Anatomy and the Clinically Orieted Researches

좌장 이혜연 연세대 • 한후재 이화여대

S1-1 **14:30-15:00**
Future of Gross Anatomy –
Clinically Oriented Anatomic Researches
왕규창 • 서울대학교 의과대학 신경외과학교실

S1-2 **15:00-15:30**
da Vinci Robot still wants to know the gross anatomy
윤영은 • 연세대학교 의과대학 비뇨기과학교실

S1-3 **15:30-16:00**
암환자의 방사선 치료에서 해부학의 중요성
금웅섭 • 연세대학교 의과대학 방사선종양학과

16:00-16:15
Intermission

S1-4 **16:15-16:45**
식도암에서의 해부학적 연구
박성용 • 아주대학교 의과대학 흉부외과학 교실

S1-5 **16:45-17:15**
Anatomy for Skull Base Surgery & Recent Advances in Neurosurgery
박현호 • 연세대학교 강남세브란스병원 신경외과학

17:15-17:30
Q&A

S1-1

Future of Gross Anatomy – Clinically Oriented Anatomic Researches

왕규창 /서울대학교 의과대학 신경외과학교실

Researches on gross anatomy which opened a dawn of modern medical science as well as the 'Renaissance' several hundred years ago is currently regarded as an old-fashioned, almost exhausted, 'historical' branch of medical science like an abandoned dead mine. Even many of faculty members of medical colleges do not pay attention to the importance of gross anatomy except its role in basic medical education.

Gross anatomy is not a field in dusk. Still up to now, however, gross anatomy is an important tool for the advance of medical science especially in the field of surgery. With advent of new methods of cross sectional and functional imaging, and complex surgical technologies such as updated stereotaxy, navigation, endoscopy, intraoperative physiologic monitoring, special dyes for visualization of certain structures, intraoperative imaging and robots, the boundary of surgical journey was tremendously expanded during the last decades. It has impacts on the clinically oriented anatomic researches and education. Because new technology shed the light on the areas of human body where previously ignored, many surgeons want knowledge on the exact dimension and spatial relationship between structures of interest, and its variations. Nowadays, the cadaver dissection is not just an interest of junior medical students but also of established surgeons who have to explore specific areas of their expertise. The level of knowledge and experience they need is totally different from that of medical students. Accordingly, the Korean government modified the regulation on the persons who can dissect the cadavers to include medical doctors who are not anatomists or pathologists. In this process of research and education on gross anatomy, of course, anatomists should be the leaders.

The medical colleges need an intimate anatomist-clinician interaction. The spectrum of researches in medical science is wide, ranging from humanity, social, basic natural, to highly complex technical or molecular ones. Among those, what only medical colleges can do has the highest priority and it is one of the main duties of medical colleges for advance of science in general. In terms of this aspect, intimate anatomist-clinician interaction is a central axis. We do not think that all, or majority of the faculty members of Department of Anatomy should be M.D.'s. But we worry about the fact that the number of M.D.'s are far below the level desired in basic medical science even in the field of anatomy. Introduction of plans to promote M.D.s to join the basic medical research and education is a vital missions in all medical colleges in Korea. Permission of M.D.'s in basic medical science to spend a part of their working hours in clinical activities may have advantages though it also has some 'risks'. It depends on 'persons'. To enhance competitiveness of medical colleges, concentration on really medical issues is one of the best options.

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S1-2

da Vinci Robot still wants to know the gross anatomy

윤영은 /연세대학교 의과대학 비뇨기과학교실

During open prostatectomy, all of the anatomic structures around the prostate could not be seen. Even though the anatomy around the pelvis was known, because of visual angles and magnification, e.g., the fine structure in the posterior aspect of the prostate remained elusive during surgery. Direct vision of anatomy is sometimes not possible during open radical prostatectomy, thus there has been a large gap between surgery and anatomy. However, after introduction of da Vinci surgical system, it is possible to view almost all of the pelvic anatomic structures during robotic prostatectomy. This enables the surgeon, in theory, to perform the operation with respect to the anatomic findings using the multi-jointed instruments, compared with the conventional laparoscopic radical prostatectomy.

Robotic surgery is increasingly being used in the world. In urology, robotic surgery is most frequently applied in prostate, urinary bladder, kidney and adrenal gland diseases. Surgical robot gives the advantages of precise, gentle and quick tissue handling with three-dimensional (3D) magnified image capability, higher grades of wristed hand movements and decreased hand tremor. Therefore, all details of the anatomical structures could be demonstrated nicely in robotic surgery with magnified vision. The surgical treatment of prostate cancer has changed remarkably because of better knowledge of prostate anatomy, which have improved cancer control and functional results. These results are closely related to the identification of a multilayered periprostatic fascia, which permits definition of dissection planes for complete oncologic excision of the prostate and preservation of both the external urinary sphincter responsible for urinary continence and the autonomic nerves responsible for erectile function and urinary control. Lack of identification of these structures during radical prostatectomy may potentially result in inferior oncologic results as well as in a higher risk of incontinence or erectile dysfunction.

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S1-3

암환자의 방사선 치료에서 해부학의 중요성

금웅섭 /연세대학교 의과대학 방사선종양학과

The first linear accelerators were applied to the clinic in the 1950s. Treatment target area was determined by plain radiography, but accuracy of localization of tumor was relatively crude. Knowledge of bony and surface anatomy was an essential skill for radiation oncologists. Twenty years later the CT scanners were incorporated into patients to reveal the position of inner structures. It did not take long for the obvious application to tumor localization to enrich radiotherapy planning. Radiotherapy education has also evolved so that radiotherapy residents must complement therapy knowledge of surface anatomy and 2-dimensional radiograph interpretation with cross-sectional anatomy and CT image interpretation. Understanding anatomy on CT image 2-dimensional recognition is basic requirement to demarcate target volume and normal organ in radiotherapy planning.
Keywords: Clusterin, Pancreas, Regeneration, Diabetes

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S1-4

식도암에서의 해부학적 연구

박성용 /아주대학교 의과대학 흉부외과학 교실

식도암 수술은 일반 흉부영역에서 행해지는 수술 중 가장 morbidity, mortality가 높은 수술로 알려져있다. 통상 수술후 3% 내외의 사망이 발생하고, 50%의 환자들에서 합병증이 발생한다. 최초로 식도암에서 수술적 치료가 시행된 것은 약 100여년전으로, 그 이후 수술에 있어서의 발전이 이루어져왔으며, 수술의 발전은 해부학적인 지식이 확대함에 따라서 이루어져왔다.

식도암에서 적절한 절제 범위에 대해서는 많은 이견이 있었으나, 최근에 이루어진 해부학적인 이해를 통해서 적절한 절제 범위에 대한 논란이 줄어들고 있다. 특히 림프절 절제에 있어서는, 식도점막하층에 위치한 submucosal lymphatic plexus가 양측 반회신경림프절과 direct communication이 있다는 카데바 연구 결과를 기반으로 하여, 양측 반회신경림프절을 철저하게 제하는 것이 원칙으로 자리잡게 되었다.

식도를 절제한 후 위를 사용한 제건 후, 문합 부위 누출의 빈도는 약 10% 내외이다. 우측 대망동맥의 주행과 해부학적 변이에 대한 해부학적인 이해뿐 아니라, 위의 혈액 공급의 양상등에 대한 지식이 축적됨에 따라서 문합 부위 누출의 빈도는 점점 감소하고 있다. 이렇듯 해부학적인 지식에 기반을 둔 수술 기법의 발전은 수술의 성적을 점차 향상시키는데 도움이 되고 있다.

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S1-5

Anatomy for Skull Base Surgery & Recent Advances in Neurosurgery

박현호 /연세대학교 강남세브란스 병원 신경외과학

Skull base surgery is the most sohpisticated and complex field in neurosurgery. The field requires comprehensive understanding of skull base anatomy in order to perform a microscopic surgery. The key objective is to maximize surgical resection while minimizing surgical morbidity and this can only be achieved with vast knowledge of anatomy. The 6 most commonly used skull base approaches are introduced for this session with special emphasis on skull base anatomy. In addition, a brief summary of recent advances in neurosurgical treatment is presented to the audience to show where contemporary neurosurgery is at.

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심포지엄-2

2016년 10월 20일(목) 14:30 ~ 17:30
무궁화홀

Current Trends in Cancer Stem Cell Research

좌장 유영현 동아대 • 한장희 강원대

S2-1 **14:30-15:00**
Specific collaboration between the microenvironment and genetic constitution regulates the self-renewal of gastric cancer stem cells
오세옥 • 부산대학교 의과대학 해부학교실

S2-2 **15:00-15:30**
Niche-independent self-modulating of cancer cell stemness
김형기 • 고려대학교 생명공학부

S2-3 **15:30-16:00**
Metabolic stress induced cancer stem-like cell state transition and metabolic reprogramming
정재호 • 연세대학교 의과대학 외과학교실 생화학 분자생물학교실

16:00-16:15
Intermission

S2-4 **16:15-16:45**
Hippo Signaling and Cancer Stem Cell
임대식 • KAIST 생명과학과

S2-5 **16:45-17:15**
Microenvironmental regulation of leukemia stem cells; implication in niche targeting therapy
오일환 • 가톨릭 대학교 의과대학, 의생명과학 교실

17:15-17:30
Q&A

S2-1

Specific collaboration between the microenvironment and genetic constitution regulates the self-renewal of gastric cancer stem cells

Sae-Ock Oh /Department of Anatomy, School of Medicine, Pusan National University, Yangsan, 50612, KOREA

Cancer stem cells (CSC) have been isolated from many solid cancers, including those of the brain, breast, colon and stomach. However, the molecular mechanisms underlying the self-renewal of CSCs are poorly characterized. Moreover, heterogeneity of the microenvironment and the genetic constitution of CSCs complicates the elucidation of mechanisms. Genomic and epigenomic studies revealed that gastric cancer stem cells (GCSCs) exhibited down-regulation of many tumor suppressor genes and up-regulation of many oncogenes, leading to the activation of NF-κB signaling and the overexpression of ERBB2. In vitro and in vivo studies indicated that NF-κB signaling is critical for the self-renewal of GCSCs. Moreover, we found that cancer-associated fibroblasts (CAFs) increase the self-renewal of GCSCs by secreting neuregulin1 (NRG1) and that NF-κB signaling mediates the effects of NRG1. The overexpression of NRG1 in stromal cells was also observed in the tumor tissues of gastric cancer patients. In addition, we found that gastric cancers exhibited amplification of the NRG1 gene, which affected the proliferation and invasion of gastric cancer cells. Overexpression of NRG1 was associated with clinical stages, lymph node metastasis and survival rate of gastric cancer patients. These results indicate that genetic and epigenetic constitutions of GCSCs affect not only the self-renewal of GCSCs but also their specific collaboration with the microenvironment.

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S2-2

Niche-independent self-modulating of cancer cell stemness

Hyunggee Kim /Department of Biotechnology, Korea University, Seoul 12841, KOREA

Glioblastomas are highly lethal cancers that display cellular hierarchies with glioma stem cells (GSCs) at the apex. Inhibitor of differentiation 1 (ID1) is highly expressed in GSCs and regulates niche-dependent growth of GSCs. However, little is known about the biological role of ID1 in GSC maintenance. Here we performed loss-of-function and gain-of-function studies for ID1 in primary human GSCs and primary Ink4a/Arf-deficient murine astrocytes, respectively. GSC properties were determined by stem cell marker expression, sphere-forming ability, and tumorigenicity. ID1 depletion in GSCs repressed gliomagenesis through inhibition of GSC properties and growth. Ectopic ID1 expression in Ink4a/Arf-deficient murine astrocytes led them to acquire a tumorigenic transformation. ID1 led to cell cycle progression through cyclin E induction by suppressing Cullin3 E3 ubiquitin ligase. Immunoprecipitation assay revealed that Cullin3 binds Dvl2 and Gli2 and induces their degradation through polyubiquitination. Cullin3 suppression also stimulated GSC properties through activation of two ligand-independent WNT and SHH signaling pathways by stabilizing Dvl2 and Gli2 protein, respectively. In silico correlative analysis revealed that ID1high-Cullin3low expression signature correlates with a poor patient prognosis, thus supporting the clinical relevance of this signaling axis. Taken together, Cullin3 represents a common signaling node for controlling the activity of multiple essential GSC pathways mediated by ID1, suggesting that targeting Cullin3 may be an effective therapeutic strategy in glioblastoma.

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S2-3

Metabolic stress induced cancer stem-like cell state transition and metabolic reprogramming

정재호 /연세대학교 의과대학 외과학교실 생화학 분자생물학교실

Tumor evolves in tumor microenvironment through bidirectional interactions and as a deadly consequence metastatic phenotype emerges. This emerging phonotype shares characteristics with cancer stem-like cells (CSCs). We recently demonstrated that chronic metabolic stress (CMS) induces a WNT-dependent CSC-like phenoconversion of cancer cells. In addition, this CMS-induced phenoconversion might be through stochastic state transition by upregulating the WNT pathway.

The abnormal and deranged metabolism of cancer has been appreciated as an important characteristic of tumors, which could contribute to the comprehensive understanding of cancer pathogenesis. To decode the biological complexity of cancer, systems biology approach which integrates and analyzes the different entities of "omics" information is imperative. Recently metabolic characterization of a number of different tumor types have been reported using metabolomics approaches. Most of the reports, however, focus on the different metabolites between tumor and normal individuals. Few have been reported regarding metabolic characteristics of metastatic CSCs in relation to core signaling pathways driving the malignant process. Here I will present the metabolomic profile of in vitro selected metastatic CSCs compared to parental cells. Further, I will discuss the integrated metabolome and transcriptome analysis which reveals that the WNT core signaling pathway mediates metabolic reprogramming which generates abnormal NAD pathway metabolites in CSCs. These results suggest that deranged core cancer signaling pathway cross talks with metabolic pathway thereby resultant 'oncometabolite' could provide selective advantage to metastatic CSCs.

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S2-4

Hippo Signaling and Cancer Stem Cell

Dae-Sik Lim /Department of Biological Sciences, KAIST, Daejeon, KOREA

The Hippo signaling pathway has emerged as a mediator of tumor suppression that is evolutionarily conserved from flies to humans. The core complex of the Hippo pathway consists of the protein kinase Hippo (MST1/2), Salvador (SAV1 or WW45), Mats (MOB1), the protein kinase Warts (LATS1/2) and transcription activator Yorkie (YAP and TAZ). Mice with genetic disruption of the Hippo pathway show two key features: expansion of tissue-specific stem /progenitor cell populations, and a hyper-regenerative response and increased cancer incidence after tissue damage. Despite YAP's powerful ability to expand adult stem cells and cancer stem cells, the downstream target genes required for its function are not fully characterized. By using mammary epithelial cells and breast cancer cells, we newly delineated downstream mechanisms underlying the stem-cell-property–inducing function of YAP. Using YAP overexpression upregulates mammary stem cell (MaSC) signature genes, including interleukin 6 (IL6), which we found to be a novel, critical target of YAP in the induction of MaSC-like properties. The transcription factor SRF (serum response factor) binds YAP, recruiting it to target genes that are specifically involved in endowing mammary epithelial cells with MaSC-like properties. SRF, YAP/TAZ and IL6 are all overexpressed in basal-like and triple-negative breast cancer cells. Moreover, having found that SRF, which is critical for YAP-induced MaSC-like properties, is expressed at a low level in luminal-type breast cancer, we proposed that YAP-SRF promotes IL6 expression and generation of cancer stem cells and is correlated with poor relapse-free survival specifically in basal-like breast cancer, and not in luminal-type breast cancer.

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S2-5

Microenvironmental regulation of leukemia stem cells; implication in niche targeting therapy

오일환 /가톨릭 대학교 의과대학, 의생명과학 교실

Leukemia stem cells are malignant counterpart of normal hematopoietic stem cells (HSCs). Xenotransplantation studies have identified a subpopulation of leukemiacells called leukemic stem cells (LSCs); they arise from the transformation of HSCs or re-acquisition of self-renewal capability in committed progenitors and can initiate and maintain their leukemic state. When transplanted into mice, like normal HSCs, these LSCs engraft in bone marrow, competing for niche with normal HSCs. Thus, LSCs are subjected to the micreonvironmental regulation by bone marrow (BM) stem cell niche.

In this presentation, we show that the leukemic cells remodel the microenvironmental cros-talk (CXCL-12 or Jagged-1) in mesenchymal stem cell niche, acquiring dominance over the normal HSCs by selective support on LSCs, while suppressing normal HSCs. Moreover, the heterogeneity in the remodeling pattern of BM niche by leukemic cells are correlated to the susequent difference in their clinical course with respect to their recurrence during 5-8 follow-up period after initial remission. Thus, we show that leukmic microenvironment contribute to the leukemogenesis and that niche remodeling by leukemia cells is another entity of leukemogenesis that can be a parameter for the heterogeneous clinical course of AML, thus servingas a prognostic marker. These studies reveal the role of microenvironment for leukemogenesis and provide insight on the significance of stem cell niche as an attractive target of therapy and regeneration for normal and cancer stem cells.

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심포지엄-3

2016년 10월 21일(금) 14:00 ~ 16:30
그린야드홀

Brain Mapping and Processing

좌장 이영호 충남대 • 유임주 고려대

S3-1

14:00-14:30
Network based longitudinal human brain transcriptome analysis in Down Syndrome
강효정 • 중앙대학교 자연과학대학 생명과학과

S3-2

14:30-15:00
Anatomical classification of retinal ganglion cells in the mouse
김진섭 • 한국뇌연구원 뇌신경망연구부

15:00-15:15
Intermission

S3-3

15:15-15:45
Temporally precise labeling and control of neuromodulatory circuits in mammalian brain
이동민 • 고려대학교 의과대학 해부학교실

S3-4

15:45-16:15
Early diagnosis of Alzheimer's disease based on brain imaging genetics
이건호 • 조선대학교 치매국책연구단

16:15-16:30
Q&A

S3-1

Network based longitudinal human brain transcriptome analysis in Down Syndrome

강효정 /중앙대학교 자연과학대학 생명과학과

Trisomy 21, or Down syndrome (DS), is the most common genetic cause of developmental delay and intellectual disability. To gain insight into the underlying molecular and cellular pathogenesis, we conducted a multi-region transcriptome analysis of DS and euploid control brains spanning from mid-fetal development to adulthood. DS brains showed genome-wide alterations in the expression of a large number of transcripts, many of which exhibited temporal and spatial specificity. Bioinformatic analyses revealed co-dysregulated genes associated with several key biological processes. In particular, our findings uncovered major expression changes in genes associated with oligodendrocyte differentiation and myelination that were validated via cross species comparison to Ts65Dn mutant mice, the most extensively studied rodent model of DS. Ts65Dn studies extended these results, demonstrating that cell-autonomous defects lead to reduced oligodendrocyte differentiation and that hypomyelination leads to slower neocortical action potential transmission. Together, these results identify defects in white matter development and function in DS and provide a transcriptional framework for further investigating DS neuropathogenesis.

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S3-2

Anatomical classification of retinal ganglion cells in the mouse

김진섭 /한국뇌연구원 뇌신경망연구부

Neural computation of visual perception begins in the retina. Retinal ganglion cells (RGCs) are the only outputs of the retina, each type of which is a channel that distinct visual information is processed through. Despite the importance of RGCs to understand the visual computation, the catalog of RGC types remains incomplete for a century. We anatomically classified an unbiased sample of almost 400 RGCs based chiefly on dendritic stratification profiles. The RGC dendrites were reconstructed from serial electron microscope (EM) images of a small patch of mouse retina inner plexiform layer. The reconstruction was carried out on EyeWire, a web-based EM reconstruction pipeline that combines artificial intelligence powered by deep learning and human intelligence of a community of 'citizen neuroscientists'. We clustered the cells into more than 40 distinct types. We used the types to systematically test heuristic rules for using structural features to predict visual response properties. This is the first time that comprehensive cells were reconstructed on a large enough area to potentially sample and identify all RGC types.

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S3-3 Temporally precise labeling and control of neuromodulatory circuits in mammalian brain

이동민 /고려대학교 의과대학 해부학교실

Dynamic modulation of neuronal pathways underlies behavior and learning, but we have limited tools to monitor these effects in situ. Here, we present "*i*Tango", a light-gated gene expression system that uses β-Arrestin and a light-inducible split tobacco-etch-virus (TEV) protease. We show that both ligand and light are necessary to induce target gene expression using an *i*Tango system, suggesting that light stimulation can be used to monitor the activity of neuromodulatory ligands in circuits over time. We delivered a dopamine (DA)-sensitive *i*Tango to mice using adeno-associated virus, and found that phasic DA release during motivation-induced learning successfully induced marker gene expression in a light-dependent way. Furthermore, inhibiting a selective neuronal population labeled by *i*Tango technique reversed cocaine-induced locomotion sensitization. We conclude that the light-gated mapping platform, *i*Tango, allows us to dissect neuromodulatory circuits in action with high temporal and spatial precision.

Keywords: Neuromodulation, High spatiotemporal resolution, Light-gated gene expression, Awake behaving animals, Optogenetic technology.

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S3-4 Early diagnosis of Alzheimer's disease based on brain imaging genetics

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Alzheimer's disease (AD) affects millions of people around the world. Currently, there are no treatments that prevent or slow the disease. Like other neurodegenerative diseases, Alzheimer's disease is characterized by protein misfolding in the brain. This process and the associated brain damage begin years before the substantial neurodegeneration that accompanies dementia. Recent advances in neuroimaging and DNA sequencing techniques allow us to acquire big dataset of both high quality brain images and individual differences in genetic variation from a large cohort. Combined analyses of these huge dataset provide novel opportunities not only to find novel genetic variations promoting brain atrophy but also to predict the onset of AD. Here we show that effects of genetic variations on AD progression as well as atrophy of cerebral cortical and subcortical regions. From more than one thousand MR brain images of cognitive normal population and late onset AD (LOAD) patients, gray matter thickness and subcortical volumes were quantified using Freesurfer software. In addition, their genome-wide genetic variations were analysed using a customized SNP chip for Korean people. Massive statistical analysis of the multimodal dataset revealed the relationship between LOAD-specific cerebral atrophies and genetic variations. In this presentation, the current and future role of imaging genetics in improved understanding of the development of LOAD will be discussed, and its potential for aiding in early and differential diagnosis and prognosis of different types of dementia. For the latter, the use of reference imaging data and reference models derived from large clinical and population imaging studies, and the application of machine learning techniques on these reference data, are expected to play a key role.

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심포지엄-4

2016년 10월 21일(금) 14:00 ~ 16:30
무궁화홀

Cancer and Immunotherapy

좌장 정채용 전남대 • 윤지희 한양대

S4-1
14:00-14:30
Cancer & immunotherapy
진동훈 • 울산대학교 의과대학 서울아산병원 융합의학과

S4-2
14:30-15:00
Multi–talented Aldose Reductase: Gene Regulation, Physiological Function and Dysfunction leading to pathological conditions
Sookja K. Chung • The University of Hong Kong

S4-3
15:00-15:30
Immune regulation via immune checkpoint PD–1 expressed on regulatory T cells during cancer progression
하상준 • 연세대학교 생명시스템대학 생화학과

S4-4
15:30-16:00
Genetically engineered T cells: A new wave of cancer immunotherapy
최경호 • 서울대학교 의과대학 생화학교실

S4-5
16:00-16:30
MDSCs : Cancer Promoting Inflammatory Cells in Breast Cancer
이동섭 • 서울대학교 의과대학 해부학교실

S4-1

Cancer & immunotherapy

진동훈 /울산대학교 의과대학 서울아산병원 융합의학과

cMET (also called MET and hepatocyte growth factor receptor (HGFR)) amplification has been reported in various human cancers. cMET represents an intriguing target for cancer therapy. Activation of cMET was regulated through HGF-dependent or –independent pathway. However, the reports are not yet which factor associated with HGF-independent mechanism. We identified a novel factor (HML) which was able to regulate phosphorylation of cMET by HGF-independent pathway. Moreover, HML binds to c-MET at the membrane and regulates activation of c-MET.
MicroRNA is noncoding RNA and regulates cancer cell proliferation and invasion. In our study, we discovered that miR-A negatively regulated cMET and HML. miR-A are expressed low level in gastric cancer cell lines. The overexpression of miR-A was suppressed cMET and HML expression. So, we demonstrated that cell growth were inhibited and cell migration/invasion was suppressed by miR-A. Therefore, we suggest that miR-A can be used as a potent therapeutic agent against gastric cancer.

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S4-2

Multi-talented Aldose Reductase: Gene Regulation, Physiological Function and Dysfunction leading to pathological conditions

Sookja K. Chung /The University of Hong Kong

Obesity is a well-known risk factor for not only metabolic syndrome and diabetes, but also closely associated with development of cancers in pancreas, liver, colon, lung, and etc. The shared underlying mechanisms for metabolic defects and cancer at the cellular level may include chronic inflammatory, oxidative, osmotic, ischemic, and immune responses due to increased insulin, high glucose and fat, reactive oxygen species (ROS), toxic lipid aldehydes, adipokine (leptin), tumor growth regulators, and nuclear factor kappa beta system. Over the years, numerous studies on aldose reductase (AR; AKR1B1 in human; AKR1B3 in mice), which is the first and rate-limiting enzyme in polyol pathway and reduces glucose to sorbitol with the aid of its co-factor NADPH, points to its role in various disease conditions. Sorbitol is then converted to fructose by sorbitol dehydrogenase (SDH) while its co-factor NAD+ is reduced to NADH. In diabetic animals, accumulation of sorbitol in the lens is thought to cause cataract due to increased osmotic stress. But in most other tissues, the level of sorbitol is too low to cause osmotic stress, presumably because of rapid conversion to fructose. Flux of glucose generates oxidative stress by several mechanisms. Depletion of AR's co-factor NADPH decreases GSH level because NADPH is also the co-factor for glutathione reductase that regenerate GSH from GSSH. In addition, fructose and its metabolites fructose-3-phosphate, and 3 deoxyglucosone are more potent glycating agents that glucose. Therefore, flux of glucose through the polyol pathway increases the formation of AGE which generates ROS when it interacts with its receptor RAGE. Conversion of SDH co-factor NAD+ to NADH would lead to increased ROS production by NAD(P)H oxidase. As a consequence of polyol pathway mediated increased oxidative stress, poly(ADP-ribose) polymerase (PARP) and mitogens activated kinases (MAPKs) are known to be activated. Activation of PARP has been shown to contribute to the pathogenesis of diabetic complications, such as endothelial dysfunction, neuropathy cardiomyopathy, cataract, and retinopathy. Several structurally unrelated AR inhibitors were found to be effective in preventing diabetic complications including cataract, retinopathy, neuropathy, and nephropathy in animal models. Recently, AR, which increased in cancer tissues, inhibitors have been used to alleviate cancers, such as liver carcinogenesis and colon cancer, and to improve cancer drug sensitivity. Although AR inhibitors showed high efficacy against diabetic complications in animal models, the number of clinical trials have failed except Epalrestat as a treatment of diabetic neuropathy. Therefore, we have revisited this old enzyme using the molecular genetics. We have cloned AR and created tissue-specific transgenic and knockout mice. The transcription factor, which regulate AR (nuclear factor active in T cells 5/osmotic response element binding protein), is isolated and characterized by generating NFAT5 knockout mice. I will discuss the research findings from these studies in the meeting and hope to convey the importance of targeting AR for treatment of diabetic complications and potentially against cancer.

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S4-3 Immune regulation via immune checkpoint PD-1 expressed on regulatory T cells during cancer progression

하상준 /연세대학교 생명시스템대학 생화학과

For more than 100 years, cancer immunotherapy has played an ever-increasing role in the understanding and treatment of cancer even though there are not many approved drugs and regimens. Activating the immune system for therapeutic benefit in cancer has long been a goal in immunology and oncology. After repetitive failures, the tide has finally changed due to the success of recent proof-of-concept clinical trials using antibodies to blockade immune checkpoint molecules such as CTLA-4 and PD-1. These successes suggest that tolerance raised by tumor microenvironment is a major obstacle for immunotherapy and therefore, blocking the tolerance is the first step to rejuvenate tumor-specific T cell immune responses. Herein, we shows that PD-1 is upregulated in tumor-infiltrating regulatory T (Treg) cells as well as CD8+ T cells in tumor microenvironment. Tumor-infiltrating Treg cells displayed greater suppressive capacity for inhibiting CD8+ T cells proliferation and subsequent cytokine production than Treg cells isolated outside tumor microenvironment. A contact between Treg cells and CD8+ T cells was necessary for the potent suppression of CD8+ T cell immune response. More importantly, the suppression required cell-specific expression and interaction of PD-1 on Treg cells and PD-1 ligand on CD8+ T cells. Our study defines PD-1 upregulated on Treg cells and its interaction with PD-1 ligand on effector T cells as one cause for the potent T cell suppression and proposes the role of PD-1 on Treg cells, in addition to that on exhausted T cells, in tumor microenvironment.

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S4-4 Genetically engineered T cells: A new wave of cancer immunotherapy

최경호 /서울대학교 의과대학 생화학교실

Whether tumor cells could be recognized and eliminated by host immune system has been a long debated issue in the field of immunology, which raised concern on cancer immunotherapy. Likewise, early clinical trials using immunological modalities based on limited information on basic immunology led to skepticism on cancer immunotherapy. However, the concept of cancer immunosurveillance is now clearly established. In recent years, we began to realize that we can use our immune system more effectively on the scientific basis, and these knowledge-based immunotherapies are slowing gaining much attention in the oncology field. Especially, in last couple of years, we observed a big enthusiasm on T cell immunotherapy including genetically engineered T cells.
In this talk, I will introduce this new trend of cancer immunotherapy and our recent experimental models on genetically engineered T cell therapy.

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S4-5

MDSCs : Cancer Promoting Inflammatory Cells in Breast Cancer

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서울대학교 의과대학 해부학교실

Tumor cell interactions with the microenvironment, especially those of bone-marrow-derived myeloid cells, are important in various aspects of tumor metastasis. Myeloid-derived suppressor cells (MDSCs) have been suggested to constitute tumor-favoring microenvironments. We evaluated whether MDSCs potentiated by cancer cells directly increased breast cancer aggressiveness, leading to spontaneous distant metastasis of cancer cells. Using a murine breast cancer cell model, we showed that murine breast cancer cells with high IL-6 expression recruited more MDSCs, and that the metastasizing capacity of cancer cells paralleled MDSC recruitment in tumor-bearing mice. Metastasizing, but not non-metastasizing, tumor-derived factors induced MDSCs to increase IL-6 production and full activation of recruited MDSCs occurred in the primary tumor site and metastatic organ in the vicinity of metastasizing cancer cells, but not in lymphoid organs. In addition, tumor-expanded MDSCs expressed Adam-family proteases, which facilitated shedding of IL-6 receptor, thereby contributing to breast cancer cell invasiveness and distant metastasis through IL-6 trans-signaling. The critical role of IL-6 trans-signaling was confirmed in both the afferent and efferent pathways of metastasis. Collectively, our findings reveal that breast cancer cells and MDSCs form a synergistic mutual feedback loop and that thus-potentiated MDSCs directly affect breast cancer cell aggressiveness, leading to spontaneous metastasis.

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구연발표

2016년 10월 20일(목) 08:45 ~ 10:30
구연발표 1 (O1~7) 그린야드홀
구연발표 2 (O8~13) 무궁화홀

2016년 10월 21일(금) 08:45 ~ 10:30
구연발표 3 (O14~19) 그린야드홀
구연발표 4 (O20~26) 무궁화홀

01~7 **육안해부학**
좌장 정민석 아주대 • 박정현 강원대

08~13 **신경과학**
좌장 유임주 고려대 • 노구섭 경상대

014~19 **신경과학**
좌장 이종은 연세대 • 한승호 중앙대

020~26 **조직 및 발생**
좌장 한기환 이화여대 • 오세옥 부산대

구연발표 1 육안해부학 (O1~7)

2016년 10월 20일(목) 08:45~10:30, 그린야드홀

좌장: 정민석 (아주대), **박정현** (강원대)

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눈구석주름의 해부와 조직소견

Anatomy and Histology of Epicanthal Fold

Kun Hwang*
Department of Plastic surgery, Inha University School of Medicine

02 ---------- 32

Histologic and Radiologic Analyses of the Retromolar Canal in the Mandible

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

03 ---------- 32

Anatomical consideration of the deep circumflex iliac artery with respect to the flap surgery

Kang-Jae Shin, Shin-Hyo Lee, Tae-Jun Ha, Ki-Seok Koh, Wu-Chul Song*
Deparment of Anatomy, Konkuk University School of Medicine

04 ---------- 33

Holistic Evaluation of Basketball players' brain with MRI Analysis

Woo Suk Tae[1], Ji Hyun Kim[2], Dae Jin Kang[2], Dai Hyun Kim[2], Soon Wook Kwon[2], Im Joo Rhyu[2,*]
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05 ---------- 33

Changes in the Orbital Rim with Aging in Korean

Anna Jeon[1], Chang-Min Seo[1], Dai-Soon Kwak[2], U-Young Lee[2], Deog-Im Kim[3], Won-Bok Lee[1], Seung-Ho Han[1,*]
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06 ---------- 34

Blood Supply to the Human Dentate Nucleus by Cerebellar Arteries : Importance of PICA

Soo-Jung Kim[1], Hyun-Joo Kim[2], Young-Han Lee[3], Ji-Hyun Lee[1], Hye-Yeon Lee[2], Hee-Jun Yang[1,*]
[1]Department of Anatomy, Gachon University College of Medicine, [2]Department of Anatomy, Yonsei University Medical College, [3]Department of Radiology, Yonsei University Medical College

07 ---------- 35

창자 발생 설명을 위한 3D 동영상과 3D 프린팅 모형 제작

Hyeon-Joo Kim[1], Dong-Su Jang[2], Hee-Jun Yang[3], Hye-Yeon Lee[1,*]
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구연발표 2 신경과학 (O8~13)

2016년 10월 20일(목) 08:45~10:30, 무궁화홀

좌장: 유임주 (고려대), **노구섭** (경상대)

08 ---------- 35

The role of heterotrimeric GTP-binding protein, Go in main olfactory system

Jung-Mi Choi[1], Sung-Soo Kim[1], Chan-Il Choi[1], Hye Lim Cha[1], Huy-Hyen Oh[1,2], Sungho Ghil[3], Young-Don Lee[1,2], Lutz Birnbaumer[4,5], Haeyoung Suh-Kim[1,2]
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09 ---------- 36

Expression of neuron-specific genes is regulated by a bHLH transcription factor, NeuroD

Taeyoung Lee, Insoo Cho, Jungmi Choi, Youngdon Lee, Sungsoo Kim, Haeyoung Suh-Kim
Departments of Anatomy, Department of Biomedical Sciences, The Graduate School Ajou University School of Medicine

010 ---------- 36

Therapeutic effects of intra-arterial delivery of neural-induced mesenchymal stem cells in the ischemic stroke

Gyu Hee Kim[1,2,*], Young Don Lee[1,2], Ji Man Hong[3], Hae Young Suh-Kim[1,2], Sung Soo Kim[1]
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011 ---------- 37
The role of microglial autophagy in normal brain development and neuropathology
Mi-Hyang Cho, Hyun-Ju Kim, Dong-Hou Kim*, Seung-Yong Yoon
University of Ulsan College of Medicine

012 ---------- 37
Protection against RAGE-mediated Neuronal cell death by sRAGE-secreting Human Mesenchymal Stem Cells in a Murine model of Alzheimer's disease
Myeongjoo Son[1,2], Kyunghee Byun[1,2], Seyeon Oh[2], Hyunjin Park[1,2], Hye-Jeong Park[3], Seung U. Kim[4], Bonghee Lee[1,5,*]
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013 ---------- 38
Enhanced long-term efficacies of GABAA-α1 receptor in the hippocampal interneuron following hyperthermic seizure
Yeon Hee Yu, Hankyu Kim, Kahyun Lee, Dae-Kyoon Park, Kyung-Ho park, Duk-Soo Kim*
Department of Anatomy, Soonchunhyang University, Cheonan, Korea

구연발표 3 신경과학 (O14~19)
2016년 10월 21일(금) 08:45~10:30, 그린야드홀

좌장: 이종은 (연세대), **한승호** (중앙대)

014 ---------- 38
Neurobiological toxicity of radiation in hippocampal cells
Joong Sun Kim[1,3,*], Miyoung Yang[2], Seungsook Lee[3], Changjoung Moon[4], Sungho Kim[4], Yeonghoon Son[1,4]
[1]Dongnam Institute of Radiological Medical Sciences , [2]Department of Anatomy, College of Medicine, Wonkwnag University , [3]Korea Institute of Radiological Medical Sciences , [4]Department of Anatomy, College of Veterinary Medicine, Chonnam National University

015 ---------- 39
Rat Odontoblasts May Use Glutamate to Signal Dentin Injury
Yi Sul Cho[1], Chang Hyun Ryu[1], Jong Hwa Won[2], Hue Vang[2], Seog Bae Oh[2], Jin Young Ro[3], Yong Chul Bae[1,*]
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016 ---------- 39
The Effect Of Prenatal Hypoxia Following Uterine Artery Ligation On PI3K/AKT Immunoreactivity
Yoonyoung Chung, Yonghyun Jun*
Department of Anatomy, School of Medicine, Chosun University

018 ---------- 40
Neuroprotective Effects of PFF in Glutamate-induced cell death
Jwa-Jin Kim[1,6,7,8,*], Yoon-Joong Kang[1], Sun-Ae Shin[6], Bong Ho Lee[2], Dong Woon Kim[3,6,7], Eun-Kyeong Jo[3,4], Jae-Min Yuk[3,5]
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019 ---------- 40
Spatiotemporal Expression of Osteopontin in the Striatum of Rats Subjected to 3-Nitropropionic Acid: Its Potential Correlation With Microcalcification
Tae-Ryong Riew[1], Hong Lim Kim[2], Jeong-Heon Choi[1], Xuyan Jin[1], Yoo-Jin Shin[1], Mun-Yong Lee[1,*]
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구연발표 4 조직 및 발생 (O20~26)

2016년 10월 21일(금) 08:45~10:30, 무궁화홀

좌장: 한기환 (이화여대), **오세옥** (부산대)

020 ---------- 41

Descending Thin Limb Of The Intermediate Loop Expresses Both Aquaporin 1 And Urea Transporter A2 In The Mouse Kidney

Wan-Young Kim[1], Hyun-Wook Lee[1], Ki-Hwan Han[2], Sun-Ah Nam[1], Arum Choi[1], Yong-Kyun Kim[3], Jin Kim[1,*]

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021 ---------- 41

3-D Imaging of Embryonic Development of *Xenopus* Using Synchrotron Radiation microCT

Hongtae Kim[1,*], Sung-Mi Han[1], Mae-Ja Park[2], Jae-Hong Lim[3]

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022 ---------- 42

NADPH Oxidase Inhibitor Inhibits The Cell Growth By EBV-induced Transformation Via LMP1-NOX4-ROS Signaling In EBV-infected ARPE-19 Cells

Ju A Shim[1], Seung-Woo Hong[1], Min hye Noh[1], Nam-Sook Park[1], Si-Kyung Kim[1], Byul-Nim Ahn[1], Yeong Seok Kim[1], Jae Wook Yang[2], Dae Young Hur[1,*]

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023 ---------- 42

The Mitotic Checkpoint Regulator RAE1 Induceses Aggressive Breast Cancer Cell Phenotypes By Mediating Epithelial-Mesenchymal Transition

Ji Hoon Oh[1], Ho Hur[2], Ji-Yeon Lee[1], Yeejeong Kim[3], Youn Soo Seo[1], Myoung Hee Kim[1,*]

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024 ---------- 43

The genetic analysis on ancient *Ascaris* discovered from archaeological sites in South Korea

Chang Seok Oh[1], Min Seo[2], Dong Hoon Shin[1,*], Jong Ha Hong[1]

[1]Department of Anatomy, Seoul National University College of Medicine, South Korea, [2]Department of Parasitology, Dankook University College of Medicine, South Korea

025 ---------- 43

Roles of Mitochondrial NADP+-dependent Isocitrate Dehydrogenase (IDH2) on Cisplatin-induced Acute Kidney Injury

Min Jung Kong[1], Sang Jun Han[1], Jee In Kim[2], Kwon Moo Park[1,*]

[1]Department of Anatomy and BK21 Plus, Kyungpook National University School of Medicine, [2]Department of Molecular Medicine and MRC, Keimyung University School of Medicine

026 ---------- 44

The First Report of the Anthropological Research Project on Zeleny Yar Mummies in Russian Federation

Sergey Mikhailovich Slepchenko[1,2,3], Alexander Vasilyevich Gusev[4], Evgenia Olegovna Svyatova[5], Jong Ha Hong[6], Dong Hoon Shin[6]

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01

눈구석주름의 해부와 조직소견
Anatomy and Histology of Epicanthal Fold

Kun Hwang*
Department of Plastic surgery, Inha University School of Medicine

목적: 눈구석주름의 해부와 조직소견을 밝히는데 있다.
재료 및 방법: 한국인 성인시신 16구 (눈구석주름이 있는 30쪽, 눈구석주름이 없는 2쪽)를 해부하였다. 피부와 연부조직을 제거하고 눈구석주름을 눈둘레근의 부분들과 관련하여 관측하였다. 눈구석성형술을 시행한 두 환자에서 눈구석주름을 채취하였다. 눈구석주름을 포함한 조직은 파라핀에 포매하여 10um 두께로 눈꺼풀틈새와 평행면으로 잘라 헤마톡실린–에오신으로 염색하한 뒤 광학현미경으로 관찰하였다.
결과: 눈구석주름이 없는 조직에서는 위사이막앞눈둘레근(upper preseptal orbicularis oculi muscle)과 아래사이막앞눈둘레근(lower preseptal orbicularis oculi muscle)이 연결되어있지 않았다. 눈구석주름이 있는 조직에서는 위사이막앞눈둘레근과 아래사이막앞눈둘레근이 연결되어있었으며(100%), 위아래 눈꺼풀판앞눈둘레근(upper and lower pretarsal orbicularis muscle)은 서로 연결되어있지 않았다. 수평절편에서 눈구석주름은 세부분으로 구성된 것이 관찰되었다: 즉, 바깥쪽 피부, 핵심구조(core structure), 안쪽피부로 구성되었다. 핵심구조는 근육섬유와 섬유조직이 혼재되어있었다.
결론: 눈구석주름을 제거하거나 재건할 때에 섬유근육핵심구조(fibromuscular core)도 제거하거나 재건되어야 한다.

Keywords: Eyelids, Anatomy and histology

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02

Histologic and Radiologic Analyses of the Retromolar Canal in the Mandible

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The aims of this study were to identify the morphology of the retromolar canal using cone-beam computed tomography (CBCT) images and histologic sections, and to provide detailed anatomic information that clinicians can use in preoperative assessments.

CBCT images of 72 patients (144 sides) and 22 hemimandibles obtained from embalmed cadavers were used in this study. The prevalence, course, opening position, and distance from the second molar were measured on CBCT images to examine the topography of the retromolar canal. The hemimandibles were prepared for routine histology and stained with hematoxylin-eosin, investigated to elucidate the histologic composition and dimensions of the retromolar canal with the aid of a light microscope.

The retromolar canal was detected on CBCT images in 26.4% of cases (in 43.1% of patients), with it mainly arising vertically from the mandibular canal and opening in the middle portion. Similarly, the retromolar canal was visible in histologic sections in 27.3% of cases. Its mean maximum horizontal and vertical diameters were 0.82 and 0.90 mm, respectively, and it had an oval shape in the vertical direction. The areas of the neurovascular bundle and of the artery and nerve contained within it were 0.59±0.42 (mean±SD), 0.07±0.06, and 0.05±0.05 mm2, respectively.

In conclusion, in individual assessments the retromolar canal was detected at a higher rate of 43.1% (31 patients), and it contained both a large artery and nerve. Clinicians need to pay closer attention to hemorrhagic damage rather than nerve injury during surgical procedures in the retromolar area of the mandible.

Keywords: Retromolar canal, CBCT, Histologic composition, Retromolar triangle

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03

Anatomical consideration of the deep circumflex iliac artery with respect to the flap surgery

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The deep circumflex iliac artery is originated from the external iliac

artery and runs laterally to the anterior superior iliac spine behind the inguinal ligament. The artery supplies the iliac crest and the skin and muscles above the iliac crest and gives off the ascending branch near the anterior superior iliac spine. Flap surgery using the deep circumflex iliac artery as the pedicle have been used in the reconstruction of the maxillary or mandibular defects, but the utilization of the flap surgery recently was decreased due to surgical disadvantages. The aim of the present study was to describe the topographic anatomy of the deep circumflex iliac artery and to provide parameters applicable to the flap surgery. Sixty sides of the deep circumflex iliac artery and inguinal region were dissected from 31 Korean cadavers. Several parameters of the artery were investigated: the diameter, the origin, the emerging points and the positional relationship with adjacent structures. The arterial variations were classified according to their origin and supply. The diameter of deep circumflex iliac artery at the origin was 2.3 mm and there was no sexual difference. The position of the origin was -2.3 mm and 4.2 mm from the inguinal ligament in male and female, respectively. The vertical distance from the anterior superior iliac spine to deep circumflex iliac artery was 11.5 mm and angulation between the artery and inguinal ligament was 24.3 degrees. The arterial variations were classified into 3 types. The results of the present study will be practical guidelines for reducing surgical complications.

Keywords: Deep circumflex iliac artery, Flap surgery, Inguinal ligament, anatomy

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04

Holistic Evaluation of Basketball players' brain with MRI Analysis

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Brain is in charge of orchestrating every activity of our life. The continuous specific stimuli trigger the corresponding functional and structural plasticity of the brain, which covers from molecular level to behavioral level as an organism.

Our laboratory has investigated brain plasticity in response to motor activity in acrobat animal model, treadmill running monkey, and elite sportsmen with wide range of tools from electron microscope to MRI. I have analyzed the brains of basketball players with MRI based on the hypothesis, brain regions related with motor control would have morphological plasticity. I found cerebellar vermis lobules (VI, VII) of basketball players are larger than that of control, which looks like to be influenced by white matter contribution. In addition to cerebellum, striatum volume was also increased in basketball players. The manual volumetric analyses of basketball players' brain limit further investigation of other brain regions might be changed in the athletes. Therefore, I employed the latest MRI analysis tools including VBM, Brain Surfer and FSL to understand holistic morphological evaluation of the basketball players.

The VBM analysis result showed that increase volume of white matter of left precentral gyrus, and right superior semiluar lobule adjacent to vermian lobule VI, VII. Free Surfer analysis revealed increased cortical thickness of left precentral gyrus. FIRST analysis showed shape alteration was detected in left thalamic nuclei such as ventral anterior, ventrolateral, and pulvinar. In addition, left amygdala also showed morphological change in basketball players.

This study implies that plastic change of cortico-striato-thalamo-cortical loop and cortico-cerebello-thalamo-cortical loop are key modules in motor activities of the basketball players. In addition, this study suggests that non-motor function might contribute to these elite athletes.

Keywords: Plasticity, Basketball player, MRI

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05

Changes in the Orbital Rim with Aging in Korean

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The facial skeleton continued remodeling in a clockwise rotation of the midface with aging has been widely accepted. Several studies have been reported that the aging process is also shown in the periorbital region. The orbital aperture becomes wider with increasing age in Caucasian according to them. In the present study, we examined that the changes of Korean's orbital rim.

Data were collected from computed tomography (CT) scans of the orbits and facial bones from 107 Korean (55 males and 52 females), at interval of 0.60mm. It was categorized according to gender and age: youg group (20 - 35 years) and old group (60 years over). CT scans were reconstructed to three dimensional (3-D) modeling programes (Mimics, Materialise, Belgium). The most lateral, medial, superior and inferior points of orbital rim were used as reference points. These points made a center point of orbital aperture and the horizontal line passing through the center point (x-axis). The distance from the x-axis to the superior and inferior rim at nine equal increments were measured. The orbital aperture area was measured on each 3D model using an analysis software program such as 3-Matic (Materialise, Belgium). Data were analyzed with a Student's t test to identify any trends between young and old groups with a value of $p < 0.05$ considered statistically significant.

The orbital aperture height showed statistically insignificant changes overall with age in both sexes. There were irregular changes with mixed decrease and increase parts. The mean orbital aperture area in the male population was 1139.6 mm2 for the young age group, and 1134.6 mm^2 for the old age group. The mean measurement in the female population was 1119.9 mm2 for the young age group, and 1112.3 mm2 for the old age group. The orbital aperture area showed no significant change with increasing age for both male ($p < 0.817$) and female ($p < 0.766$) study populations.

The measurement data in the present study differs from previous studies with Caucasian subjects, in which they found a significant increase in orbital aperture area. In our study, there was no significant enlargement of the orbital rim in Korean.

Keywords: Aging, Orbital rim, Orbital aperture area, Korean

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06

Blood Supply to the Human Dentate Nucleus by Cerebellar Arteries : Importance of PICA

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The major roles of human cerebellum are planning, initiation, and modulation of voluntary movements. In addition, the cerebellum is known to be related with the cognitive function. The dentate nucleus is the largest deep nucleus in human cerebellum. Like cerebral cortex and cerebellar cortex, the dentate nucleus is also known to have somatotopic arrangement in itself in relation with upper limb and lower limb. Series of cognitive function tests revealed that the cognitive domains are located in arrangement as well. However, the mapping of arterial supply to each regions of the dentate nucleus by cerebellar arteries has not been clarified anatomically. The aims of this study are to clarify the arterial territories in the dentate nucleus and to match them with the known somatotopy and the arrangement of cognitive area in the dentate nucleus which should be useful for research and clinical situation of various cerebellar disease. Twelve cerebellar hemispheres from six adult cadavers were used in this study. Red-colored radio-opaque silicon dye was injected into the vertebral arteries and internal carotid arteries or their branches supplying the cerebellum. Computed tomographs of the cerebellar hemispheres were taken. The cerebellar hemispheres were sliced into sections of 5 mm thickness. The sliced cerebellar hemispheres were stained by Mulligan method. The stained sections were microdissectioned under surgical microscopes. Most of the dentate nuclei were mainly supplied by two or three direct branches of posterior inferior cerebellar arteries. Some of the dentate nuclei were supplied by microcirculation which are invisible under surgical microscope. Between the known suppliers to the dentate nucleus, the dominant artery is the posterior inferior cerebellar artery.

Keywords: Cerebrovascular accident, Stroke, Dementia

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07

창자 발생 설명을 위한 3D 동영상과 3D 프린팅 모형 제작

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복막과 창자의 구조를 이해하기 위해서는 창자의 발생과 회전 및 창자간막의 융합으로 인하여 창자들의 위치가 정해지는 과정을 아는 것이 중요하다. 교과서의 그림만으로 다음과 같은 발생과정을 이해시키기는 쉽지 않다. 태아 발생 14기에 나타나는 midgut과 몸통의 성장속도의 차이로 인해 발생 15기부터 관찰되게 되는 창자고리는 시계반대방향으로 90도 회전을 한 채로 umbilical coelom으로 진입한다. 이 시기로부터 몇 주일 동안 더 이어지는 창자의 회전에 의해 태어났을 때의 각 소화기계통 장기들의 위치, 창자간막혈관의 주행, 복막의 여러 구조의 모양이 결정진다. 이러한 발생 과정을 관찰할 수 있는 표본을 준비하여 학생들에게 보여주는 것은 매우 쉽지 않으며, 점토모형을 제작하여 시도한 결과 그림만으로 이해시키는 것보다는 효과가 있었으나, 잘 설명하기 어려운 것은 여전하였으므로, 3D 애니메이션으로 창자만 회전시키는 모델을 제작한 바 있다. 그러나 이 모델에 복막이나 혈관이 없는 상태인 것이 단점으로 지적되었으므로 이를 보완하기 위해 우선 창자에 위창자간막동맥(superior mesenteric artery, SMA) 축을 추가하여 3D 애니메이션을 제작하고, 이를 이용한 3D 프린팅 모델을 제작하였으며, 이를 보조할 수 있는 2D 애니메이션도 제작하였다. 3D 모델 제작에는 유저 인터페이스(user interface, UI)가 편리하고 렌더링 속도가 빠른 Cinema4D 소프트웨어가 사용되었고, 2D 애니메이션 제작에는 AfterEffect 소프트웨어가 사용되었다. 완성단계의 편집에는 Premier 소프트웨어가 사용되었다. 이미 제작한 바 있는 점토 모형과 여러 가지 발생학 교과서를 참고로 하여 창자가 90도, 180도, 270도 회전한 후의 배열 형태를 8단계로 나누어 제작하였다. 각 단계에서 관찰되는 발달 과정 형태를 모델링하고 point level animation(PLA) 방식을 이용하여 각 단계의 주요 포인트를 키로 설정하여 시간 순서로 연결하여 애니메이션으로 만들었다. 발생 과정 중 뒤바뀌는 창자의 앞뒤관계를 구별할 수 있도록 소화관의 앞쪽과 뒤쪽에 각각 색을 입혔다. 창자 모델이 완성된 후에는 SMA를 모델 안에 추가하였다. 완성된 애니메이션 중에서 몇 가지 단계의 모델은 3D 프린터로 출력하였다. 별도로, 횡단면에서 볼 수 있는 발달단계를 나타내는 2D 애니메이션 작업을 시행하였다. 포인트들이 움직이며 다음 단계로 형태를 변형시키는 방식을 사용하였다. 이에 그 과정과 애니메이션 모델을 소개하고 그 효과에 대해 토의하고자 한다.

Keywords: Greater Omentum, Lesser Omentum, Appendix, Greater Sac, Lesser Sac

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08

The role of heterotrimeric GTP-binding protein, Go in main olfactory system

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In mammals, initial detection of olfactory stimuli is mediated by sensory neurons in the main olfactory epithelium (MOE) and the vomeronasal organ (VNO). The heterotrimeric GTP-binding protein, Go, is widely expressed in the MOE and VNO of mice. Early studies indicated that Go expression in VNO sensory neurons is critical for directing social and sexual behaviors in female mice [Oboti L, et al. (2014) BMC Biol 12:31]. However, the physiological functions of Go in the MOE have remained poorly defined. Here, we examined the role of Go in the MOE using mice lacking the a subunit of Go. Development of the olfactory bulb (OB) was perturbed in mutant mice as a result of reduced neurogenesis and increased cell death. The balance between cell types of OB interneurons was altered in mutant mice, with an increase in the number of tyrosine hydroxylase-positive interneurons at the expense of calbindin-positive interneurons. Sexual behavior towards female mice and preference for female urine odors by olfactory sensory neurons in the MOE were abolished in mutant male mice. Our data suggest that Go signaling is essential for structural and functional integrity of the MOE and for specification of OB interneurons, which in turn are required for pheromone signal transmis-

sion and initiation of mating behavior with the opposite sex.

Keywords: Heterotrimeric Go protein, Olfactory mucosa, Olfactory bulb interneuron, Tyrosine monooxygenase, Sexual behavior

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09

Expression of neuron-specific genes is regulated by a bHLH transcription factor, NeuroD

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NeuroD1 is a transcription factor with a basic-helix-loop motif, which is known to regulate differentiation and survival of neuronal cells, enteroendocrine cells, and pancreatic beta cells. Previous reports showed that targeted depletion of NeuroD1 caused decreases in proteins involved in secretory machinery in neuronal and endocrine cells, suggesting that NeuroD1 may be a master transcription factor that regulates expression of members of secretory machinery. Here, we report a potential role of NeuroD1 in the regulation of transcription of neuron specific genes in neuronal cells. Since NeuroD1 is known to be highly phosphorylated by diverse protein kinases, we also investigated the effects diverse phosphorylation sites of NeuroD1. We will also discuss the diverse phosphorylation mutations with respect to the functions of NeuroD1.

Keywords: NeuroD, Transcription factor

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010

Therapeutic effects of intra-arterial delivery of neural-induced mesenchymal stem cells in the ischemic stroke

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Cerebral ischemic stroke is a serious public health concern. It causes considerable death and disability. Only limited treatment options are available in the acute phase of stroke.

Mesenchymal stem cells (MSCs) have been shown to improve a variety of neurological dysfunction by their paracrine effects. Neurogenin-1 (Ngn1) is a proneural gene that directs neuronal differentiation of progenitor cells during development. In recently study, intracranial injection of Ngn1-expessing MSCs showed the remarked improvement of motor dysfunction in stroke model compared to MSC and PBS treated group. However, intracranial injection is not feasible method to use in clinical field. Therefore, we conducted the study to investigate that intra-arterial injection of Ngn1-expressing MSCs can improve motor deficit in ischemic rat model.

Fifteen Sprague-Dawley rats were subinjected to transient middle cerebral artery occlusion(tMCAo) of 2 hours with the suture occlusion model. Magnetic resonance image (MRI), including diffusion-weighted imaging (DWI) and T2-weighted imaging was performed at 2, 7 and 28days after withdrawal of the suture. Motor function evaluation including ratarod test and adhesive removal test was performed at 1, 7, 14 and 28 days. Amimals were divided into 3 subgroup. Each group received 1×10^6 MSC-Ngn1 cells, 1×10^6 MSC-lacZ cells and normal saline respectively. The distribution and phenotype of injected stem cells were compared among the groups.

Rat injected with MSC-Ngn1 showed the tendency of motor dysfunction improvement compared to MSC-LacZ and control groups. The induction of neural stem cell number were greater in MSC-Ngn1 injected rat than in other groups.

Intra-arterial injection of MSC-Ngn1 cell in stroke model showed the remarkable improvement of motor dysfunction . Intra-arterial injection can be the feasible method of stem cell transplant.

Keywords: Ischemic stroke, Mesenchymal stem cells, Neurogenin1, Intra-arterial injection

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011

The role of microglial autophagy in normal brain development and neuropathology

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Autism spectrum disorders (ASDs) are neurodevelopmental disorders caused by various genetic and environmental factors resulting in the abnormalities of synapses. Microglia are suggested to be related with ASDs and play a role in refining synapses during development. Autophagy and related pathways are also suggested to be related with ASDs. However, the precise roles of autophagy in microglia on synapses and ASDs are unknown. Here we show that microglial autophagy refines synapses and regulates neurobehaviors. We found that atg7 deletion in the myeloid cell specific lysozyme-M cre mice showed social behavioral defects and repetitive behaviors, characteristic features of ASDs. These mice also showed increased dendritic spines, synaptic markers and altered connectivity between brain regions indicating defects in synapse refinement. Degradation of synaptosomes was impaired in atg7-deficient microglia and immature dendritic filopodia were increased in neuron cultures with atg7-deficient microglia. Our results first demonstrate the role of microglial autophagy in synapse regulation and neurobehaviors.
Accumulation of β-amyloid (Aβ) and resultant inflammation are critical pathological features of Alzheimer's disease (AD). Microglia is a primary immune cell in brain and ingests and degrades extracellular Aβ fibrils via lysosomal system. Autopagy is a catabolic process that degrades native cellular components, however, the role of autophagy in Aβ degradation by microglia and its effects on AD are unknown. Here we demonstrate a novel role for autophagy in the clearance of extracellular Aβ fibrils by microglia and in the regulation of the Aβ-induced NALP3 (NACHT, LRR and PYD domains-containing protein 3) inflammasome using microglia specific Atg7 knockout mice and cell cultures. We found in microglial cultures that Aβ interacts with LC3-II via optineurin and is degraded by an autophagic process mediated by the AMPK pathway.
We anticipate our results to be a starting point for more comprehensive understanding of microglial autophagy in the brain and enhancing microglial autophagy may be a promising new therapeutic strategy for ASDs and AD.

Keywords: Microglia, Autophagy, Alzheimer's disease, Autism spectrum disorders, Brain

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012

Protection against RAGE-mediated Neuronal cell death by sRAGE-secreting Human Mesenchymal Stem Cells in a Murine model of Alzheimer's disease

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Alzheimer's disease (AD), which is the most commonly encountered neurodegenerative disease, causes synaptic dysfunction and neuronal loss due to the accumulation of amyloid beta (Aβ). Aβ stimulates secretion and synthesis of Receptor for Advanced Glycation Endproducts (RAGE) ligands from activation microglial cells and then, it caused neuronal cell death in AD animal model. Soluble form of RAGE (sRAGE) are known to reduce inflammation, and decrease microglial cell activation, Aβ deposition, and thus, protect from neuron death in AD. However, general sRAGE protein has a short half-life for use as a therapeutic material. Here, we developed the sRAGE-secreting MSC to improve sRAGE effects for inhibition of Aβ deposition and reduction of secretion and synthesis of RAGE ligands in an $A\beta_{1-42}$ induced AD model. In addition, this novel cells improved viability of injected MSC and finally, enhanced protective effects by inhibiting binding of RAGE and RAGE ligands in an $A\beta_{1-42}$ induced AD model. These findings showed sRAGE protein from sRAGE-secreting MSC might be an effective materials for protecting neu-

ronal cell death, perhaps by inhibiting RAGE cascade cell death or inflammatory than sRAGE protein or MSC single treatment.

Keywords: Alzheimer's disease, soluble RAGE, human UC-MSC, neuronal death, RAGE, Aβ deposition, AGE, HMGB1, S100β

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013

Enhanced long-term efficacies of GABAA-α1 receptor in the hippocampal interneuron following hyperthermic seizure

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Febrile seizure (FS) is the most common seizure type in the infant and young child. FS may induce functional changes in the hippocampal circuitries and then contributed toward the development of temporal lobe epilepsy (TLE). Hippocampal interneuron is central role of regulating the excitability in the hippocampal circuits, thus it is important to comprehend the mechanism of γ-aminobutyric acid (GABA)ergic signaling. It is well known that phasic and tonic inhibitions are mediated by synaptic and extrasynaptic GABAA receptors. Among them, tonic inhibition plays a critical role of control in the excitability of hippocampal network, and these inhibitory efficacies are increases in diverse animal models of absence epilepsy and promotes the generation of spike-wave discharges. Previously, we investigated that expressional alteration of GABAA-α1 receptor in the hippocampal interneuron was abnormally enhanced at recurrent seizures stage following FS. Therefore, this study was investigated to confirm whether the hyperthermic seizure may be related to a consequence of compensated functional responses of excessively increased inhibitory circuits by GABAA-α1 receptor in the hippocampus. In the results of this study, EEG signal was shown characteristic amplitudes in each model. In addition, we were investigated filed excitatory postsynaptic potential (fEPSP) and paired-pulse responses in the hippocampus for identifying the functional alterations of GABAergic inhibition after the applications of GABAA receptor drugs and FS. Following bicuculline and FS, despite the slope of fEPSP was markedly reduced more than control level, the paired-pulse response was enhanced as similar to level of muscimol application. Moreover, vesicular GABA transporter (VGAT) expression and GABA immunoreactivity in the GABAA-α1 positive interneurons was significantly enhanced in the hippocampus following FS. However, although chloride channels (ClC) immunoreactivities were un-changed, two-pore-domain K+ channel (TASK-1) expression in the dentate gyrus (DG) was decreased after hyptethermic seizure. Therefore, our findings in present study revealed that enhanced tonic current in the inhibitory hippocampus interneuron may lead to alterations of interneuronal excitability, thus it may accompanied with sustained hyper-excitability of hippocampus circuits following FS.

Keywords: Hyperthermic seiuzre, GABAA receptor, Epilepsy, Tonic inhibition, Phasic inhibition

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014

Neurobiological toxicity of radiation in hippocampal cells

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Current events throughout the world underscore the growing radiation exposure of different forms, such as nuclear accidents, space travels, and atomic weapons use and testing, as well as the side effects of cancer therapy. Hippocampal neurogenesis in adult animals is significantly impacted by ionizing radiation and such change may be associated with hippocampal functions, including cognition. However, there is considerable uncertainly about exactly how these changes evolved, and new *in vivo* and *in vitro* approaches have provided a means by which new mechanistic insights can be gained. This study shows that the data from animal-based and cell culture studies provide complementary information relevant to a potentially serious complication of radiation exposure and should enhance our understanding of the tolerance of the normal brain to radiation exposure.

Keywords: Hippocampus, Radiation, Cognitive impairment, Mice

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015

Rat Odontoblasts May Use Glutamate to Signal Dentin Injury

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Accumulating evidence indicates that odontoblasts act as sensor cells, capable of triggering action potentials in adjacent pulpal nociceptive axons, suggesting a paracrine signaling via a currently-unknown mediator. Since glutamate can mediate signaling by non-neuronal cells, and peripheral axons may express glutamate receptors (GluR), we hypothesized that the expression of high levels of glutamate, and of sensory receptors in odontoblasts, combined with an expression of GluR in adjacent pulpal axons, is the morphological basis for odontoblastic sensory signaling. To test this hypothesis, we investigated the expression of glutamate, the thermo- and mechanosensitive ion channels TRPV1, TRPA1, and TREK-1, and the glutamate receptor mGluR5, in a normal rat dental pulp, and following dentin injury. We also examined the glutamate release from odontoblast in cell culture.

Odontoblasts were enriched with glutamate, at the level as high as in adjacent pulpal axons, and showed immunoreactivity for TRPV1, TRPA1, and TREK-1. Pulpal sensory axons adjacent to odontoblasts expressed mGluR5. Both the levels of glutamate in odontoblasts, and the expression of mGluR5 in nearby axons, were upregulated following dentin injury. The extracellular glutamate concentration was increased significantly after treating of odontoblast cell line with calcium permeable ionophore, suggesting glutamate release from odontoblasts.

These findings lend morphological support to the hypothesis that odontoblasts contain glutamate as a potential neuroactive substance that may activate adjacent pulpal axons, and thus contribute to dental pain and hypersensitivity.

Keywords: Odontoblast, Glutamate, Glutamate Receptor, Neuroactive Substance, Electron Microscopy

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016

The Effect Of Prenatal Hypoxia Following Uterine Artery Ligation On PI3K/AKT Immunoreactivity

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Prenatal hypoxia affects neurogenesis, which is a process of generation of new neurons from progenitor neuronal stem cells. There is no consensus on the effect of hypoxia on neurogenesis. It was reported that prenatal hypoxia induced neurogenesis in developing rat brain. In our previous study, we showed that cell proliferation in SVZ and DG was not different between normal and hypoxic fetuses, but cell survival in the cerebral cortex and dentate gyrus of the hypoxic group was different from the normal group. BDNF is important in neuronal cell proliferation, growth and survival. BDNF activates PI3K/Akt signaling, which affects the nervous system development. In this study, we investigated the relation between BDNF and PI3K/Akt signaling after uterine artery ligation in pregnant rats. Rats were mated and checked for the vaginal plug to confirm the pregnant status. Unilateral uterine artery ligation was performed at 16 days of gestation. Fetuses were delivered by cesarean section at 21 dg. Fetuses from one horn with the unligated uterine artery were allocated to the control group and those from the other horn with the ligated artery were allocated to the hypoxic group. Immunohistochemistry was performed with antibodies; NeuN, BDNF, PI3K, Akt and pAkt. The densities of NeuN- and BDNF-IR cells in the cerebral cortex were lower in the hypoxic fetuses than in the controls at 21 dg. The density of PI3K and pAkt-IR cells in the cortex significantly differed between the control and hypoxic fetuses. The results in dentate gyrus were similar to the results in the cerebral cortex. In this study, prenatal hypoxia reduced the density of PI3K-IR cells and also affected Akt phosphorylation. This suggests that the response of PI3K/Akt signaling to hypoxic stress is not sufficient to prevent hypoxia-induced changes after uterine artery ligation.

Keywords: Prenatal hypoxia, Neurogenesis, Akt, BDNF

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017

전시발표 P25로 변경

018

Neuroprotective Effects of PFF in Glutamate-induced cell death

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Stroke is a complex neurodegenerative disorder with a clinically high prevalence and mortality. Despite many efforts to protect against ischemic stroke, its incidence and related permanent disabilities continue to increase. In this study, we found that pretreatment with phlorofucofuroeckol (PFF), isolated from brown algae species, significantly increased cell viability in glutamate-stimulated PC12 cells. Additionally, glutamate-stimulated cells showed irregular morphology, but PFF pretreatment resulted in improved cell morphology, which resembled that in cells cultured under normal conditions. We further showed that PFF pretreatment effectively inhibited glutamate-induced apoptotic cell death in a caspase dependent manner. Reactive oxygen species (ROS) induced by oxidative stress are closely associated with ischemia-induced neurological diseases. Exposure of PC12 cells to glutamate induced abundant production of intracellular ROS and mitochondrial dysfunction, which was attenuated by PFF in a dose-dependent manner. In vivo studies revealed that PFF-mediated prevention was achieved predominantly through inhibition of apoptosis and mitochondrial ROS generation. Taken together, these results suggest the possibility of PFF as a neuroprotective agent in ischemic stroke.

Keywords: Ischemic stroke, Phlorofucofuroeckol, PC12 cells, Apoptosis, Reactive oxygen species

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019

Spatiotemporal Expression of Osteopontin in the Striatum of Rats Subjected to 3-Nitropropionic Acid: Its Potential Correlation With Microcalcification

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Osteopontin (OPN), an adhesive glycoprotein, has recently been shown to be involved in striatal lesion elicited by 3-nitropropionic acid (3-NP) that can be a good model for better understanding of the mechanisms underlying the ectopic microcalcification. The aim of the present study was to examine the expression and subcellular localization of OPN and its correlation with the microcalcification in the striatum of rats treated with 3-NP. Immunohistochemistry and immunoblotting revealed that OPN was specifically induced in the injured striatal tissue by 3-NP. OPN protein, expressed in a punctate pattern at the light-microscopy level, was shown to be increased in number and size by visual inspection and morphometry using image analysis. Ultrastructural investigation revealed that OPN protein was initially localized to the mitochondria within degenerating dendrites at 3 days post-lesion that was followed by the profuse OPN accumulation along the membrane of degenerating dendrites on days 7-14. Combination of electron probe analysis, immunoelectron microscopy and osmium/potassium dichromate method revealed that the OPN protein accumulates selectively on the surface of degenerating neurites that were filled with calcium precipitates, indicating that OPN protein accumulates selectively on the surface

of degenerating neurites by a possible interaction between OPN and calcium. In addition, the combined use of focused ion beam milling/scanning electron microscopy with 3-diemnsional reconstruction revealed that the OPN profiles of variable sizes and shapes were randomly distributed in the lesioned striatum, and some profiles directly connected to their parent dendrites that were negative to OPN. Thus, our data indicate that time-dependent localization of OPN protein correlates with the spatial profile of intracellular and extracellular calcification progression that occurs in the striatum, suggesting that OPN may play an important role in the initiation and progression of the microcalcification in response to brain insults.

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Keywords: Mitochondrial toxin, Microcalcification, Dendrites, Mitochondria, Osteopontin

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020

Descending Thin Limb Of The Intermediate Loop Expresses Both Aquaporin 1 And Urea Transporter A2 In The Mouse Kidney

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A new intermediate type of Henle's loop has been reported that it extends into the inner medulla and turns within the first millimeter beyond the outer medulla. This study aimed to identify the descending thin limb (DTL) of the intermediate loop in the adult C57Bl/6 mouse kidney using aquaporin 1 (AQP1) and urea transporter A2 (UT-A2) antibodies. In the upper part of the inner stripe of the outer medulla (ISOM), AQP1 was expressed strongly in the DTL with type II epithelium of the long loop, but not in type I epithelium of the short loop. The DTL of the intermediate loop exhibited weak AQP1 immunoreactivity. UT-A2 immunoreactivity was not observed in the upper part of any DTL type. AQP1 expression was similar in the upper and middle parts of the ISOM. UT-A2 expression was variable, being expressed strongly in the DTL with type I epithelium of the short loop, but not in type II epithelium of the long loop. In the innermost part of the ISOM, AQP1 was expressed only in type III epithelium of the long loop. UT-A2-positive and UT-A2-negative cells were intermingled in type I epithelium of the intermediate loop, but were not observed in type III epithelium of the long loop. UT-A2-positive DTLs of the intermediate loop extended into the UT-A2/AQP1-negative type I epithelium in the initial part of the inner medulla. These results demonstrate that the DTL of the intermediate loop is composed of type I epithelium and expresses both AQP1 and UT-A2. The functional role of the DTL of the intermediate loop may be distinct from the short or long loops.

Keywords: Loop of Henle, Intermediate Loop, Aquaporin 1, Urea Transporter A, Mouse Kidney

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021

3-D Imaging of Embryonic Development of *Xenopus* Using Synchrotron Radiation microCT

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Understanding developmental processes requires accurate visualization and parameterization of three-dimensional embryos. In *Xenopus laevis*, the South African clawed frog, cell and tissue movements have been studied in explants, in fixed embryos, in vivo using fluorescence microscopy or microscopic magnetic resonance imaging. None of these methods allows cell behaviors to be observed with micrometer-scale resolution throughout the optically opaque embryos over developmental time. Here we use non-invasive synchrotron radiation microCT, based on single distance phase contrast and/or combined with simple staining methods, to examine the course of embryonic development. We demonstrate that this powerful three-dimensional imaging technique provides high resolution views of developmental processes of each stage in wild-type *X. laevis* embryos, including cleavage, gastrulation and neurulation.

Synchrotron radiation microCT provides a useful tool for comparative developmental studies, embryo phenotyping, and quantitative modeling of development.

Keywords: Xenopus, Embryonic development, 3-D imaging, Synchrotron radiation microCT

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022

NADPH Oxidase Inhibitor Inhibits The Cell Growth By EBV-induced Transformation Via LMP1-NOX4-ROS Signaling In EBV-infected ARPE-19 Cells

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Epstein-Barr virus is a γ-herpes virus that has been known primary B cells by its infection can be transformed to immortalized lymphoblastoid cell lines (LCL). EBV-induced malignancy has been well understood on such as Burkitt's lymphoma and Nasopharyngeal carcinoma, but the role of EBV in EBV-infected retinal cells poorly understood. Previously, we established and reported a cell line model to address the relationship between EBV infection and retinal cell proliferation using adult retinal pigment epithelium (ARPE-19) by EBV infection. In this study, we found that reactive oxygen species (ROS) were dramatically increased in EBV-infected ARPE19 cells (APRE19/EBV) than parental cell line. And, the expression level of NADPH oxidase 4 (NOX4), a main resource of ROS, was upregulated by EBV infection. Interestingly, downregulation of LMP1 which is one of EBV viral onco-proteins completely decreased EBV-induced ROS accumulation and the upregulation of NOX4. Treatment of NOX inhibitor, induced apoptotic cell death of the only EBV-infected ARPE19 cells but not parental cell line. Pretreatment of z-VAD, a pan-caspase inhibitor, inhibited NOX inhibitor-induced cell death in ARPE19/EBV cells. Furthermore, Nox inhibitor-induced cell death mediated the activation of JNK and ERK. These our results suggested that NOX inhibitor could be therapeutic potential agents for treatment in EBV-infected retinal cells or diseases by inhibiting LMP1-NOX-ROS signaling.

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

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023

The Mitotic Checkpoint Regulator RAE1 Induceses Aggressive Breast Cancer Cell Phenotypes By Mediating Epithelial-Mesenchymal Transition

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The gene *RAE1*, which encodes ribonucleic acid export 1 (RAE1), is involved in mRNA export and is known to serve as a mitotic checkpoint regulator. In addition, haplo-insufficiency of *RAE1* leads to chromosome missegregation and early aging-associated phenotypes. In humans, a positive correlation has been found between RAE1 copy number abnormalities and gene amplification in breast cancer cells. However, the precise functional role of RAE1 in breast cancer remains to be determined. An *in silico* analysis of data retrieved from GENT and cBio-Portal identified RAE1 upregulation in breast cancer tissues, compared with normal breast cells. Functional studies of various cell lines showed that RAE1 induced invasive and migratory abilities by regulating epithelial-mesenchymal transition signals. A tissue microarray was constructed to demonstrate the interrelationship between clinicopathological features and RAE1 expression. Immunohistochemistry revealed a positive correlation between RAE1 expression and a high histologic grade. Furthermore, *RAE1* overexpression was associated with considerably poorer disease-free

survival and distant metastasis-free survival, especially in patients with oestrogen receptor-positive tumours. In summary, RAE1 may be a prognostic marker and therapeutic intervention target in malignant breast cancers.

Keywords: RAE1, Breast cancer, Invasion, migration, Epithelial-mesenchymal transition

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024

The genetic analysis on ancient *Ascaris* discovered from archaeological sites in South Korea

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In paleoparasitological study, the genetic research on ancient *Ascaris* found in archaeological samples is very useful for physical anthropologists to elucidate the ancient-to-modern secular changes in parasitic infection pattern. However, the data on ancient *Ascaris* obtained up to now were too insufficient to reconstruct comprehensive evolutionary history of *Ascaris* spp. In this regard, we tried to get in much information on the genetic traits of ancient *Ascaris* by molecular studies on the archaeological samples. We analyzed *Ascaris* ancient DNA with various multiple genetic markers, obtaining consensus sequences of each ancient *Ascaris* gene, and further performing phylogenetic analyses on them. Our study clearly showed that the genetic characteristics of ancient *Ascaris* spp. prevalent in ancient Korea was not uniform but was diverse to a certain degree. Genetic analyses on ancient *Ascaris* also represented that they could be helpful in molecular diagnosis of ancient *Ascaris* infection. This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (NRF-2016R1A2B4015669).

Keywords: Paleoparasitology, Ascaris, ancient DNA, Phylogenetic analysis, Korea

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025

Roles of Mitochondrial NADP+-dependent Isocitrate Dehydrogenase (IDH2) on Cisplatin-induced Acute Kidney Injury

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Mitochondrial $NADP^+$-dependent isocitrate dehydrogenase (IDH2) plays an important role on the formation of NADPH, which is critical for maintenance of mitochondrial redox balance. Cisplatin has been used for cancer therapy. However, its nephrotoxicity limits the use. Here, we investigated the role of IDH2 in cisplatin-induced nephrotoxicity. IDH2 gene-deleted ($IDH2^{-/-}$) and wild type ($IDH2^{+/+}$) mice were injected intraperitoneally cisplatin. Some mice were treated with the Mito-Tempo (MT), a mitochondria-specific antioxidant.IDH2 deficiency aggravated cisplatin-induced renal functional and morphological impairments. MT reduced those cisplatin-induced renal functional and morphological impairments in both $IDH2^{-/-}$ and $IDH2^{+/+}$ mouse kidneys. Cisplatin-induced reduction of NADPH levels was greater in $IDH2^{-/-}$ mouse kidneys than $IDH2^{+/+}$ mouse kidneys. Cisplatin increased hydrogen peroxide production and lipid peroxidation with decrease of glutathione (GSH) level. These increases were greater in the $IDH2^{-/-}$ mouse kidneys than $IDH2^{+/+}$ mouse kidneys. MT treatment attenuated those cisplatin-induced changes in NADPH, hydrogen peroxide, lipid peroxidation, and GSH levels of both $IDH2^{-/-}$ and $IDH2^{+/+}$ mouse kidneys. Mitochondrial damage and renal cell death after cisplatin injection were greater in the $IDH2^{-/-}$ than $IDH2^{+/+}$ mouse kidneys. MT reduced those cisplatin-induced mitochondrial damage and cell death in both $IDH2^{-/-}$ and $IDH2^{+/+}$ mouse kidneys. In conclusion, IDH2 deficiency aggravates cisplatin-induced nephrotoxicity via increase of mitochondrial oxidative damage, suggesting that IDH2 plays a crucial role in the pathogenesis of cisplatin-induced acute kidney injury (AKI).

Keywords: Cisplatin Nephrotoxicity, Mitochondria, Oxidative stress

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026

The First Report of the Anthropological Research Project on Zeleny Yar Mummies in Russian Federation

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Archaeologists have excavated the Zelyeny Yar archaeological site in Yamalo-Nenets Autonomus Okrug for the past several years. While they investigated two medieval necropolises, dated 9th to 13th centuries, seventy-two burials with a number of 12th to 13th century aboriginal Siberian mummies have been discovered. Although these mummies are very important to understand the physical and pathological traits of the Siberian people in history, scientific studies were not performed sufficiently on them by for now. In this regard, we, the Russian and South Korean researchers agreed to make collaborative studies on the Siberian aboriginal mummies. In the forthcoming years, our research will be mainly focused on a full and detailed anthropological picture about the pre-modern Siberian people, using various techniques such as archaeological, anatomical, histological, paleoparasitological, ancient DNA, stable isotope analysis, and craniofacial reconstruction. In fact, this is the first report of our long-term studies on invaluable 12th to 13th century Siberian Zeleny Yar mummies. Correspondences for this project: Sergey Mikhailovich Slepchenko (s_slepchenko@list.ru) of Russian Federation or Dong Hoon Shin (cuteminjae@gmail.com) of South Korea.

Keywords: Russia, Siberian Mummies, Anthropology, Medieval necropolis

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Poster

전시발표-1 (P001-P067)
2016년 10월 20일(목) 13:30 ~ 14:30 지하1층 포스터전시장
■ 육안해부학 분야: P1~P19
■ 신경과학 분야: P20~P67

전시발표-2 (P068-P145)
2016년 10월 21일(금) 13:00 ~ 14:00 지하1층 포스터전시장
■ 조직 및 발생: P68~P79
■ 면역 및 종양: P80~P120
■ 기타: P121~P145

P1

Anatomical Study of the Genicular Artery Branching Patterns and Its Clinical Applications

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Purpose: The total knee arthroplasty is increasingly recognized as a standard treatment option, and the number of this surgery has increased substantially. Although the vascular complications in total knee arthroplasty occur continually, precise studies are scarce.
Methods: In this study, 42 lower limbs were dissected. The horizontal line which extends between the most prominent point of the lateral and medial margins of patella was defined as a reference line. The distance of branching point of the genicular artery from the reference line was measured.
Results: The superior lateral and medial genicular arteries were located at + 38.17 ± 3.10 mm and + 32.68 ± 3.83 mm, the middle genicular artery was located at + 7.57 ± 3.98 mm and the inferior lateral and medial genicular arteries were located at - 18.46 ± 2.63 mm and - 24.09 ± 3.52 mm. When the middle genicular artery was combined with the other genicular arteries, the superior lateral genicular artery was located + 23.77 ± 6.61 mm and branched separately, + 42.82 ± 3.13 mm. In addition, the middle genicular artery had positive relationship with the inferior medial genicular artery and the inferior lateral genicular artery, respectively.
Conclusions: In this study, topography of the genicular artery and its anatomical association were demonstrated for the first time in Korean. Knowledge of the topography about frequent variation would be useful for safe surgery and clinical procedures. Moreover this data also encourages further development of this concept of variation study.

Keywords: Genicular artery, Variations, Branching patterns, Topography

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P2

Colonoscopy Tutorial Software Made with a Cadaver's Sectioned Images

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In training for actual or computed tomograph (CT) colonoscopy, novice doctors may watch tutorial videos. The conventional learning videos can be complemented by virtual colonoscopy software made with a cadaver's sectioned images (SIs). The objective of this study was to assist colonoscopy trainees with the new interactive software. Submucosal segmentations on the SIs were carried out through the whole length of the large intestine. With the SIs and segmented images, a volume model was reconstructed. Six-hundred seventy-one proximal colonoscopic views (conventional views) and corresponding distal colonoscopic views (simulating the retroflexion of a colonoscope) were produced. Not only navigation views that showed the current location of the colonoscope tip and its course but also supplementary description views were elaborated. The four corresponding views were put into convenient browsing software to be downloaded free from the homepage (anatomy.co.kr). The SI colonoscopy software with the realistic images and supportive tools was available to anybody. Users could readily notice the position and direction of the virtual colonoscope tip and recognize meaningful structures in colonoscopic views. The software is expected to be an auxiliary learning tool to improve technique and related knowledge in actual and CT colonoscopies. Hopefully, the software is updated using raw images from the Visible Korean project.

Keywords: Colonoscopy, Three-dimensional imaging, User-computer interface, Virtual colonoscopy, Visible Human Projects

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P3

Transnasal Endoscopic Ultrasound-Guided Reduction Of Maxillary Sinus Wall Fracture

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Maxillary sinus wall fracture is one of the most common types of fracture caused by maxillofacial trauma. Surgical morbidity from open reduction and internal fixation (ORIF) of maxillary sinus wall fracture often surpasses the benefits of ORIF. The authors devised transnasal endoscopic-assisted reduction of maxillary sinus wall fracture (TERM) without internal fixation as a minimally invasive surgery for maxillary sinus wall fracture. The purpose of this study was to investigate the feasibility of TERM in cadavers and patients. Six cadavers were dissected to evaluate the feasibility of TERM. In addition, twenty patients with maxillary sinus wall fractures who visited the ENT department from August of 2013 to December of 2015 were enrolled in this study.Cadaver dissections were performed to identify the most feasible route to the maxillary anterior wall. In addition, various methods of providing counterforces were tested in cadavers. In the clinical arm, demographic factors, type of anesthesia, and presence and type of fractures in patients who underwent TERM were analyzed. Patient satisfaction with surgery and postoperative computed tomography (CT) scans were obtained and compared to those of ORIF. Endoscopic inferior meatus antrostomy (IMA) is a feasible method of approaching the maxillary sinus wall in cadavers. In addition, counterforce could be applied to the maxillary sinus wall by pushing packed Vaseline-soaked gauze or using a zygomatic process approach via a Gillies incision. Clinical experience with patients showed that TERM could be performed under local anesthesia. Patients experienced good facial contour restoration postoperatively. The extent of fractured bony segments was reduced on postoperative CT without complications. Patient satisfaction with TERM was greater than that with ORIF (p=0.031). TERM was demonstrated to be feasible in a cadaveric study. In addition, TERM also showed favorable results in patients. The authors suggest that TERM without internal fixation is feasible for treating maxillary sinus wall fracture, or tripod fracture without severe dislocation. In addition, in patients who are reluctant to undergo a facial incision, TERM is a good alternative to ORIF.

Keywords: Facial Bone, Maxillofacial Injury, Maxillary Fracture, Endoscopic Surgical Procedure, Ultrasonography

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P4

엄지발가락가쪽휨증 교정시 종자뼈를 재배치하는 개선된 첫마디뼈 뼈자름술

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엄지발가락가쪽휨증 (무지외반증; Hallux Valgus)은 첫째발허리발가락관절에서 첫째발허리뼈가 안쪽으로, 엄지발가락이 가쪽으로 변형되며, 첫째발허리발가락관절의 부분탈구 및 관절염, 첫마디뼈의 안쪽돌림 그리고 첫째발허리뼈의 통증 등을 특징으로 하는 질환이다. 특히 대부분의 엄지발가락가쪽휨증 환자에서 종자뼈의 가쪽 이동 혹은 부분탈구가 발견되는데, 이는 엄지발가락가쪽휨증의 초기 발생 및 진행과, 수술 후 재발, 통증에 관여하고 있기에 종자뼈의 원래 위치로의 재배치는 엄지발가락가쪽휨증의 수술 시 중요한 고려 요소 중 하나라고 할 수 있다. 그러나 기존 알려진 수술방법으로 종자뼈를 정확히 재배치할 수 있는가에 대해서는 이견이 있다. 따라서 이 연구에서는 시신 연구를 통하여 개선된 뼈자름술을 이용해 종자뼈를 재배치할 수 있는지 알아보고자 하였다.

엄지발가락가쪽휨증을 가진 시신 2구 4쪽을 대상으로 하였다. 4쪽 모두에서 발허리뼈몸통의 몸쪽 1/3지점의 갈매기 뼈자름 교정 및 첫마디뼈의 개선된 뼈자름술을 시행하였다. 수술 전후의 발의 앞뒤 및 종자뼈 접선 단순 방사선 영상을 얻어 엄지발가락가쪽휨각과 첫째/둘째발허리뼈사이 각도를 기록하고 종자뼈의 재배치 정도를 Hardy와 Smith 등의 방법에 따라 각각 분류하여 비교하였다.

4쪽의 수술 전 엄지발가락가쪽휨각은 29.87도, 28.13도, 39.12도, 24.23도였으며, 첫째/둘째발허리뼈사이 각도는 8.45도, 8.02도, 13.23도, 9.01도 였다. 수술 전 안쪽 종자뼈의 위치는 degree 7(Gr 3), 5(Gr 3), 5(Gr 3), 4(Gr 1) 였다. 수술 후 엄지발가락가쪽휨각은 각각 1.36, 9.91, 12.12, 0.69도, 첫째/둘째발허리뼈사이 각도는 2.28, 2.42, 0.82, 1.58도, 수술 후 안쪽 종자뼈의 위치는 degree 2(Gr 0), 3(Gr 1), 2(Gr 1), 1(Gr 1) 이었다.

이 연구를 통하여 발허리뼈머리의 안쪽돌림 및 종자뼈의 가쪽이동은 기존의 발허리뼈 교정술과 함께 실시한 개선된 엄지발가락 몸쪽 뼈자름술로 만족스러운 재배치를 얻을 수 있었다. 수술 관절면 및 주변 조직 손상을 최소화 하고 안전성을 높이기 위해 첫마디뼈 절단면에 대한 세부적인 해부연구를 진행 할 계획이다.

Keywords: 엄지발가락가쪽휨증, 첫마디뼈, 종자뼈 재배치, Akin 뼈자름술

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P5

Three dimensional measurement of periodontal surface area for quantifying inflammatory burden

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Measurement of root surface area (RSA) is important for classification of periodontal diseases as a risk factor for the other diseases, The aim of this study is to measure the RSA at 6 mm below the cemento-enamel junction (CEJ) by using Mimics software (Materialise, Leuven, Belgium).

Thirty three representative human cone-beam computed tomography (CBCT) images were obtained from the Department of Oral and Maxillofacial Radiology, Dankook University Dental Hospital, Cheon-an, South Korea. In this study, maxillary third molars and mandibular third molar were excluded for high stain value. The CBCT scans were read into the visualization software after separating teeth, maxilla and mandible by uploading the CBCT image into Mimics. Twenty eight separate three-dimensional (3D) teeth files were transformed into the STL format using 3-Matic research (Materialise, Leuven, Belgium). In 3-matic, each tooth was separated into crown and root based on the cervical line. Cross-section surface is located at 6 mm below the CEJ. Also, it was used on measurement of the root surface area at 6 mm.

Remaining RSA was compared by gender, maxilla/mandible. Each RSA of all teeth was larger in male than female. Also, average of maxillary RSA was larger than mandibular RSA.

In this study, using CBCT and Mimics software demonstrated that it can easily generate 3D data and evaluate the RSA values. Further studies are warranted to fully evaluate the relationship between root surface area and periodontal diseases.

Keywords: Mimics, Periodontal diseases, Root surface area, Three-dimensional, Cemento-enamel junction

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P6

The Prevalence and Genetic Pattern of Clinodactyly in Korean Populations

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Clinodactyly, as rare congenital malformation, refers to a curvature of a digit in a radial or ulnar direction in the coronal plane. The abnormality is inherited as an autosomal dominant trait. And its frequency was low, however, it was higher by accompanying other congenital anomaly. In present study, the frequency and genetic characteristics of clinodactyly were investigated. In 100 family (382 peoples), clinodactyly was found in 4.7% (n =18). All clinodactyly were bilateral and it was more frequently in female (6.8%) than male (2.6%), without statistical difference (p = 0.056). Its inheritance was autosomal dominant trait in 80% (4/5) families, however, one family did not have this inheritance pattern. We described the frequency and clinical implication of clinodactyly, and this description will be lead to an improved understanding of its spectrum and inheritance.

Keywords: Clinodactyly, Autosomal dominant, Hand deformity, Smartphone pinky

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P7

Condylar size in maloc clusion skeletal patterns: Measurements of Three Dimensional models

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Objectives: As the primary center of mandible growth, the condyle undergoes a remodeling process as the responses to continuous stimuli during jaw movements. The condyle and the fossa might differ in shape between people with various malocclusions. 3-dimensional (3-D) reconstruction with CBCT can provide more information about the configuration and bone changes of condyles other than simple distances and angles measurement reported by the previous researchers.

Purpose: The purpose of this study was to assess condylar size in volumetric 3D imaging in patients with class I, class II, class III malocclusions.

Methods: Our study included 60 young patients with skeletal class I, class II and class III (20 patients for one class) of Dankook university dental hospital. CBCT data images were imported and reconstructed into 3D models by an interative medical image control system, Mimics 17.0 software. We evaluated the condylar volume, surface size, width, height, and length.

Result : The measurements for skelletal class I and class III did not show significant differences on condylar size. Condylar size of class II is the smallest. There also was little difference between right condyles and left sides. Male's condylar size was bigger than female's.

Conclusions: The present study provides details of the connection between malocclusion and condyle morphology.

Keywords: Condylar size, Malocclusion, Measurements of Three Dimensional models, Mimics

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P8

Anatomical Basis for Injection around First Dorsal Compartment of the Wrist: A Fresh Cadaveric Study

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People performing tasks that require frequent finger motions often experience pain in the dorsal wrist compartment due to synovitis and tendinopathy caused by friction from overuse of the fingers and wrists. Among the 6 dorsal compartments of the wrist, the first dorsal compartment is the most common site for such problems; therefore, procedures involving this area are commonly required. During these procedures, the adjacent SRN may be vulnerable to injury. So it is important to understand the anatomical relationship between the medial and lateral branches of superficial radial nerve (SRN) and the first dorsal compartment around the tip of radial styloid process (RSP). However, few studies have identified the anatomical proximity of these structures, or suggested a safe approach for performing procedures in this area. Through fresh cadaver dissection, this study aimed to delineate the anatomical relationship between the SRN and tendons of the first dorsal compartment, and suggest a safe approach for interventions or procedures performed around the RSP. We used 17 wrists from 9 fresh cadavers (6 men, 3 women) with no known history of disease or trauma around the wrist, were dissected. The mean age was 70 years (58 to 98 years). One limb was excluded due to its poor state of preservation. The width of the first dorsal compartment, distance between the extensor pollicis brevis (EPB) tendon and the closest medial branch of the SRN, and distance between the abductor pollicis longus (APL) tendon and the closest lateral branch of the SRN were measured. The distances were measured at the RSP (the tip of the RSP) and RSP+1 (1 cm proximal to the tip of the RSP) levels. The median distances between the EPB tendon and the closest medial branch of the SRN at the RSP and RSP+1 were 6.0 mm (range: 1.6~11.0 mm) and 3.2 mm (range: -2.0~9.4 mm), respectively. The median distances from the APL tendon to the closest lateral branch of the SRN at the RSP and RSP+1 were -2.0 mm (range: -9.0~8.4 mm) and 1.0 mm (range:

-7.2~8.0 mm), respectively. A high percentage of overlap (up to 59%) was observed between the lateral branch of the SRN and the APL tendon. Due to the anatomical proximity of the branches of the SRN and the first dorsal compartment around the RSP, physicians must be cautious during procedures near this location. It is important to approach from above the EPB, rather than from above the APL, when performing blind procedures, although ultrasound guidance is preferable.

Keywords: Superficial radial nerve, Abductor pollicis longus, Extensor pollicis brevis, Wrist, First dorsal compartment

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P9

Three concurrent variations of the aberrant right subclavian artery, the non-recurrent laryngeal nerve and the right thoracic duct

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We herein report a case showing three anatomical variations including the aberrant right subclavian artery (ARSA), the non-recurrent laryngeal nerve (NRLN) and the right thoracic duct in a 59-year-old male cadaver. The right subclavian artery arose from the descending aorta next to the left subclavian artery and coursed in between the oesophagus and the thoracic vertebrae. The recurrent laryngeal nerve did not coil around the right subclavian artery but directly entered the larynx. Lastly the thoracic duct terminated into the right brachiocephalic vein. This study makes an embryological assumption that the abnormal development of the right subclavian artery would had happened first and subsequently caused NRLN and the thoracic duct drainage variation. As to our knowledge, only two reports have been made previously concerning such concurrent variations. Therefore, this case report alerts the possibility of simultaneous occurrence of ARSA, NRLN and the right thoracic duct to the anatomical and the clinical fields.

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Keywords: ARSA, NRLN & right thoracic duct

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P10

귓바퀴관자신경과 얕은관자동맥 및 정맥의 국소해부학적 위치 관계

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귓바퀴관자신경은 편두통을 일으키는 통증유발 요인 중 하나로 알려져 있다. 서양인을 대상으로 관자부위에서 통증유발점이 될 수 있는 부위는 귓바퀴관자신경과 얕은관자혈관의 해부를 통해 보고되었지만, 동양인을 대상으로 귓바퀴관자신경의 전체 주행경로에서 신경이 얕은관자혈관에 의해 눌려 통증을 유발할 수 있는 위치에 대한 연구는 부족한 실정이다. 이에 본 연구에서는 귓바퀴관자신경과 얕은관자혈관의 위치관계를 관찰하고 신경과 혈관이 교차하는 지점을 계측하였다.

재료는 한국인 및 태국인 성인 시신 머리 21쪽 (오른쪽: 10쪽, 왼쪽: 11쪽, 평균나이: 71.8세)을 사용하였다. 관자부위의 피부를 벗긴 후 귓바퀴관자신경, 얕은관자동맥, 얕은관자정맥을 노출시켰다. 이 부위에서 신경과 혈관의 위치관계를 계측하기 위해 2개의 기준선을 설정하였다. 귀구슬과 눈확아래모서리를 연결한 선을 x축, 이 축에서 귀구슬을 수직으로 지나는 선을 y축으로 설정하였다.

귀구슬 앞쪽에서 귓바퀴관자신경은 1 개의 가지로 나오는 형태가 52.4% (11쪽/21쪽), 2 개의 가지로 나오는 형태가 47.6% (10쪽/21쪽)로 관찰되었다. 관자부위에서 귓바퀴관자신경과 얕은관자동맥 및 정맥의 위치관계에 따라 2가지 형태로 분류할 수 있었다. Type Ⅰ은 귓바퀴관자신경이 얕은관자동맥과 정맥보다 얕게 주행하며 교차하는 형태로 66.7% (14쪽/21쪽)에서 관찰되었다. Type Ⅱ는 귓바퀴관자신경이 얕은관자동맥과 정맥보다 깊게 주행

하며 교차하는 형태로 33.3% (7쪽/21쪽)에서 관찰되었으며 교차하는 혈관 유형에 따라 다시 2가지 형태로 분류하였다. 귓바퀴관자신경이 얕은관자동맥만 교차하는 형태는 Type Ⅱa로 14.3% (3쪽/21쪽)에서, 얕은관자정맥만 교차하는 형태는 Type Ⅱb로 19% (4/쪽21쪽)에서 관찰되었다. Type Ⅱa의 경우 귓바퀴관자신경은 귀구슬에서 앞쪽으로 10±5.6mm, 위쪽으로 36.7±6.2mm에서, Type Ⅱb의 경우 앞쪽으로 9.5±5.2mm 위쪽으로 27.7±8.4mm 에서 각각 교차하였다. 신경과 혈관이 교차하는 위치에서 귓바퀴관자신경과 얕은관자동맥 및 정맥의 두께는 각각 0.8±0.2mm, 1.9±0.6mm, 2.1±0.3mm였다. 서양인에서는 귓바퀴관자신경이 얕은관자동맥을 80%에서 깊게 교차하는 반면 한국인 및 태국인에서는 33%만이 혈관보다 깊게 교차하는 양상이었다.
이러한 해부학적 구조를 통해 동양인에서 귓바퀴관자신경 눌림 현상에 의한 편두통이 상대적으로 서양인보다 적게 나타날 것으로 예상할 수 있다. 신경과 혈관이 교차하는 계측 자료를 활용하여 두통 완화를 위한 신경감압술 시 보다 안전하게 수술을 수행할 수 있을 것으로 생각된다.

Keywords: 귓바퀴관자신경, 얕은관자동맥, 얕은관자정맥, 편두통

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P11

The Positional Relationship Between the Pectoralis Major and the External Abdominal Oblique Muscles for Applying the Dual Plane Breast Augmentation

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In breast augmentation, surgeons usually choose a pocket location for the implant subglandular, subfascial, or submuscular. Each pocket location has specific benefits and indications, but each also has unique tradeoffs in specific breast types. In comparison, the dual plane breast augmentation has more potential benefits and less tradeoffs than single pocket planes. For making dual plane pocket, the costal part of pectoralis major muscle(PM) should be cut down, and during this procedure, surgeons sometimes make wrong plane and muscular incision especially for the external abdominal oblique muscle(EAO).
The aim of this study is to clarify the positional relationship between the PM and the EAO for making the correct location of the implant and the exact muscular incision during the dual plane breast augmentation.
In this study, we dissected 15 cadavers (7 females and 8 males). We confirmed the distances from the midclavicular line to the borders of each muscles and measured the widths of overlap portion between the PM and the EAO in 4th, 5th and 6th costal levels.
The origin of lowermost portion of the costal part of PM was 6th rib in 86%. And also, it was originated from the 5th and 7th rib in 7%, respectively. The distances from the midclavicular line(MCL) to the lateral border of the PM at 4th, 5th and 6th rib were 50mm, 31mm and 5mm, respectively. In 97% of all cases, the PM and the EAO were overlapped in nearby the MCL. In one case, the PM and the EAO was separated from each other, as the EAO did not attached to the 6th rib and was originated from the 7th rib. The widths of overlap portion between the PM and the EAO at the 5th and 6th rib were 24mm and 25mm, respectively.
During dual plane breast augmentation, the pocket for implant should be made correct plane at just under the PM, and the muscular incision line must be located at the lowermost portion of the costal part of PM. Therefore, surgeon need to consider that in almost cases the PM and the EAO overlapped each other about 25mm at nearby the MCL, and the lowermost portion of the costal part of PM was originated from the 5th or 7th rib in 14% of cases, not from the 6th rib.

Keywords: Pectoralis Major Muscle, External Abdominal Oblique Muscle, Dual Plane Breast Augmentation

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P12

Topographic Anatomy of the Infraorbital Artery and its Clinical Implications for Nasolabial Fold Augmentation

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Introduction: A prominent nasolabial fold (NLF) makes creases in the nasolabial region, causing esthetic problems. Facial soft-tissue augmentation procedures is used to alleviate this problem. However, inappropriate procedure of injectable treatments to the NLF can result in vascular complications. In the nasolabial region, the infraorbital artery (IOA) anastomoses with the facial artery (FA). In cases where the FA is "non-dominant", the blood supply of nasolabial region belongs to IOA. The purpose of this study was to provide detailed topographic information on the IOA during nasolabial fold augmentation.

Materials and methods: Sixty-two hemifaces from 20 Thai and 11 Korean cadavers were used in this study. The FA and the IOA were observed in the midface area, and the running layers of the IOA and infraorbital nerve (ION) were compared in the infraorbital foramen. Also, changes in the IOA were observed according to vascular dominance of the FA.

Results: In 72% of the cases, the IOA was located superficial to the infraorbital nerve branches. The IOA divided into three main branches—palpebral, nasal, and labial branches—in 58%, 100%, and 93.5% of the specimens, respectively. In bilateral FA topography, vascular dominance of the FA was observed in 7 specimens (16.5%). In the non-dominant side of the FA, the IOA was observed to be thicker with a wider distribution while the IOAn penetrated the LLS and anastomosed with the FA in the lateral nasal region in 4 out of 7 specimens.

Conclusions: During nasolabial fold augmentation, a deep injection should be made after the needle or cannula establishes contact with the bone to avoid vascularly compromising the IOA. Moreover, a physician should be aware prior to designing needle entry that the arterial branches locate at the region next to the nose ala.

Keywords: Infraorbital Artery, Facial Artery, Nasolabial Fold

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Tracheal Compression by Aberrant Innominate Artery and Variant Origin of the Vertebral Artery

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The aorta is the main arterial trunk in the human body, however, its variation was extremely variable. During an educational dissection, aberrant branching pattern of aortic arch was found in a Korean cadaver. The innominate artery (brachiocephalic trunk) originated from the aortic arch at the left side of the trachea. It crossed the trachea and divided into the right common carotid and subclavian arteries. The left vertebral artery originated from the aortic arch between the origins of the left common carotid artery and the left subclavian artery. Ant then, the left vertebral artery coursed upward to the transvers foramen of the C7. The author describes this previously novel case report and discusses the clinical implications of such a variant.

Keywords: aberrant innominate artery, aortic arch, tracheal compression, variation, vertebral artery

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한국인 소아청소년 3차원 머리뼈 모델을 이용한 뼈콧구멍과 코 사이의 형태학적 관계 분석

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얼굴에서 코는 가장 두드러진 부분이며 얼굴인식 및 얼굴복원에 있어 중요한 형태소이다. 뼈콧구멍의 형태 특징을 바탕으로 코의 형태를 추정할 수 있는 연구를 통해 얼굴복원에 필요한 형태소

자료를 제공할 수 있으나 한국인의 경우 이와 관련한 객관적인 분석 자료가 부족하며 소아청소년의 경우는 더욱 그러한 실정이다. 이 연구는 한국인 소아청소년의 3차원 모델을 이용하여 뼈콧구멍과 코 주변의 형태에 대한 계측을 수행하고 선형회귀분석을 통하여 뼈콧구멍으로부터 코의 형태를 추정할 수 있는 공식을 도출하고자 하였다.

한국인 소아청소년 남자 155명, 여자 152명의 컴퓨터단층촬영 영상으로부터 제작한 3차원 머리뼈 및 얼굴 모델을 대상으로 조사하였다. 20살까지의 표본들을 5살 간격으로 나이 집단을 4개로 나누어 분석하였다. 코 주변의 계측을 위해 9개의 표지점과 9개의 계측항목을 선정하였고 뼈콧구멍 주변 계측을 위해 7개의 표지점과 5개의 계측항목을 선정하였으며 뼈콧구멍과 코의 표지점 사이의 관계를 직접적으로 확인할 수 있는 4개의 계측항목을 측정하였다. 각 계측 항목에 대한 기술통계, 성별와 나이 집단에 따른 평균값 차이를 비교하였다. 선형회귀분석은 계측 항목으로 조합할 수 있는 모든 경우를 분석하여 뼈콧구멍으로부터 코의 형태를 추정하는 방정식을 도출하였다.

성별과 나이집단에 따라 모형 적합성을 대표하는 R-제곱값이 높은 회귀방정식의 종류는 다소 달랐지만 공통적으로 높은 R-제곱값을 보인 방정식을 뼈콧구멍으로부터 코의 형태를 추정할 수 있는 회귀방정식으로 최종 선택하였다. 이 회귀방정식들은 코의 폭, 코의 높이, 코끝 위치를 추정할 수 있어 한국인 소아청소년의 얼굴복원에 있어 코의 형태를 추정하는 데 도움이 될 것으로 기대한다.

사사: 이 초록은 2015년도 정부(미래창조과학부)의 재원으로 한국연구재단의 지원을 받아 수행된 연구임(No. 2015R1C1A1A01052630).

Keywords: Nose, Piriform aperture, Three dimensional model, Regression equation, Morphometric study

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The sensory innervation of the tentorium cerebelli of human cranial dura

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Intoduction: Trigeminal nociceptive system within intracranial meninges have been postulated as possible causes of certain headaches. Knowledge about them may be also important for the neurosurgeon in order to avoid contact that may result in postoperative headache and trigemino-cardiac reflex. Investigations of human dura mater is comparatively rare, particularly in the studies by macroscopic observation. From above, we examined human cranial dura in whole-mounts in order to understand comprehensive and global features of sensory nerve distribution patterns on cranial dura mater.
Methods: The supratentorial part of cranial dura mater from human cadaveric specimens (N = 29) were stained for Sihler's method to examine the pattern and distributions of the nerve fibers. Stained specimens were treated with graded glycerin and photographed.
Summary: Linear projection of the ophthalmic division of trigeminal nerve ran on the tentorium cerebelli with diverse directions, as recurrent meningeal branch. The recurrent meningeal branch of trigeminal nerve predominantly innervated the tentorium cerebelli in all specimen, projecting to the straight sinus and the transverse sinus. The posterior part of the falx cerebri and straight sinus were innervated by medially directed nerve fibers elongated from the tentorium cerebelli. Laterally mediated nerve fibers on the tentorium cerebelli projected to transvers sinus and lateral convexity. Stained nerve fibers are not observed in the anterior and middle part of falx cerebri and superior sagittal sinus.
Conclusions: The ophthalmic division of trigeminal nerve on the tentorium cerebelli showed significant variations in the projection pattern with more widespread, implicating their sensitization under physiological or pathological conditions.

Keywords: Tentorium cerebelli Cranial dura mater Trigeminal nerve Headache Trigemino-cardiac reflex

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Comparison of Fore Limb Digital Length Between Rat and Guinea Pig

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Rodents are mammals of the order Rodentia that comprises 5 suborders, 33 families, 481 genera and 2277 species. The shape of bone such as scapula, carpal bones, metacarpal bones and phalanges is a characteristic indicator for each animal. Differences of food manipulation with digits in rodents were reported in various mammals. In this study, comparison of fore limb digital length between in rat and guinea pig was performed using computer based radiographic system.

Digits were collected from 20 adult male SD rats and guinea pigs. Digital radiographic images of each digit were taken from computer based radiation system. Digital length was measured by Image J and statistical analysis was performed by SPSS program. Student t-tests and one-way ANOVA with post hoc Bonferroni were performed at significance levels of 0.01 to 0.05.

Significant difference between phalangeal lengths was found in all digits except for middle to distal phalanges of the 2nd digits and 5th digits in rat. In guinea pigs, there were significant differences between phalangeal lengths in all the digits. In comparison of phalangeal length between rat and guinea pig, significant differences were found in all digits except for middle phalanges of 2nd and 4th digits. The differences of digital length between rat and guinea pig were also found in 2nd and 5th digits. The ratio of the lengths of the 2nd and 4th digits was significantly differed between both animals. The ratio of phalangeal lengths of the 2nd and 4th digits between rat and guinea pig was found in proximal and distal phalanges not in middle phalanges.

Keywords: Rat, Guinea pig, Forelimb, Phalangeal length

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P17

Anatomy of the Anterior Pennate Part of the Soleus Muscle: Various Externally, Bipennate Internally

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Introduction: Soleus muscle is one of the chief plantar flexors of the foot. However, the information about the functional role of soleus in standing and walking is poorly understood yet. In this study, the shape and sectional images of soleus were analyzed.

Methods: Sixty-two soleus muscles from 31 adult Korean cadavers were examined. The length and width of the muscles were measured. The shapes of the muscular fibers in median part of anterior surface were examined and grouped into bipennate type and unipennate type, and the width of median part was measured. The muscles were stained in Lugol's solution for ten days and their CT scans were obtained. The comparison between external observation and CT image was made. The size and shape of the pinnate muscle fibers were examined on the sectional images.

Summary: The length and maximal width of the soleus were 343.0 mm and 78.6 mm, respectively. The muscular fibers in the median part of anterior surface were in bipennate arrangement in 75.9% of specimens or in unipennate arrangement in 6.9%. In 17.2%, because muscular fibers in median part were absent or too scarce to be examined eyes or by CT scan, the arrangement was not identifiable. The maximal width of median part of anterior surface occupied by anterior muscular fibers and intramuscular tendon was 35.6 mm in average. In coronal CT images, the median part was bipennate in all specimens. It formed an internal core structure which ran vertically in most part of the soleus muscles.

Conclusions: The median part of anterior surface of soleus was not only in bipennate shape, but also in unipennate shape, or unidentifiable. However, it was bipennate internally in every specimen. The median pennate part formed central core of the muscle, which suggest that it might contribute the functional role of soleus in standing and walking. (This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology(NRF-2014R1A1A2055742)).

Keywords: Gait, Running, Endurance, Triceps Surae, Biomechanics

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Aging change of epidermal thickness in Korean

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Skin is composed of epidermis and dermis and varied depend on the region and gender. Previous studies have examined the thickness of facial soft tissue for facial reconstruction, and there has been no detailed study focusing on the epidermis, specifically with regard to its thickness with age.

In Korean, it has been reported that the partial of the face without aging. We attempted to examine the thickness of epidermis on the face with aging in korean.

We performed 273 specimen biopsies on 12 different regions of the normal skin of Korean men and women, It was categorized according to gender and age(20~39 year-old, 40~59 year-old, and 60~79 year-old groups). The biopsy specimens were stained H&E and epidermal thickness was measured using dotSlide program(slide microsocope BX 51, Olympus, Poland).

The average of men and women groups by age was compared in 12 region, the epidermis thickness was 159μm for 20-39 men group, 116μm for 40-59 group, and 92μm for 60-79 group. For women, the epidermis thickness was 149μm for 20-39 group, 103μm for 40-59 group, and 90μm for 60-79 group.

The epidermis was the thickest in the 20-30 year olds in both men and women and thinnest was in the 60-79 year-olds. These results showed that epidermis became thinner with aging. As for regional, lower lip was the thickest and the upper eyelid was the thinnest for both sexes.

Moreover, the thickness of forehead became thinner with aging as it was 128μm for 20-39 group, 102μm for 40-59 group, and 63μm for 60-79 group in men while it was 95μm for 20-39 group, 72μm for 40-59 group, and 67μm for 60-79 group in women. The thickness of lower lip also became thinner with aging as it was 585μm for 20-39 group, 384μm for 40-59 group, and 365μm for 60-79 group in men and it was 499μm for 20-39 group, 372μm for 40-59 group, and 97μm for 60-79 group in women.

Keywords: Aging, Epidermis, Thickness, Korean

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근치적전립샘암절술의 위치표지로서의 활용과 남성요실금 방지 및 음경등동맥 보호를 위한 두덩전립샘인대의 형태학 연구: 형태와 크기의 폭넓은 다양성

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두덩전립샘인대는 남성의 전립샘과 방광의 연결부위로부터 두덩뼈까지 이어지는 인대로서, 근치적전립선암절제술 등에서 생식기능 보호를 위해 중요한 위치표지로 쓰인다. 또한, 이 인대는 요도를 지지할 수 있는 구조로서, 남성의 요실금을 방지하는 데에 중요한 역할을 하므로, 수술적 처치시의 이 인대의 손상은 요실금의 발병 빈도를 높이게 된다. 본 연구에서는 두덩전립샘인대의 손상을 줄일 수 있도록 그 형태를 분석하고, 위치표지로서의 형태학적 특징을 이용하기 쉽도록 주변 구조와의 관계를 구명하였다. 성인 남성 시신 13 구의 골반에서 골반근막을 제거한 뒤, 방광을 뒤로 젖힌 상태에서 전립샘의 앞쪽 가장자리, 두덩전립샘인대, 음경등정맥의 위치를 확인하였다. 결합조직을 제거하여 두덩전립샘인대의 가장자리, 전립샘에 붙은 자리, 두덩뼈에 붙는 자리를 노출시킨 뒤, 두덩전립샘인대의 개수, 모양, 두덩뼈에 붙는 범위, 왼쪽과 오른쪽 두덩전립샘인대 사이의 거리, 음경등정맥의 개수, 음경등정맥과 두덩전립샘인대 사이의 위치관계를 조사하였다. 두덩전립샘인대는 두덩뼈와 방광목에 붙는 위치의 개수가 다양하여, I, X, ㅅ, Y, M, W 등의 모양을 하고 있었다. 두덩전립샘인대가 두덩뼈에 붙는 위치의 개수는 1-3 곳이었고, 방광목

에 붙는 위치의 개수는 1–5 곳이었다. 인대가 두덩뼈에 붙은 자리의 너비는 1.23 mm – 29.43 mm로 다양하였다. 양쪽 인대 사이의 거리는 두덩뼈 쪽에서는 5.41 mm – 15.61 mm, 전립샘 쪽에서는 4.21 mm – 21.67 mm였다. 일부 표본에서는 두덩전립샘인대가 항문올림근의 인대활과 합쳐지는 것도 관찰되었다. 대부분의 표본에서 두덩뼈 – 전립샘 – 양쪽 인대 사이의 공간으로 음경등동맥이 노출되었다. 두덩전립샘인대의 위치를 확인하는 것은 수술 도중 음경등동맥을 보호하는데에 도움이 될 것이며, 단일 두덩전립샘인대만 존재하는 경우에 인대의 손상은 수술 후 요실금을 유발하기 쉬우므로 주의하여야 할 것이다.

Keywords: 전립샘암, 비뇨생식가로막, 요도

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Volume Reconstruction of Neural Circuits using Serial Block-Face Scanning Electron Microscopy

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Each of the 100 billion neurons in the human brain has thousands of connections to other neighboring neurons. These 100 trillion contact points between neurons are called synapses where the signals from presynaptic neuronal axons are delivered to postsynaptic neuronal dendrites. Although the light microscopy has long been used to explore neuronal connections, even state-of-the-art light microscopy has a limited resolving power to observe synaptic ultrastructures. In contrast, electron microscopy is currently the only available technique with a spatial resolution sufficient to identify fine neuronal processes and synaptic structures in densely packed neuropil. For large-scale volume reconstruction of neuronal connectivity, KBRI recently installed serial block-face scanning electron microscopy. This advanced EM technology allows us to acquire thousands of serial images in an automated fashion and reconstruct neural circuits faster by reducing the alignment task. Here we introduce the whole reconstruction procedure of synaptic network in the rat hippocampal CA1 area and discuss technical issues to be resolved for improving image quality and segmentation. Compared to the serial section transmission electron microscopy, serial block-face scanning electron microscopy produced much reliable 3D data sets and accelerated reconstruction by reducing the need of alignment and distortion adjustment. This approach will generate invaluable information on organizational features of our connectomes as well as diverse neurological disorders caused by synaptic impairments.

Keywords: Electron Microscopy, Hippocampus, Synapse, Connectomics, Mapping

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Effects of a mitochondrial division inhibitor on neuroprotection in kainic acid-induced hippocampal cell death

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Kainic acid (KA)-induced excitotoxicity promotes cytoplasmic calcium accumulation, oxidative stress, and apoptotic signaling, leading to hippocampal neuronal death. Mitochondria play a critical role in neuroinflammation and the oxidative stress response. Mitochondrial morphology is disrupted during KA-induced seizures; however, it is not clear whether mitochondrial fission or fusion factors are involved in KA-induced neuronal death. We investigated the effect of Mdivi-1, a chemical inhibitor of the mitochondrial fission protein Drp1, on mitochondrial morphology and function in KA-injected mice. Mdivi-1 pretreatment significantly reduced seizure activity and increased survival rates of KA-treated mice. Mdivi-1 was protective against mitochondrial morphological disruption, and it reduced levels of phosphorylated Drp1 (Ser616) and Parkin recruitment to mitochondria. By contrast, levels of mitochondrial fusion factors did not change. Mdivi-1 also reduced KA-induced neuroinflammation and glial activation. We conclude that inhibition of mitochondrial fission attenuates Parkin-mediated mitochondrial degradation and protects from KA-induced hippocampal neuronal cell death.

Keywords: Drp1; Mitochondrial fission; Neuroinflammation; Neuronal cell death

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A Significant Effect Of Trichostain A On Delaying Wallerian Degeneration In Sciatic Nerve.

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Trichostatin A(TA) has been widely applied for biomedical research fields such as production of cloned mouse embryos, inhibition of histone deacetylase. However, its effect on peripheral nerve have been poorly understood. Thus, we tried to reveal its effect on Wallerian degeneration(WD) through 3 days in vitro(3DIV) sciatic nerve explant culture. Firstly, we found that 3DIV cultured nerves on complete DMEM with 1mM of TA keeps its unaltered morphology compared to positive control(3DIV cultured nerve without TA). To be more specific, the fibers showed almost same ovoid index, neurofilament(NF) index, myelin index as negative control(unaltered nerve). Also, we scrutinized both its dedifferentiation and proliferation, using diverse markers including LAMP1(lysosomal marker), p75 NGR(dedifferentiation marker), pERK1/2(dedifferentiation marker), Ki67(proliferation marker), Krox-20(demyelination marker). From that, we confirmed that TA successfully help drop all of the level of the gene expression markers, which means TA really acts on WD inhibition on molecular scale. To sum up, TA could be a powerful drug for delaying onset of WD.

Keywords: Trichostain A, Schwann Cell, Sciatic nerve, Wallerian Degeneration

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Induction of Schwann cell demyelination correlates with carbon monoxide during wallerian degeneration

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Carbon monoxide (CO), a gaseous second messenger, arises in biological systems during the oxidative catabolism of heme by the heme oxygenase (HO) enzymes. Till date, three isoforms of HO (HO-1, HO-2, and HO-3) have been identified. HO-1 expression is induced ubiquitously in response to oxidative stress, whereas HO-2 is constitutively expressed and not inducible. Previous studies revealed that CO can modulate a variety of physiological processes, including gasotransmitter. Similar to CO, H_2S is the most recently described gasotransmitter and is essential for Schwann cell responses to peripheral nerve injury. However, the effect of CO on peripheral nerve injury is still unknown. Thus, we examined role of CO on peripheral nerve injury. First, we investigated the effect of CO in Schwann cell de-differentiation and proliferation during Wallerian degeneration (WD) using ex vivo sciatic nerve explant system. We demonstrated that HO inhibitors reduced p75NGFR/LAMP1 and Ki67 as factors implicated in Schwann cell de-differentiation and proliferation during WD, respectively. In addition, inhibition of HO prevented the process of demyelination via ovoid observation of sciatic nerve fiber and immunochemistry for MBP using HO inhibitors. These findings suggest that CO has a strong protective effect on WD.

Keywords: Carbon monoxide, Schwann cell, Wallerian degeneration, Heme oxygenase

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P24

Anatomical difference and distributional defect between mutant gene lead to expression dissimilarities in adenoviral vector-mediated mouse model of Dominant intermediate Charcot-Marie-Tooth disease type C (DI-CMTC).

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Dominant intermediate Charcot-Marie-Tooth disease type C (DI-CMTC) used to be classified on the basis of motor conduction velocity but now revealed for having axonal and demyelination features, is a dominantly inherited neuropathy. DI-CMTC is linked with tyrosyl-tRNA synthetase (YARS) associated neuropathy which is caused by three different types of mutations [E196K and G41R missense mutation and one *de novo* deletion (153-156delVKQV)]. It is clear that YARS mutant induces neuronal dysfunction, morphological symptoms of axonal degeneration, and impaired motor performance. For the first time, here we describe a novel YARS associated mouse neuropathy model that consists of a neuronal specific promoter. YARS fusion proteins are expressed with Flag-tag (wild-type WT, E196K, and G41R mutants) in spinal cord, peripheral axons, and dorsal root ganglion (DRG-neuron) using adenovirus vectors *in vivo*. We discovered significant distribution of WT YARS in all expressed regions whereas after the transfection, expression of E196K mutant was found substantially greater than that of G41R mutant in all areas of expression. However, proportion of Flag/GFP-double-positive signal in E196K mutant type was statistically similar to WT in DRG neurons. Immunohistochemistry experiments displayed that the double positive signal was higher in cross section slides than that of longitudinal section of axons in E196K mutant which may be due to the anatomical difference in tissue that lead to expression dissimilarities. Similarly, anti-Flag immunostaining pattern was different for each adenovirus in spinal cord.

Thus, our result using this animal model provide not only distributional defect between mutant genes and WT in neuron but also convenient information regarding morphology of DI-CMTC. This is also a potential lead and strategy for the treatment of incurable neuropathy.

Keywords: Tyrosyl-tRNA synthetase, DI-CMTC, Recombinant adenovirus, E196K mutation, G41R mutation

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P25

Down Regulation of DICER Acivate Inflammasomes in Astrocytes

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DICER is RNase III enzyme that cleave double-stranded RNA (dsRNA). It is core enzyme in microRNA (miRNA) processing and Short interspersed elements (SINEs). Down regulation of DICER is associated with multiple types of cancers and inflammatory diseases. Inflammasomes are responsible for the innate immune responses. It recognizes microbial, stress and damage signals and directly activates caspase-1, which subsequently induces secretion of pro-inflammatory cytokines. In age-related macular degeneration (AMD), down regulation of DICER induces accumulation of Alu-RNA as a result Nlrp3 inflammasomes activated. In brain, various neurodegenerative diseases associated with inflammasomes activation, but there are any direct interaction between deregulated DICER and inflammasomes activation. In our study, DICER expression are down-regulated with various stressful conditions and as a results, dsRNA are accumulated in the cells along with increased concentration of cleaved caspase-1 and interleukin-1 β in human glioblastoma cell lines can be estimated as inflammasomes activation.

Keywords: DICER, Inflammasomes, Astrocyte

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P26

Protein Disulfide-Isomerase A3 Significantly Reduces the Neuronal Damage by Decreasing the Oxidative Stress

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Ischemia causes oxidative stress in the endoplasmic reticulum (ER), accelerates the accumulation of unfolded and misfolded proteins, and can finally lead to neuronal cell apoptosis. In the present study, we investigated the effects of protein disulfide-isomerase A3 (PDIA3), an ER-resident chaperone that catalyzes disulfide-bond formation in a subset of glycoproteins, against oxidative damage in the hypoxic HT22 cell line and against ischemic damage in the gerbil hippocampus. The HT22 cell line showed effective (dose-dependent and time-dependent) penetration and stable expression of the Tat-PDIA3 fusion protein 24 h after Tat-PDIA3 treatment, compared to that in control-PDIA3. Furthermore, Tat-PDIA3 significantly reduced the formation of H2O2-induced reactive oxygen species and apoptosis in the HT22 hippocampal cell line, which were demonstrated using 2′,7′-dichlorofluorescein diacetate and a terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) assay, respectively. The administration of Tat-PDIA3 significantly reduced the ischemia-induced hyperactivity seen a day after ischemia/reperfusion, and the ischemia-induced neuronal damage and glial (astrocytes and microglia) activation seen in the hippocampal CA1 region four days after ischemia/reperfusion. In addition, the administration of Tat-PDIA3 significantly reduced lipid peroxidation and nitric oxide generation in the hippocampal homogenates 3–12 h after ischemia/reperfusion. These results suggest that Tat-PDIA3 can act as a neuroprotective agent against ischemia by decreasing glial activation and oxidative damage.

Keywords: Protein disulfide-isomerase A3; Hippocampus; Gerbil; Oxidative stress; Tat peptide

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P27

Increased expression of suppressor of cytokine signaling 2 in the subventricular zone after transient focal cerebral ischemia in adult rats

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Suppressor of cytokine signaling 2 (SOCS2) is a well-established negative regulator of growth hormone signaling that acts on adult hippocampal neurogenesis during ischemic insults. To explore whether SCOS2 is involved in poststroke neurogenesis, we studied the temporal expression of SOCS2 mRNA in the subventricular zone (SVZ) of rats after transient focal cerebral ischemia. We found that SOCS2 expression was upregulated in the SVZ of the infarcted hemisphere. The number of SOCS2-expressing cells was significantly increased in the ipsilateral SVZ compared with that on the contralateral side on days 7–10 after reperfusion, and SOCS2-expressing cells were highly proliferative, coinciding both spatially and temporally with stroke-induced neurogenesis. Almost all SOCS2-expressing cells in the SVZ were colabeled with the neural stem cell markers nestin and musashi1 and the neural/glial progenitor transcription factor Sox-2. In addition, SOCS2 was highly expressed in newly generated neurons that were immunoreactive for polysialic acid-neural cell adhesion molecule, indicating that SOCS2 expression may be persistent during neuronal differentiation. Thus, our data demonstrated that SOCS2 mRNA was highly expressed in proliferating neural stem/precursor cells and postmitotic migratory neuroblasts in the SVZ niche after focal cerebral ischemia, suggesting that SOCS2 may be actively involved in regulating adult neurogenesis induced by ischemic stroke.

Keywords: Suppressor of cytokine signaling 2; Neural stem cells; Immature neurons; Focal ischemia; Subventricular zone

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P28

The protective roles of alpha B-crystallin in oligodendrocyte precursor cells under oxidative stress

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Alpha B-crystallin (aBC) is a member of small heat shock protein family, and it is expressed in mature oligodendrocytes but not oligodendrocyte precursor cells (OPCs) in the central nervous system. Recently, we observed *in vitro* that survival rate of OPCs is lower than mature oligodendrocytes under oxidative stress and this result suggested that aBC may play a protective role in mature oligodendrocytes. In the present study, we prepared the aBC recombinant lentiviral vector for aBC overexpression in OPCs from the cerebrum of neonate rats (postnatal day 1) and investigated how aBC could protect OPCs under oxidative stress induced by hydrogen peroxide (H_2O_2) treatment. We demonstrated that the survival rate of aBC-overexpressed OPCs was higher than those of control groups (vector control and normal OPCs) under oxidative stress condition. Under the condition without H2O2, Akt activities (p-Akt/t-Akt) were not different between aBC-overexpressed OPCs and control groups. However, under oxidative stress condition, Akt activities in control groups were suppressed, whereas Akt activity in aBC-overexpressed OPCs was not suppressed and maintained to the level of the condition without H_2O_2. In aBC-overexressed OPCs under oxidative stress condition, proapoptotic protein such as Bax and caspase-3 expression was suppressed, whereas antiapoptotic protein such as Bcl-2 expression was increased. The present results showed that aBC overexpression can inhibit the downregulation of Akt pathway in OPCs under oxidative stress, which suggests that aBC protects OPCs from oxidative stress-induced apoptosis.

Keywords: Alpha B-crystallin, Oligodendrocyte Precursor Cell, Oxidative Stress, Akt Pathway

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P29

Neuronal Origin of Neuropeptide Y (NPY) or Cocaine- and amphetamine-regulated transcript (CART) Fibers Projecting to the Tuberomammillary Nucleus of the Rat

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Based on the importance of tuberomammillary nucleus (TMN) as a target for feeding/arousal-related functions, we aimed in the present study to investigate neuronal origin of neuropeptide Y (NPY) and cocaine- and amphetamine-regulated transcript (CART) fibers projecting to the histaminergic nucleus. In the first series of experiments, we examined fiber distribution of NPY and CART in the TMN. Extensive NPY (or CART)-immunoreactive (ir) axon terminals were observed within the boundary of adenosine deaminase (ADA)-ir TMN regions. NPY-ir varicosities co-contained vesicular GABA transporters (vGAT). CART boutons, however, contained either vGAT or vesicular glutamate transporters (vGLU), which suggested the dual origins of CART fibers. In the second series of experiments, we investigated the neuronal origin of NPY or CART fibers projecting to the TMN using retrograde tracing method. The arcuate nucleus (Arc) was the sole source of NPY fibers projecting to the nucleus. In contrast, CART fibers in the TMN originated from the Arc as well as the other hypothalamic nuclei including the retrochiasmatic nucleus, paraventricular nucleus, perifornical region of the lateral hypothalamus, zona incerta, and dorsal hypothalamic area. Quantitative analysis showed that the Arc occupied approximately 23.5% of the total CART input to the TMN, while the rest (76.5%) came from the remaining hypothalamic nuclei. The present observations suggested that the TMN might play a key role in energy balance and arousal, by receiving peripherally-originated, first-order NPY and CART inputs from the Arc as well as second-order (and downstream) CART inputs from the other hypothalamic nuclei.

Keywords: Neuropeptide Y (NPY), Cocaine- and amphetamine-regulated transcript (CART) peptide, Tuberomammillary nucleus (TMN)

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P30

The Neuroprotective Effect of Brain-Specific Angiogenesis Inhibitor-1 in a Parkinson's Disease Model

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Brain-specific angiogenesis inhibitor-1 (BAI-1) is a seven-transmembrane protein that belongs to the adhesion G protein-coupled receptor family. It has been reported that BAI-1 has anti-angiogenic and anti-tumorigenic properties. However, the role of BAI-1 in Parkinson's disease is still unknown. In this study, we investigated the function of BAI-1 in Parkinson's disease using a cellular model. To identify the expression pattern of BAI-1 protein in specific cell type, we performed immunostaining using striatum and substantia nigra of MPTP-injected mouse brain. The BAI-1 protein was expressed in neuronal cells including dopaminergic neurons, however, we could not detect in both microglia and astrocytes. Moreover, we found that expression of BAI-1 was reduced in 1-methyl-4-phenylpyridinium (MPP^+)-treated mouse primary mesencephalic cells and SH-SY5Y cells. Because we have previously reported that AMPK inhibits MPP^+-induced neuronal cell death, we examined the relationship between AMPK and BAI-1. Interestingly, we found that BAI-1 expression was increased by AICAR, which is a specific activator of AMPK. In addition, overexpression of BAI-1 reduced MPP^+-induced neuronal cell death. Taken together, these results suggest that BAI-1 may act as cell survival factor in Parkinson's disease.

Keywords: Brain-Specific Angiogenesis Inhibitor-1, MPP+, AMPK, Parkinson's Disease

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P31

GlcNAc Kinase Modulates Dynein Motor

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N-acetylglucosamine kinase (GlcNAc kinase or NAGK) is a ubiquitously expressed enzyme which phosphorylates GlcNAc to GlcNAc-6-phosphate in amino sugar metabolism. Our lab recently found that NAGK interacts with dynein light chain roadblock type 1 (DYNLRB1) and upregulates axo-dendritic growth, which is an enzyme activity-independent, non-canonical structural role. Cytoplasmic dynein is primarily involved in intra-cellular cargo transport, mitotic cell division, and cell migration. We reported that NAGK interacted with dynein motor at neuronal Golgi outpost, modulated the transportation of golgi as a cargo and upregulated the axo-dendritic growth. Next, during cell division, authors examined the distributions of NAGK and NAGK-dynein complexes during the cell cycle in HEK293T cells and found NAGK-dynein complex at nuclear envelope, spindle microtubules (MTs), and kinetochores (KTs) where KTs were marked with CENP-B ICC and nuclear membrane with lamin ICC. NAGK-DYNLRB1 PLA followed by Lis1/NudE1 immunostaining showed NAGK-dynein complexes were colocalized with Lis1 and NudE1 signals where NAGK functioned as a regulator of dynein-Lis1-NudE1 complex. Furthermore, knockdown of NAGK by small hairpin (sh) RNA was found to delay cell division. To sum up the modulatory roles of NAGK on different factes of dynein function establish its non-canonical function as an accelerator for dynein motor.

Keywords: Cell division, Dynein, Golgi outpost, NAGK, Neuron

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P32

The effect of central GLP-1 and GIP on feeding behavior in mice

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The Glucagon-like peptide-1(7-36) amide (GLP-1) is a 30-amino

acid peptide hormone produced in the intestinal epithelial endocrine L-cells and also Gastric inhibitory polypeptide (GIP) is a 42 amino acid peptide hormone released from small intestinal mucosa in response to eating a meal. In the present study, we investigated the role of GLP-1 with GIP in central regulation of body weight homeostasis. The effect of GLP-1 with GIP on food intake, body weight, locomotor activity were determined following intracerebroventricular (ICV) administration of GLP-1 and GIP in male C57BL/6 mice. For single hormone experiment, mice were injected with GLP-1 (0.3~3nmol/mouse), GIP (1~6nmol/mouse) or vehicle. For combination hormone experiment, co-administration of sub-effect dose GLP-1 (0.3nmol/mouse) with sub-effect dose GIP (1nmol/mouse) were performed. Food intake, body weight were measured 24 hours after the injection. Finally, the locomotor activity of hypothalamic GLP-1 and GIP was studied. ICV administration of GLP-1 into mice significantly decreased in a dose dependent manner (0.3~3nmol/mouse). GIP also decreased food intake and body weight. Furthermore, ICV co-administration of sub-effect dose GLP-1 (0.3nmol/mouse) with sub-effect dose GIP (1nmol/mouse) significantly decreased food intake, body weight and locomotor activity compared with saline group. ICV administration of GLP-1 and GIP showed synergetic effect on food intake and body weight. These results suggest that co-administration of GLP-1 and GIP may represent a promising option for treating obesity through central nervous system mechanism.

Keywords: Glucose like peptide-1(GLP-1), Gastric inhibitory peptide(GIP), Food intake, Intracerebroventricular (I.C.V), Hypothalamus.

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P33

Neuregulin 1 Controls Glutamate Uptake by Upregulating Excitatory Amino Acid Carrier 1

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Neuregulin 1 (NRG1) is a trophic factor that is thought to have important roles in the regulating brain circuitry. Recent studies suggest that NRG1 regulates synaptic transmission, although the precise mechanisms remain unknown. Here we report that NRG1 influences glutamate uptake by increasing the protein level of excitatory amino acid carrier (EAAC1). Our data indicates that NRG1 induced the up-regulation of EAAC1 in primary cortical neurons with an increase in glutamate uptake. These *in vitro* results were corroborated in the prefrontal cortex (PFC) of mice given NRG1. The stimulatory effect of NRG1 was blocked by inhibition of the NRG1 receptor ErbB4. The suppressed expression of ErbB4 by siRNA led to a decrease in the expression of EAAC1. In addition, the ablation of ErbB4 in parvalbumin (PV)-positive neurons in PV-ErbB4-/- mice suppressed EAAC1 expression. Taken together, our results show that NRG1 signaling through ErbB4 modulates EAAC1. These findings link proposed effectors in schizophrenia: NRG1/ErbB4 signaling perturbation, EAAC1 deficit, and neurotransmission dysfunction.

Keywords: neuregulin 1, amino acid carrier (EAAC1), NRG1/ErbB4

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P34

Protective Effect of Glycyrrhizic Acid against Retinal Degeneration Induced by Blue Light-Emitting Diode Exposure in Mice

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The root and rhizomes of licorice (*Glycyrrhiza*) have been used as an herbal medicine, because they have various therapeutic effects, such as anti-inflammatory and antioxidative activities. Glycyrrhizic acid (GA) is a major component in the root and rhizomes of licorice. In this study, we examined the effect of GA in an animal model for retinal degeneration (RD), which is the

leading cause of blindness and characterized by the irreversible and progressive degeneration of photoreceptor cells in the retina. RD was induced in BALB/c mice by exposure to a blue light-emitting diode (LED) (460 nm) for 2 hours. To examine retinal functions, electroretinography (ERG) was performed. To assess histopathological changes, hematoxylin and eosin (H&E) staining were conducted. Apoptotic cell death was evaluated by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay. In addition, changes in proinflammatory cytokines were detected by real time RT-PCR and retinal stress and inflammation were evaluated by immunohistochemistry with anti-ionized calcium binding adaptor molecule 1 (Iba-1) and anti-glial fibrillary acidic protein (GFAP). Scotopic ERG showed that both a- and b-waves were significantly reduced in RD mice, while amplitudes of both waves were significantly increased in GA-treated RD mice, compared to those in non-treated RD animals. H&E and TUNEL assay showed that the outer nuclear layer where photoreceptors reside appeared to be more preserved and less apoptotic cells were observed in GA-treated RD retinas than in non-treated RD retinas. GA reduced expression of proinflammatory cytokines, such as TNF-α, interleukin (IL)-6, IL-1β, CCL2 and 6, iNOS, and Cox-2. In addition, GA reduced expression of Iba-1 and GFAP, indicating decreased glial response, retinal stress and inflammation. These results demonstrate that GA reduces retinal inflammation and prevents photoreceptor cell death from experimentally induced RD, suggesting that GA may have a potential for the treatment of RD as a medication.

Keywords: Glycyrrhizic Acid, Retinal Degeneration, Animal Model

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P35

Neuregulin-1 Improves Cognitive Dysfunction in Alzheimer's Disease Mouse Model

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The neuregulin (NRG) family of epidermal growth factor-related proteins is composed of a wide variety of soluble and membrane-bound proteins that exert their effects via the tyrosine kinase receptors ErbB2-ErbB4. In the nervous system, the functions of NRG1 are essential for peripheral myelination, the establishment and maintenance of neuromuscular and sensorimotor systems and the plasticity of cortical neuronal circuits. In the present study, we report that an intracerebroventricular infusion of NRG1 attenuated cognitive impairments in 13-month-old Tg2576 mice, an animal model of Alzheimer's disease (AD). In addition, according to Golgi-Cox staining, NRG1 rescued the reduction in the number of dendritic spines detected in the brains of Tg2576 mice compared with vehicle (PBS)-infused mice. This result was also corroborated in vitro as NRG1 attenuated the oligomeric amyloid beta peptide$_{1-42}$ (Aβ_{1-42})-induced decrease in dendritic spine density in rat primary hippocampal neuron cultures. NRG1 also alleviated the decrease in neural differentiation induced by oligomeric Aβ_{1-42} in mouse fetal neural stem cells. Collectively, these results suggest that NRG1 has a therapeutic potential for AD by alleviating the reductions in dendritic spine density and neurogenesis found in AD brains.

Keywords: Alzheimer's disease, NRG1, ErbB4, Amyloid beta peptide

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Introducing a new strategy for an early time detection of HFD-induced AD using Touchscreen-based behavior test

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Epidemiological and clinical studies show that beta amyloid aggregation at any stage is insufficient to develop a sporadic Alzheimer's

disease(AD) which accounts for more than 85% of both sporadic and familial AD. Moreover, recent studies show that sporadic AD arises from dysregulation of brain glucose metabolism that the amyloid hypothesis does not explain and that it occurs before beta amyloid plaques accumulates in the brain.In our previous results, mice were fed high-fat diet(HFD) for 24 weeks and subjected to dynamic nuclear polarization-enhanced hyperpolarized 13C magnetic resonance spectroscopic imaging (DNP-MRSI). Abnormal pyruvate-lactate conversion was observed in the medial temporal lobe. Spatial memory loss was confirmed with Morris Water Maze (MWM) and accumulation of beta amyloid was found in CA1 and DG. These results demonstrate that HFD-induced metabolic stress plays pivotal role of AD-like pathogenesis. As the disease develops gradually, it is essential to have a certain criterionto detecta potential AD pathophysiologybefore a severe cognitive decline affects the patient's quality of life. Therefore we investigated early-time pathophysiology of AD andthe possibility of early detection of cognition impairment using adultHFD mouse models. The MRS images and MWM results in this group showed no significance between normal and HFD mice. However, a touchscreen-based behavior test tool allows us to detect the tendency towards the mild cognitive decline in relatively young adult mice. The object-location-paired-associated learning tasks (PAL) depends specifically on hippocampal region which is related to spatial memory of the mouse.Tomake sure there is nomotivation differencebetween the groups, Fixed Ratio (FR) task wasconducted prior to the PAL.This non-invasive behavior test tool will help us find an earlier-time mechanism of the metabolic AD.

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Keywords: Touchscreen, Animal behavior, Memory, Alzheimer's disease, Metabolic disease

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P37

Role of Follistatin in assigning the apical cochlear identity

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The vertebrate cochlea is tonotopically organized, such that hair cells located in the base respond to high frequency sounds and their counterparts towards the apex progressively respond to lower frequency sounds. Recent studies suggest that the tonotopic organization is established by a decreasing apex-to-base gradient of Sonic hedgehog (Shh) signaling both in birds and mammals. In the chicken basilar papilla, *Bmp7* appears to be a key downstream target of Shh in mediating the tonotopy. In the mouse organ of Corti, however, the downstream mediators of Shh are not known. A likely candidate is *Follistatin* (*Fst*), which encodes an antagonist for Bmp/TGFβ signaling. The expression pattern of *Fst* is in a similar apex-basal gradient in the developing mouse cochlea as the gradient of Shh signaling and *Fst* expression is regulated by Shh as well. Here, we investigated the role of *Fst* in the tonotopic organization of the mammalian cochlea, especially in assigning the apical cochlear identity. In *Fst* KOs, the cochlear length was largely normal, yet its apical end displayed a slightly irregular shape. Within the cochlear duct, an extra row of outer hair cells was evident only in the apical cochlear region and hair cells appeared more mature than those in the wild type. Importantly, genes that are preferentially expressed in the apical cochlea such as *Msx1* and *Efnb2* were abolished or down-regulated, respectively in *Fst* KOs. These results suggest that apical cochlear patterning is disrupted in the absence of Fst function. Since the neonatal lethality of *Fst* KOs, we generated inner ear-specific *Fst* cKOs, which are viable and closely recapitulate the cochlear phenotypes of *Fst* KOs. Their ABR results show low-frequency specific hearing impairment which supports our hypothesis that *Fst* cKOs have disrupted apical patterning, resulting in the lessened ability to detect low frequency sounds. On the whole, our data suggest that *Fst* is required for proper organization and differentiation of hair cells and is also an important downstream mediator of the Shh signaling in the apex to facilitate tonotopy of the mammalian cochlea.

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Keywords: Fst (Follistatin), Shh (Sonic Hedgehog), Cochlea, Apex,

Low-frequency

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P38

Blocking the phosphatidylinositol 3-kinase pathway inhibits neuregulin-1-mediated rescue of neurotoxicity induced by $A\beta_{1-42}$

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

Keywords: Neuregulin-1 (NRG1), Beta amyloid peptide1-42(Aβ1-42), Alzheimer's disease (AD), Neurotoxicity, PI3K/Akt

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P39

Increased Expression of Slit2 and its Robo Receptors during Astroglial Scar Formation after Transient Focal Cerebral Ischemia in Rats

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Slit2, a secreted glycoprotein, has recently been implicated in the post-ischemic astroglial reaction. The objective of this study was to investigate the temporal changes and cellular localization of Slit2 and its receptors, Robo1, Robo2, and Robo4, in a rat transient focal ischemia model induced by middle cerebral artery occlusion. We used double- and triple-immunolabeling to determine the cell-specific changes in Slit2 and its receptors during a 10-week post-ischemia period. The expression profiles of Slit2 and the Robo receptors shared overlapping expression patterns in sham-operated and ischemic striatum. Constitutive expression of Slit2 and Robo receptors was observed in striatal neurons with weak intensity, whereas in rats reperfused after ischemic insults, these immunoreactivities were increased in reactive astrocytes. Astroglial induction of Slit2 and Robo in the peri-infarct region was distinct on days 7–14 after reperfusion and thereafter increased progressively throughout the 10-week experimental period. Slit2 and Robo were prominently expressed in the perinuclear cytoplasm and main processes of reactive astrocytes forming the astroglial scar. This observation was confirmed by quantification of the mean fluorescence intensity of Slit2 and Robo receptors over reactive astrocytes localized at the edge of the infarct area. However, activated microglia/macrophages in the peri-infarct area were devoid of any specific labeling for Slit2 and Robo. Thus, our data revealed a selective and sustained induction of Slit2 and Robo in astrocytes localized throughout the astroglial scar after ischemic stroke, suggesting that Slit2/Robo signaling participates in glial scar formation and brain remodeling following ischemic injury.
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Keywords: Reactive astrocytes, Slit2/Robo signaling, Glial scar, Ischemic stroke, Rat

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P40

Mice Subjected To Unpredictable Electric Shocks Show Anhedonia-like Behavior Irrespective Of Their State Of Helplessness

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The unpredictable and inescapable electric shock-induced "learned helplessness" paradigm has long been used to produce an animal model of depression to identify the molecules associated with depressive symptoms or to assess the efficacy of pharmacological treatments for depression. After exposure to inescapable shocks, mice show vulnerability (learned helplessness; LH) or resilience (non-learned helplessness; NLH) to aversive stimulation in an active avoidance task. Here, we investigated whether mice with LH exhibited depression-like behaviors, including anhedonia, anxiety, and despair. We found that compared with control naïve mice those with electric shock-induced LH showed anhedonia-like behavior, but not anxiety and despair. Notably, mice subjected to unpredictable electric shocks showed similar behaviors, irrespective of whether they also showed LH or NLH. Furthermore, since both LH and NLH mice showed only anhedonia-like behavior but not anxiety or despair, this model may be generally inadequate for classic depression assessment. In conclusion, active avoidance test-based validation of LH in mice should be interpreted carefully when used as a model of depression.

Keywords: Electric foot shock, Learned helplessness, Anhedonia, Active avoidance, Depression animal model

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P41

Reduction of Habenula Cholinergic Signaling Induces Anhedonic-like Behavior in Rat

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Objective: Dysfunction of cholinergic signaling in the central nervous system has long been believed to be associated with depressive disorders. Habenula is emerging as a therapeutic target for depression and its cholinergic projection is one of the most prominent cholinergic pathways in the brain. However, it remains unclear whether the habenular cholinergic signaling is associated with depression symptoms.
Method: We measured habenular cholinergic system gene expression in humans and a rat model of depression by quantitative polymerase chain reaction. We used the habenula tissues obtained from humans (12 suicide victims and 11 matched control subjects) and rats exposed to chronic restraint stress (CRS). To comprehensively evaluate the role of altered habenular cholinergic signaling in depression symptoms, we stereotaxically injected viral vector encoding short hairpin RNA for knockdown of the essential cholinergic gene *CHAT* into the habenula and depressive behaviors were assessed 3 weeks later.
Results: We found that the expression levels of cholinergic signaling genes (*CHAT, VACHT, CHT, CHRNA3, CHRNB3* and *CHRNB4*) were downregulated in the postmortem habenula of suicide victims who were diagnosed with major depressive disorder (MDD). This cholinergic gene downregulation in the habenula was recapitulated in a CRS rat model of depression. Moreover, knockdown of *CHAT* in the rat habenula was sufficient to evoke anhedonia-like behavior.
Conclusions: These human and rodent studies implicate the habenular cholinergic system as a therapeutic target for MDD by illuminating how reduction of cholinergic signaling in the habenula contributes to the induction of depressive behavioral symptoms.

Keywords: Major Depressive Disorder; Habenula; Cholinergic Signaling; Anhedonia

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P42

Vessel-associated Nestin Expression and its Possible Implication for Fibrotic Scar Formation in the Striatum of Rats Subjected to 3-Nitropropionic Acid

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Nestin, a type VI intermediate filament protein, has been reported to be induced in the vasculature-associated cells that undergo dynamic structural changes in the ischemic core in a rat model of ischemic stroke. The current study was designed to investigate the potential role of vessel-associated nestin-positive cells in the fibrotic scar formation, which is characterized by excess deposition of fibrous extracellular matrix, in the striatum of rats treated with the mitochondrial toxin 3-nitropropionic acid (3-NP). Nestin expression was exclusively induced within the vasculature in the lesion core, where the blood-brain barrier is broken and astrocytes are virtually absent, while nestin-positive cells in the peri-lesional area were indeed GFAP-positive reactive astrocytes. Vasculature-associated nestin was induced by day 3 post-lesion, and persisted until least 28 days, when long intertwined nestin-positive processes appeared to form a network within or around the vascular profiles. Double-labeling study revealed that vessel-associated nestin-positive cells were clearly distinguishable from endothelial cells, smooth muscle cells and microglia/macrophages. Instead, the expression profiles of nestin and platelet-derived growth factor receptor beta (PDGFRβ), a specific marker for pericytes, shared overlapping expression patterns. In addition, we observed the close relationship between nestin and fibronectin or collagen IV, which are the most commonly used markers for the fibrotic scar. Immunoelectron microscopic findings demonstrated that nestin-positive cells in the lesion core were fibroblast-like cells that had flattened nucleus and extremely long, tenuous processes, suggesting that nestin could be induced in pericytes or fibroblast-like cells. Thus, our data indicate nestin expression was induced in PDGFRβ-positive pericytes that occupied the lesion core, suggesting that nestin may be involved in cellular structural remodeling of pericytes that contribute to the fibrotic scar formation in response to brain insults.

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Keywords: Nestin, Pericytes, Fibrotic scar, 3-nitropropionic acid, platelet-derived growth factor receptor beta

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Microglial HO-1/Nrf2 induction by Terminalia chebula provides antioxidant, antineuroinflammatory effects

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HO-1/Nrf2 signaling regulates multiple anti-oxidative factors and exerts anti-neuroinflammatory effects. Plants of the genus Terminalia are amongst the most widely used plants for traditional medicinal purposes worldwide. Many species are used for their anti-bacterial, anti-fungal, anti-protozoal, anti-viral, anti-diarrhoeal, analgesic, anti-malarial, anti-oxidant, anti-inflammatory and anti-cancer activities. In this study, we studied the neuro-inflammatory effects of Terminalia chebula on BV2 microglial cells. Terminal chebula was shown to suppress the inflammation process in LPS-stimulated BV2 cells. Furthermore, the anti-neuroinflammatory activities of Terminalia chebula were associated with unregulated expression of heme oxygenate (HO)-1 and nuclear factor-E2-related factor 2 (Nrf2) in BV2 cells. We also found that Terminalia chebula activated p38 mitogen-activated protein kinases (MAPK), resulting in reduction of TNF-alpha and IL-1beta production, but not IL-6 production. Collectively, these results demonstrated that Terminalia chebula exerts anti-

neuroinflammatory effects against LPS inducing HO-1/Nrf2 via the activation of the p38 MAPK pathways.

Keywords: Terminalia chebula, inflammation, HO-1, Nrf2, MAPK, microglia

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P44

20(S)-Protopanaxadiol (PPD) inhibits survival of glioblastoma multiforme through regulation of Akt

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20(S)-Protopanaxadiol (PPD), an aglycone saponin ginsenoside isolated from Panax ginseng C.A. Mey., has been shown to inhibit the growth and proliferation in several cancer lines. However, the underlying molecular mechanisms remain poorly understood. In this study, we investigated its inhibitory effect on glioblastoma multiforme (GBM) and the mechanism of 20(S)-PPD on GBM cells. 20(S)-PPD showed a potent anti proliferative activity, cause cell cycle arrest and DNA damage. 20(S)-PPD triggered apoptosis in GBM via significant activation of caspase-3. Importantly, temozolomide with 20(S)-PPD combination-induced cell death was found to be associated with down regulation of phosphorylated Akt. These results revealed an unexpected mechanism of temozolomide and 20(S)-PPD, triggering caspase-dependent apoptosis via down-regulation of the Akt in GBM cells. Together, these data demonstrate that 20(S)-PPD may suppress the growth and survival of GBM through inhibiting Akt. Thus, our data highlight a previous unappreciated role for 20(S)-PPD in suppressing GBM.

Keywords: 20(S)-Protopanaxadiol (PPD), glioblastoma, Akt, caspase-3

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P45

RGD-motif-containing osteopontin icosamer stimulates migration and phagocytosis of microglia.

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Osteopontin (OPN), a secreted glycoprotein, possesses an arginine-glycine-aspartate (RGD)-motif, which binds to integrins and mediates a wide range of cellular activities. In a previous study, we demonstrated that RGD-containing icosamer OPN peptide (OPNpt20) has a robust neuroprotective effects in the ischemic rat brain after middle cerebral artery occlusion (MCAO, 60min). In the present study, we showed OPNpt20 mediated cellular movements, phagocytosis of microglia and clearance of apoptotic neuron by microglia. OPNpt20 bound to αvβ3 integrin and regulated downstream signaling pathways, consequently, F-actin polymerization was activated. As a result, in OPNpt20 treated microglia, cellular movements were markedly increased compared to that in sham controls. FGF or recombinant OPN treated BV2 cells were also increased cellular movements, however, Cytochalasin B (CytB) treated group was suppressed the movement. Next, we investigated OPNpt20-mediated phagocytosis. After BV2 cells were incubated with FITC-labeled zymosan particles in the presence or absence of OPNpt20, phagocytosis was markedly increased in OPNpt20 treated group. Furthermore, OPNpt20 induced efferocytosis after cocultures of BV2 with staurosporine-mediated apoptotic N2A. Together these results indicate OPNpt20 increased cellular movements and phagocytosis via integrin signaling.

Keywords: Osetopontin, OPNpt20, Cellular movement, Phagocytosis, Efferocytosis

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P46

IKKβ-mediated inflammatory myeloid cell activation exacerbates experimental autoimmune encephalomyelitis by potentiating Th1/Th17 cell activation and compromising blood brain barrier

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Background: The inflammatory myeloid cell activation is one of the hallmarks of experimental autoimmune encephalomyelitis (EAE), yet the in vivo role of the inflammatory myeloid cell activation in EAE has not been clearly resolved. It is well-known that IKK/NF-κB is a key signaling pathway that regulates inflammatory myeloid activation.

Methods: We investigated the in vivo role of inflammatory myeloid cell activation in myelin oligodendrocyte glycoprotein (MOG) peptides-induced EAE using myeloid cell type-specific *ikk*β gene conditional knockout-mice (*LysM-Cre/Ikk*$\beta^{F/F}$).

Results: In our study, LysM-Cre/Ikk$\beta^{F/F}$ mice had alleviated clinical signs of EAE corresponding to the decreased spinal demyelination, microglial activation, and immune cell infiltration in the spinal cord, compared to the wild-type mice (WT, *Ikk*$\beta^{F/F}$). Myeloid *ikk*β gene deletion significantly reduced the percentage of $CD4^+$/IFN-γ^+ (Th1) and $CD4^+$/IL-17^+ (Th17) cells but increased the percentages of $CD4^+$/$CD25^+$/$Foxp3^+$ (Treg) cells in the spinal cord and lymph nodes, corresponding to the altered mRNA expression of IFN-γ, IL-17, IL-23, and Foxp3 in the spinal cords of *LysM-Cre/Ikk*$\beta^{F/F}$ EAE mice. Also, the beneficial effect of myeloid IKKβ deletion in EAE corresponded to the decreased permeability of the blood brain barrier (BBB).

Conclusions: Our findings strongly suggest that IKK/NF-kB-induced myeloid cell activation exacerbates EAE by activating Th1 and Th17 responses and compromising the BBB. The development of NF-κB inhibitory agents with high efficacy through specific targeting of IKKβ in myeloid cells might be of therapeutic potential in MS and other autoimmune disorders.

Keywords: Myeloid cell, IKKβ conditional deletion, Experimental autoimmune encephalomyelitis, T cell, Blood brain barrier

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P47

Establishment of Pure Mouse Primary Oligodendrocyte Culture for Studying the Effects of Extracellular Alpha-synuclein on Multiple System Atrophy

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Alpha-synuclein (α-Syn) is a natively unfolded cytosolic protein that is linked to several neurodegenerative diseases such as Parkinson's disease, dementia with Lewy bodies, multiple system atrophy (MSA), etc. MSA is an adult-onset, neurodegenerative disorder characterized by progressive loss of neuronal and oligodendroglial cells in the central nervous system (CNS). The presence of glial cytoplasmic inclusions (GCIs), which is mainly composed of aggregated α-syn in oligodendrocytes and astrocytes, is a major neuropathological hallmark of MSA. Previous studies showed that α-syn could be secreted from neurons and internalized by not only adjacent neurons but also by glial cells. However, the physiological and pathological effects of these transmitted α-syn on oligodendroglial cells are still unclear.

To this end, we are in the process of establishing pure primary oligodendrocyte culture method from mouse embryos. Brain cortices are removed from E13~E14 mice and neurospheres are generated from neural stem cells. These neurospheres are then transformed into 'oligoshperes', which are clonal aggregates of oligodendroglial precursor cells (OPCs). We are currently working to generate mature oligodendrocytes from these OPCs. These mature oligodendroytes will

then be used to study transmission of extracellular a-syn into oligodendrocytes and its effect on gene expression changes by microarray analysis and further into unveiling the pathological mechanism of MSA and possible therapeutic interventions.

Keywords: Multiple system atrophy, Alpha-synuclein, Oligodendrocyte, Glial cytoplasmic inclution

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ZL006, an Inhibitor of the Neuronal Nitric Oxide Synthase-postsynaptic Density 95 Interaction, Ameliorates Pathology in a Mouse Model of Alzheimer's Disease

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In Alzheimer's disease (AD), a most common age-related neurodegenerative disorders showing impaired cognition, it is reported that accumulated amyloid beta (Aβ) peptides over-activates calcium (Ca_{2+})-permeable and membrane-bounded NMDA receptors (NMDAR). Upon Ca_{2+} influx, the Ca_{2+}-dependent neuronal NO synthase (nNOS) is activated and the resulting cytotoxic NO overproduction contributes the excitotoxic damage. Although PSD95, the scaffolding protein located in postsynaptic density, can recruit the nNOS to the mouth of the NMDAR, the possibility that selective uncoupling of nNOS from PSD95 might be neuroprotective is unexplored. Herein, we investigated whether the ZL006, a novel inhibitor of nNOS and PSD95 interaction, can exert the therapeutic effect in AD mouse model which was established by intra-hippocampal injection of Aβ. Experimental animals were divided by 3 groups: sham-operated (SHAM, a group injected with 3μl normal saline as a vehicle), operated (OP, a group injected with 10 μM Aβ diluted in vehicle), and ZL006-treated group (TX, a group intravenously injected with 1.5mg/kg ZL006 at 1hr after operation). At 1 week after operation, we analyzed the translocation of nNOS from cytosol to membrane, the AD-related behavior, the viability of hippocampal CA1 pyramidal neurons, and the synaptic strength in different groups. Compared with OP, in western blot using cytoplasmic and membranous lysate of hippocampus, TX showed increased cytoplasmic level of nNOS and reduced membranous level of nNOS, respectively. Compared with OP, in behavioral tests using Y-maze test and passive avoidance test, TX showed the higher frequency of spontaneous alteration and the elongation of latency time, respectively. Furthermore, we observed that the hippocampal CA1 pyramidal neurons of TX were relatively intact compared with those of OP. In immunofluorescence study using the antibodies against the pre-synaptic marker synaptophysin (SNP) and post-synaptic marker PSD95, when compared with SHAM, OP showed the marked impairment on synaptic strength, which was significantly attenuated in TX. By these results, we suggest that ZL006 can ameliorate the AD-related symptoms and histology in AD mice via inhibition of nNOS and PSD95 interaction.

Keywords: Alzheimer's disease, amyloid beta, nNOS, synaptophysin,

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Oriental medicine Woohwang-chungsimwon attenuates kainic acid-induced seizures and neuronal cell death in the hippocampus

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Woohwangchungsimwon (WCW) is an oriental medicine that has been extensively prescribed in Asia to patients with apoplexy, high blood pressure, acute/chronic convulsion, etc. However, the potential therapeutic value of WCW in treating the pathologic brain has not

yet been fully investigated. In the present study, we evaluated whether WCW has beneficial effects on kainic acid (KA)-induced excitotoxicity. An intraperitoneal injection of KA (40 mg/kg) and an intracerebroventricular (i.c.v.) injection of KA (0.2 μg) produced typical seizure behavior and neuronal cell death in the CA1 and CA3 pyramidal layers of the hippocampus, respectively. However, the systemic administration of WCW significantly attenuated the seizure behavior and neuronal cell death. WCW was found to exert the best protective effect when it was administrated 2 hours before a KA-injection. Moreover, this WCW-induced neuroprotection was accompanied by a reduction in microglia activation and tumor necrosis factor-alpha, interleukin (IL)-1beta, IL-6, heme-oxygenase-1, inducible nitric-oxide synthase, and cyclooxyganase-2 in the hippocampus. These results suggest that WCW has therapeutic potential to suppress KA-induced pathogenesis in the brain by inhibiting inflammation.

Keywords: Woohwangchungsimwon, kainic acid, seizure behavior, hippocampus cell death, anti-inflammation

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Robust Neuroprotective Effects of A Novel Neuroprotectant 2-((2-Oxopropanoyl)oxy)-4-(Trifluoromethyl)Benzoic Acid (OPTBA), A HTB/Pyruvate Ester, In The Postischemic Brain

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Cerebral ischemia causes brain damages via complicated pathological events, and so multimodal drug treatments may offer better therapeutic means for improving clinical outcomes. In the present study, we report a novel neuroprotectant, 2-((2-oxopropanoyl) oxy)-4-(trifluoromethyl)benzoic acid (OPTBA), a 2-hydroxy-4-trifluoromethyl benzoic acid (HTB, a metabolite of triflusal)-pyruvate ester. Administration of OPTBA (5 mg/kg, i.v.) 3 or 6 h after middle cerebral artery occlusion (MCAO) in Sprague-Dawley rats reduced infarct volumes to 38.5±11.4% and 46.5±15.3%, respectively, of that of MCAO controls, and improved neurological deficits and motor impairment. Importantly, infarct suppression of OPTBA were far greater than those afforded by combined treatment of HTB and pyruvate. Furthermore, OPTBA further suppressed microglial activation and proinflammatory cytokine inductions than HTB/pyruvate co-treatment in postischemic brains and LPS-treated cortical slice cultures and also attenuated NMDA-induced neuronal death in hippocampal slice cultures. LC-MS analysis demonstrated that OPTBA was hydrolyzed to HTB and pyruvate with a t1/2 of 38.6 min in blood and 7.2 h and 2.4 h in cortex and striatum, respectively. Interestingly, HTB was maintained for more than 24 h both in blood and brain tissue. Together these results indicate OPTBA acts directly and via its hydrolysis products, thus acting as a multimodal neuroprotectant in the postischemic brain.

Keywords: OPTBA, Triflusal, HTB, Pyruvate, MCAO, Neuroprotection

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Neuroanatomical distribution of Galectin-3 in the adult rat brain

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Galectin-3 is a subfamily of lectin, β-galactoside sugar specific binding protein. It is expressed in a broad spectrum of species and organs, and known to have various functions related to cell adhesion, signal transduction and proinflammatory responses. Although, in the central nervous system, the galectin-3 expression in some activated neuroglia under neuroinflammation has been well documented, little is known about the neuronal expression and distribution of galectin-3 in normal brain. To describe the cellular and neuroanatomi-

cal expression map of galectin-3, we performed galectin-3 immunohistochemistry through the entire normal rat brain and analyzed neuronal distribution. Galectin-3 expression was found not only in some neuroglial cells (mainly in ependymal cells; barely in some astrocytes and microglia) but also in neurons. The galectin-3 expression in neurons was observed in many functional parts of cerebral cortex, some deep cerebral nuclei, and various other subcortical nuclei in hypothalamus, thalamus, and brainstem. Neuroanatomical analysis revealed that robust galectin-3 immuno-signals were present in many hypothalamic nuclei related with a variety of physiological functions mediating anxiety responses, energy balance, and neuroendocrine regulation (dorsomedial, ventromedial, arcuate, supraoptic, and paraventricular nuclei). In addition, the regions where functionally and neuroanatomically connected with the indicated hypothalamic nuclei also showed intensive galectin-3 expression (central and medial amygdaloid nuclei, bed nuclei of stria terminalis, nucleus of the solitary tract, and so on). In addition, the multiple key regions regulating autonomic functions such as Edinger-Westphal nucleus, A5 noradrenaline cells, superior salivatory nucleus, and vagal motor nucleus showed high level of galectin-3 expression, too. In contrast, the subcortical nuclei which control voluntary motor functions (basal nuclei, substantia nigra, and cerebellar cortex) and limbic system (hippocampal formation and most part of olfactory areas) showed no galectin-3 immunoreactivity. These observations suggest that galectin-3 expression in rat brain seems to be regulated by developmental cascades and, eventually, functionally and neuroanatomically related nuclei seem to constitutively express galectin-3 in adulthood.

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Keywords: Galectin-3, Central Nervous System

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

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Parkinson's disease (PD) is a common age-related neurological motor disorder, marked by the relatively selective and progressive neuronal degeneration of dopaminergic (DA) neurons in the substantia nigra (SN). 6-Hydroxydopamine (6-OHDA) is able to induce retrograde degeneration of the nigrostriatal DA neurons and has been the most widely used tool for replicating a PD pathology. Galectin 3, a member of the Galectin family of β-galactoside binding lectins, plays an important role in the cell adhesion, immune responses, and signal cascades. Activating transcription factor 3 (ATF3), a member of CREB/ATF family, is induced in wide spectrum of tissues by various types of insults and suggested to be an important immediate early gene to initiate the signal cascades related in cell death or survival. To elucidate the neurobiological role of these molecules in DA neuronal degeneration. we investigated temporal and spatial profiles of Galectin-3 and ATF3 expression in 6-OHDA PD animal model. The 6-OHDA cytotoxicity in the striatum induced the retrograde DA neuronal cell death in SN. in time point dependent manner with occurance with its degeneration, ATF3 and Galectin-3 expression were also induced the SN. Triple immunofluorescence of tyrosine hydroxylase(TH;DA neuronal marker), Galectin-3, and ATF3 revealed that DA neurons co-expressed Galectin-3 and ATF3. Finally, Fluorogold retrograde labeling confirmed the 6-OHDA neurotoxicity specifically induced the Galectin-3 and ATF3 expression. these results suggest that Galectin-3 and ATF3 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 ATF3.

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Keywords: Parkinson's disease 6-hydroxydopamine Neurodegeneration Galectin-3

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P53

Inhibition of Matrix Metalloproteinase 9 Enhances Rod Survival in the S334ter-line3 Retinitis Pigmentosa Model

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Retinitis Pigmentosa (RP) is one of the most common forms of inherited visual loss with the initial degeneration of rod photoreceptors, followed by a progressive cone photoreceptor deterioration. Coinciding with this visual loss, the extracellular matrix (ECM) is reorganized, which alters matrix metalloproteinase (MMP) activity levels. A potential pathological role of MMPs, MMP-9 in particular, involves an excitotoxicity-mediated physiological response. In the current study, we examine the MMP-9 and MMP-2 expression levels in the rhodopsin S334ter-line3 RP rat model and investigate the impact of treatment with SB-3CT, a specific MMP-9 and MMP-2 inhibitor, on rod cell survival was tested. Retinal MMP-9 and MMP-2 expression levels were quantified by immunoblot analysis from S334ter-line3 rats compared to controls. Gelatinolytic activities of MMP-9 and MMP-2 by zymography were examined. The geometry of rod death was further evaluated using Voronoi analysis. Our results revealed that MMP-9 was elevated while MMP-2 was relatively unchanged when S334ter-line 3 retinas were compared to controls. With SB-3CT treatment, we observed gelatinolytic activity of both MMPs was decreased and diminished clustering associated with rod death, in addition to a robust preservation of rod photoreceptors. These results demonstrate that up-regulation of MMP-9 in retinas of S334ter-line3 are associated with rod death. The application of SB-3CT dramatically interferes with mechanisms leading to apoptosis in an MMP-9-dependent manner. Future studies will determine the feasibility of using SB-3CT as a potential therapeutic strategy to slow progression of vision loss in genetic inherited forms of human RP.

Keywords: Retinitis Pigmentosa; Matrix metalloproteinase-9 (MMP-9); Rod survival; Cluster cell death; SB-3CT

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6-Hydroxydopamine Induces Nuclear Translocation of Apoptosis Inducing Factor in Nigral Dopaminergic Neurons in Rat

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Parkinson's disease (PD) is a progressive neurodegenerative disorder, characterized by relatively selective death of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc). Although understanding of the pathogenesis of PD remains incomplete, increasing evidence from human and animal studies has suggested that oxidative stress is an important mediator in its pathogenesis. 6-hydroxydopamine (6-OHDA), a neurotoxin that causes the death of DA neurons, is commonly used to produce experimental PD model in rodents. It is generally assumed that programmed cell death (PCD), especially caspase-dependent apoptosis is the main cell death mechanism in various neurodegenerative diseases. However, accumulating evidences also suggest that caspase-independent neuronal PCD can be involved in the progression of neurodegen-

erative diseases. Apoptosis-inducing factor (AIF), a mitochondrial intermembrane oxidoreductase, has been identified as a key protein implicated in caspase-independent apoptosis. However, little is known about the role of AIF in death of nigral DA neurons in PD. Therefore, we undertook this study in an effort to clarify the involvement of AIF in DA neuronal death by 6-OHDA administration. Ten and twenty micrograms of 6-OHDA was infused into the medial forebrain bundle (MFB) unilaterally, and the experimental rats were sacrificed at various time point. The DA neuronal loss was identified in the ipsilateral SN in the dose-dependent manner by using NeuN and tyrosine hydroxylase immunohistochemical staining and western blot assay. Numerous degenerating neurons, showing apoptotic features which are characterized by the shrunken nuclei with eosinophilic perikarya were observed in the ipsilateral SNpc. Activating transcription factor 3 (ATF3), the specific marker for neuronal damage, was expressed in the ipsilateral DA neurons only. Immunohistochemistry and immunofluorescence staining demonstrated that nuclear localization of AIF in the ipsilateral degenerating DA neurons. These results suggest that AIF mediated caspase-independent apoptosis could induce DA neuronal death in 6-OHDA PD animal model, although other cell death cascades should not be rule out.

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Keywords: Apoptosis inducing factor (AIF), Parkinson's disease, Activating transcription factor 3 (ATF3), 6-hydroxydopamine (6-OHDA), Caspase-independent apoptosis

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P55

마트리젤과 bFGF를 이용한 대뇌 허혈 손상 복구에 대한 연구

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뇌 허혈 (Brain ischemia) 은 뇌혈전, 심장질환, 뇌동맥폐색증 등의 다양한 원인으로 인하여 뇌에 국소적으로 뇌혈류장애가 발생하는 질병이다. 뇌 허혈이 일어나면 세포 조직이 괴사하고 뇌 조직 구조가 소실 된다. 이러한 소실은 혈관과 세포외 지지물질의 소실과 동반되어 신생 신경세포들의 이주, 생존 및 조직의 재형성 등을 어렵게 한다. 마트리젤 (Matrigel) 은 세포증식, 이주 분화, 혈관 형성 촉진 등의 특징을 가지고 있어 신경조직 회복의 지지대 (scaffold) 역할을 할 가능성이 있다. 따라서 본 연구에서 마트리젤과 성장인자 (Basic Fibroblast Growth Factor; bFGF) 를 이용하여 광혈전 뇌 허혈 (Photothrombotic ischemia) 후 마트리젤과 bFGF의 뇌 신경 조직 손상 복구에 대하여 관찰하였다.
C57BL/6 생쥐에 로즈벵갈 (Rosebengal) 을 꼬리정맥 (tail vein) 에 주사한 후 cool light (halogen lamp) 를 머리뼈 (skull) 위에 쬐어 광혈전 허혈 모델을 제작하였다. 수술 다음날 마트리젤과 bFGF를 대뇌 손상 부위에 주입하고 4주 후 인도시아닌그린 (Indocyanine green; ICG) 을 이용한 영상분석과 면역조직화학 등을 실시하였다. 그 결과, ICG를 이용한 영상분석에서 마트리젤과 bFGF를 주입한 생쥐들이 대조군에 비해 손상 부위의 혈관 구조들이 더 많이 관찰되었다. 또한 니슬 (Nissl) 염색법을 실시하여 마트리젤이 조직의 소실 된 부분을 지지하고 있으며 마트리젤 안에서 이주한 세포들을 발견하였다. 면역조직화학을 이용하여 이주한 세포를 동정한 결과 신경아교세포 (GFAP+) 와 혈관세포 (CD31+) 를 관찰할 수 있었다. 이 결과는 마트리젤과 bFGF가 뇌 허혈 후 뇌 신경 조직의 복구를 촉진할 수 있음을 보여준다.

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Keywords: brain photothrombotic ischemia, matrigel, bFGF, Indocyanine green

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P56

Primary cilium mediates Shh signaling to control cochlear growth and hair cell differentiation

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The primary cilium serves as a signaling center for several cellular pathways important for animal development and homeostasis including Sonic hedgehog (Shh), Wnt, and PDGF. Defects in the primary cilium are associated with a range of genetic disorders known as ciliopathies, which include hearing loss. Previous studies showed that ciliary defects resulted in shortened cochlear duct and abnormal hair cell polarization. While the hair cell polarization defect is attributed to defective planar cell polarity (PCP) signaling, the cause for shortened cochlear duct remains unclear. Given the role of Shh signaling in cochlear patterning and growth, we analyzed Shh signaling in inner ears of three different ciliary mutants, Broad-mined (*Bromi*) mutant, *Intestinal cell kinase* (*Ick*) knockout (KO), and conditional knockout of *Ift88* (*Pax2-Cre; Ift88*$^{lox/lox}$, *Ift88* cKO), which all display a shortened cochlear duct.

As previously reported, *Ift88* cKO mutants lack the primary cilium. Both *Bromi* and Ick mutants showed abnormal morphology and increased length of the cilium, respectively. Our results indicate that Shh signaling was compromised in the cochlea of these mutants. First, all three cochleae showed a reduction in *Ptch1* expression, which is a direct readout of Shh signaling. Second, the expression of a bona-fide apical cochlear marker, *Msx1*, was reduced or absent, suggesting that the patterning of the apical cochlear region is compromised. Third, *Bromi* and *Ift88 cKO* developed premature hair cells and ectopic sensory patches containing vestibular-like hair cells in the Kölliker's organ, which is also a phenotype associated with reduced Shh signaling. Taken together, our results underscore the complexity of ciliary mutants and the importance of disrupted Shh signaling in contributing to the cochlear phenotypes of ciliary mutants including shortened cochlear duct, which is generally regarded as the result of PCP defect.

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Keywords: Primary cilia Hearing loss Sonic hedgehog signaling Hair cell Development

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The Relationships between Cerebrovascular Structural Change and Cerebral Blood Flow in Aged Mouse Brain

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Age-related degeneration of the brain vasculature may reduce the blood flow and cognition, although the related mechanism is unclear. To investigate the relationships between aging and changes in cerebral blood flow and vasculature, we used indocyanine green (ICG) dynamics and angiography imaging with young (2-month-old) and old (12-month-old) mice. We also visualized the cortical pial arterial trees in these mice using clarification with methyl salicylate. As a result, we found that the blood flow in old mice's brains is lower than that in young mice and that old mice had more curved pial arteries and fewer pial artery junctions than young mice. Second, using western blotting, we showed that the ratio of collagen to elastin (related to cerebral vascular wall distensibility) increased with age. Finally, we found that the peak ICG intensity and blood flow index decreased, whereas the mean transit time increased, with age in the middle cerebral artery (MCAs) and superior sagittal sinus (SSS). Age-related changes in pial arterial structure and composition, concurrent with the observed changes in the blood flow parameters, suggest that age-related changes in the cerebral vasculature structure and distensibility may induce altered brain blood flow.

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Keywords: Aging, Cerebral blood flow, 3D cerebral vascular angiography, Optical imaging

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P58

Effect of Voluntary Wheel Running Exercise on the FoxO3a Expression in the Brain of Mice Exposured by 853 MHz Radiofrequency Radiaion

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Mammalian FoxO transcription factor regulates a variety of physiological responses in oxidative stress condition. However, under various intrinsic or extrinsic stress, the study of the expression and physiological function of FoxO proteins in the hippocampus is not sufficient. Therefore, in this study, we observed the phosphorylation of FoxO3a in the hippocampus following 835 MHz RF-EMF(SAR: 4.0 W/kg, 6 hr/day) and voluntary wheel running during 8 wks. ICR mice were randomly selected and divided into four groups: control group (CON), voluntary wheel runnng group (VWR), 835 Mhz RF-EMF exposure group (RF-EMF), and 835 Mhz RF-EMF exposure plus VWR group (RF-EMF+VWR). We investigated the changes of body weight and number of wheel rotation during 8 wks. Body weight of CON continuously increased and VWR was significantly reduced as compared to CON. Interestingly, the significant body weight loss observed in RF-EMF compared to CON. In addition, RF-EMF+VWR showed weight loss as compared to RF-EMF or VWR. The number of wheel rotation were significantly increased in RF-EMF+VWR, but not VWR during 8 wks. By using immunohistochemistry, the expression of phosphorylated FoxO3a (pFoxO3a) protein was investigated in the mice hippocampus which is divided into three parts as CA1, CA3, and the dentate gyrus. The pFoxO3a expression in all hippocampal regions were significantly increased in all experimental groups compared to CON. Taken together, RF-EMF and exercise may be act as a stressor and then can lead to weight loss and hyperactivity. Furthermore, the phosphorylation of FoxO3a can be induce to protect neuronal cells against stress condition in mice hippocampus.

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Keywords: Radiofrequency Radiaion; FoxO3a; Voluntary Exercise; Mice

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Effect of GABAA-α1 positive interneurons in the chronic epilepsy following febrile seizure

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Febrile seizure (FS) is the most common seizure type in the infant and young child, because prolonged FS may induce the alteration in hippocampal circuitry. These changes may sustain enhanced hippocampal excitatory and contribute toward the development of temporal lobe epilepsy (TLE). Hippocampal interneuron is central role of regulating the excitability in the hippocampal circuits, thus it is important to comprehend the mechanism of γ-aminobutyric acid (GABA)ergic signaling. It is well known that phasic and tonic inhibitions are mediated by synaptic and extrasynaptic GABAA receptors. Among them, tonic inhibition plays a critical role of control in the excitability of hippocampal network, and these inhibitory efficacies are increases in diverse animal models of absence epilepsy and promotes the generation of spike-wave discharges. In a previous study we found that GABAA-α1 receptor expression of interneuron was abnormally enhanced in recurrent seizures stage at FS. Therefore, we needed confirm whether hyperthermic seizure may be related to a consequence of compensated functional responses of excessive

increased inhibitory circuits in the hippocampus. In the results of this study, EEG signal was shown characteristic amplitudes in each model. In addition, we were investigated filed excitatory postsynaptic potential (fEPSP) and paired-pulse responses in the hippocampus for identifying the functional alterations of GABAergic inhibition after the applications of GABAA receptor drugs and FS. Following bicuculline and FS, despite the slope of fEPSP was markedly reduced more than control level, the paired-pulse response was enhanced as similar to level of muscimol application. Moreover, vesicular GABA transporter (VGAT) expression and GABA immunoreactivity in the $GABA_A$-α1 positive interneurons was significantly enhanced in the hippocampus following FS. However, although chloride channels (ClC) immunoreactivities were un-changed, two-pore-domain K^+ channel (TASK-1) expression in the dentate gyrus (DG) was decreased after hyptethermic seizure. Therefore, our findings in present study indicated that enhanced tonic current in the interneuron may lead to reduced of interneuron excitability, result in sustained hyperexcitability of hippocampus following FS.

Keywords: Hyperthermic seiuzre, GABAA receptor, Epilepsy, Tonic inhibition, Phasic inhibition

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P60

Angiogenic properties of osteopontin icosamer peptide via interacting with $\alpha_v\beta_3$ integrin

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Osteopontin (OPN) is a phosphorylated glycoprotein that is secreted into body fluid after being synthesized in various cells and tissues. OPN contains arginine, glycine, aspartate (RGD) and serine, leucine, alanine, tyrosine (SLAY) motifs. They bind to several cell surface integrins which mediate a wide range of cellular processes such as adhesion, migration, and proliferation of a variety of cell types. In the present study, authors examined the pro-angiogenic effects of a RGD and SLAY-containing 20 amino acids OPN peptide (OPN20) in human umbilical vein endothelial cells (HUVECs) and in a rat model of focal cerebral ischemia and reperfusion injury. We found that OPN20 exerted a robust pro-angiogenic effect in HUVEC cultures, including proliferation, migration, and tube formation. However, a mutant peptide (OPN20-RAA) replaced RGD to RAA was failed in a scratch assay but the proliferation assay. Moreover, a mutant peptide (OPN20-Db) replaced RGD and SLAY by RAA and SLAA failed to activate all of pro-angiogenic processes. It shows that both of motifs are required for pro-angiogenic effect and SLAY motif is especially needed in the proliferation aspect but migration and tube formation. In OPN20-treated HUVEC cultures, PI3K/AKT and ERK signaling pathways were activated. Moreover, the blocking $\alpha_v\beta_3$ integrin by antibody suppressed OPN20-mediated pro-angiogenic function. It indicate that OPN20 stimulates angiogenesis via $\alpha_v\beta_3$/PI3K/AKT and ERK signaling pathways in HUVEC cultures. Pro-angiogenic function of OPN20 was further confirmed in the postischemic brain, OPN20 induced an increase of the rat endothelial cell antigen (RECA-1) immunoreactivity as well as the expression of angiogenesis related proteins such as vascular endothelial growth factor (VEGF) and alpha smooth muscle actin (α-SMA) in the cortex penumbras of OPN20 administered animals. Together these results demonstrate that the RGD and SLAY motifs containing OPN icosamer peptide has a robust pro-angiogenic effects and it might contribute to a robust neuroprotective effects in the postischemic brain.

Keywords: Osteopontin icosamer, RGD motif, $\alpha v\beta 3$ integrin, Stroke, Angiogenesis

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P61

Alterated expression of PEA-15 immunoreactivity in the gerbil hippocampus after ischemic insults

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Global cerebral ischemia is leading to selected and delayed neuronal cell death in the pyramidal neurons of hippocampal CA1 and it is developing cognitive damage and epileptic seizure in rodents, primates, and humans. This phenomenon is known for various mechanisms that including excitotoxicity, free radical stress and apoptotic neural cell death. On the other hand, the regulations of cellular apoptosis and cell cycle is modulated by phospho PEA-15 protein that is a multifunctional phosphoprotein. Thus, these signaling are play an important role for controlling survival signaling pathways and results in neuronal cell death in the ischemic brain insults. Therefore, in present study, we investigated whether distributional alterations of phospho PEA-15 are involved to delayed neuronal cell death in the gerbil hippocampus following ischemic brain damage. In this present result, EEG signals and cognitive behavior tests were significantly altered after ischemic attack. In addition, we were investigated filed excitatory postsynaptic potential (fEPSP). At 4 day following ischemia, slope of fEPSP was markedly reduced more than control levels. Moreover, although phospho PEA-15 immunoreactivities were significantly increased within the glia in the dentate gyrus (DG) and CA1 regions, its immunoreactivity in the hilar interneuron was decreased after ischemic insult. Furthermore, phospho PEA-15 immunoreactivities in the GFAP-positive astrocyte were enhanced in the CA1 and DG at 4 day following ischemia. Therefore, these distributional alterations of phospho PEA-15 protein may involved in the apoptotic neural cell death and the cognitive behavior phenotype after ischemic insults through functional decline of phospho PEA-15 protein.

Keywords: Ischemia, Phospho PEA-15, epilepsy, gerbil

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P62

Light-gated Mapping System to Label Neuronal Ensembles

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Although higher complexity of the brain allows its amazing function and performance, it is working as a physical hindrance for revealing the function of neuronal circuit in the brain. Minor population of neurons, called neuronal ensembles, involves to specific neural computation such as memory, motor learning, sensation, and cognition in response to specific stimuli. Therefore, if we selectively define these neuronal ensembles, we will control and manipulate neuronal computation selectively. To achieve these demands, we developed new type of mapping system, called Cal-light, which can translate neuronal activity to gene-expression in the guidance of blue light. Simultaneous induction of neuronal activity and light will provide instant recovery of the split-TEVprotease system, and it leads a proteolytic cleavage of transactivation domain. Cal-light will be a new optogenetic toolkit for the neuroscience and will be very helpful for manipulating a specific circuit.

Keywords: Optogenetics, Neural ensembles, Mapping system, TEV protease, Neural circuit

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The activation of Microglia and Blood-derived macrophages on neuroinflammation following ischemic stroke using transgenic mice: *In vivo* and *Ex vivo* system

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Ischemic stroke is a devastating disease, second only to cardiac ischemia as a cause of death worldwide and a common type of strokes caused by blood clots that stop the flow of the blood to an area of the brain. As the blood supply is insufficient to the brain tissue followed by occlusion of the cerebral artery, molecular cues generated by cerebral ischemia activate the components of innate immunity, promote inflammatory signaling and contribute to tissue damage. Microglia known as an immune cell in the central nervous system (CNS) has functions similar to those of macrophages in the periphery. At the functional point of view, resident microglia (M0) can be polarized by molecular cues: M1 phase microglia and M2 phase

microglia – former is related to pro-inflammatory responses and the latter is associated with anti-inflammatory responses. Moreover, blood-brain barrier (BBB) causes the extravasation of blood-derived macrophage. However, the interaction between the microglia and blood-derived macrophage is still unknown. We used two types of transgenic mice -CCL2::mRFP mice and CX3CR1::GFP mice- to visualize the microglia and macrophage dynamics on neuroinflammatory responses. CCL2 known as chemokine monocyte chemoattractant protein-1 (MCP1) is expressed in glial cells and increased in cerebral ischemia, Alzheimer's disease and traumatic brain injury. Furthermore, CX3CL1, a cell surface–bound chemokine constitutively expressed by neurons, suppresses microglial activation through its microglial receptor CX3CR1. In this study our goal is to observe the activation of microglia and the migration of activated microglia and infiltrated macrophage to the injured area using double transgenic mice - CCL2::RFP-CX3CR1::GFP and two-photon microscope technique on neuroinflammatory responses by transient middle cerebral artery occlusion (tMCAO) in *ex-vivo* culture, time-dependently. Our preliminary data showed that it is morphologically possible to distinguish activated microglia from the resident microglia specifically. Therefore, the overall data demonstrated that dynamics of microglia and blood-derived macrophage using specific type of transgenic mice could be a novel strategy for maintaining the M2 anti-inflammatory microglia phenotype rather than M1 pro-inflammatory microglia and finding the optimal time point of drug treatment attenuating ischemic stroke.

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Keywords: neuroinflammation, microglia activation, Transgenic mouse, intravital imaging, ex-vivo system

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P64

Overexpression arginine decarboxylase by viral vector improves neuronal differentiation of neural stem cells by regulating microRNA *let-7a*

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Neural stem cells (NSCs) have been investigated to solve central nervous system (CNS) disorders due to the potential of differentiation into neuron. Several studies have reported that microRNA is a key player of cell differentiation with roles in regulating genes associated with CNS neurogenesis. Recently, we demonstrated that agmatine, an endogenous primary amine and a novel neurotransmitter synthesized from the decarboxylation of L-arginine catalyzed by arginine decarboxylase (ADC), shows neuroprotection and contributes to cellular proliferation and differentiation. In this study, we investigated whether agmatine and retrovirus-delivered human ADC (*vh*ADC) modulated the expression of crucial regulators of NSC differentiation including DCX, TLX, c-Myc, and ERK by regulating microRNA *let-7a* (*let-7*a). Our data showed that high levels of *let-7a* promoted the expression of TLX and c-Myc, as well as repressed DCX and ERK expression. In addition, vhADC attenuated expression of TLX and increased expression of ERK by negatively regulating *let-7a* compare to control and agmatine. Our study therefore suggest that *vh*ADC and miRNA administration may improve the differentiation of NSCs.

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Keywords: Neural stem cells (NSCs), microRNA let-7a (let-7a), agmatine, arginine decarboxylase (ADC)

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Effect of Ischemic Preconditioning on the Expression of Cyclin-Dependent Kinase 5 in the CA1

Region of the Gerbil Hippocampus to Transient Global Ischemia

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The deregulation of cyclin-dependent kinase 5 (Cdk5) activity is associated with pathological conditions. Ischemic preconditioning (IPC) provides neuroprotection against subsequent lethal ischemic insults by activating specific mechanisms. We examined the effect of IPC (2 min of transient ischemia) on expressions of molecules related with Cdk5 in the hippocampus induced by a subsequent lethal transient ischemia (LI, 5 min of transient cerebral ischemia) in gerbils, which were assigned to 4 groups; group subjected to sham operation (sham group), group subjected to LI (LI group), group with IPC and sham operation (IPC+sham group), group with IPC and LI (IPC+LI group). Pyramidal neurons in the CA1 region were dead 5 days after LI; however, IPC effectively protected the neurons from a subsequent LI. In the LI group, Cdk5 and p53 expressions were significantly in nuclei of pyramidal neurons 1 and 2 days after LI; however, the expressions were abolished by IPC. In addition, expressions of calpain-I and p25 were increased in pyramidal neurons 1 and 2 days after LI. On the other hand, in the IPC+LI group, Cdk5, calpain-I, p25 and p53 expressions were significantly decreased in pyramidal neurons, in particular, Cdk5 and p53 immunoreactivities in pyramidal nuclei significantly decreased. Furthermore, apoptosis of pyramidal neurons occurred days after LI with significant increases of Bax, PUMA and caspase-3 expressions, and the apoptosis and increases of the molecuels were abolished by IPC.
In brief, IPC protected CA1 pyramidal neurons from LI through down-regulating of Cdk5, p25 and p53 in their nuclei, and the down-regulation of Cdk5 by IPC might be a key factor in attenuation of p53-dependent apoptosis in CA1 pyramidal neurons after LI. In this regard, we suggest that an inhibition of Cdk5 translocation into neuronal nuclei is critical in neuroprotection against ischemic insults.

Keywords: Ischemia-reperfusion, Ischemic tolerance, Cyclin-dependent kinase 5, P25, P53

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Immunoreactivities of Calbindin-D28k, Calretinin and Parvalbumin in the Somatosensory Cortex of Rodents During Normal Aging

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Calbindin-D28k (CB), calretinin (CR) and parvalbumin (PV), which regulate cytosolic free Ca2+ concentrations in neurons, are chemically expressed in GABAergic neurons that regulate the degree of glutamatergic excitation and output of projection neurons. In this study, we investigated age-related changes of CB, CR and PV immunoreactivities in the somatosensory cortex at young (1 month), adult (6 month) and aged (24 month) ages in three species of rodents (mouse, rat and gerbil) using immunohistochemistry and western blotting. Abundant CB-immunoreactive neurons were distributed in layers II and III, and age-related change in their number was different according to the species. CR-immunoreactive neurons were not abundant in all layers; however, the number of them was highest in all adult species. Many PV-immunoreactive neurons were found in all layers, especially in layers II and III, and they were increased in all layers with age in all species. We demonstrate that the distribution pattern of CB, CR and PV containing neurons in the somatosensory cortex were apparently changed in number with normal aging and that CB and CR showed a tendency to decrease in aged rodents, whereas PV displayed a tendency to increase with age. These finding indicates that CB, CR and PV are distinctively changed in the somatosensory cortex in normal aging and the change might be associated with normal aging.

Keywords: Somatosensory Cortex; Rodents; GABAergic neurons;

Calbindin-D28K; Calretinin; Parvalbumin

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Dynamin-related protein 1 controls the migration and neuronal differentiation of subventricular zone-derived neural progenitor cells

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Mitochondria mediate many cellular functions required for cell survival and maintenance, as they play a prominent role in energy production and calcium homeostasis. The organelles are scattered throughout the cytoplasm, but their distribution can be altered in response to local energy demands, such as cell division and neuronal maturation. Mitochondrial distribution is closely associated with mitochondrial fission, and blocking dynamin-related protein 1 (Drp1) activity often results in mitochondrial elongation and clustering. In this study, we observed that mitochondria were preferentially localized at the leading process of migratory adult neural stem cells (aNSCs), whereas neuronal differentiating cells transiently exhibited perinuclear condensation of mitochondria. Inhibiting Drp1 activity altered the morphology of migrating cell from elongated to round, while the polarized mitochondrial distribution was maintained. With these changes, aNSCs failed to migrate and differentiate. Because blocking Drp1 activity also impaired the mitochondrial membrane potential, we tested whether supplementing with L-carnitine, a compound that restores mitochondrial membrane potential and ATP synthesis, could rescue the defects induced by Drp1 inhibition. Interestingly, L-carnitine fully restored the impaired cell morphology, migration and differentiation in aNSCs. These results suggest that Drp1 is important for regulating mitochondria to produce ATP for proper migration and differentiation, and supplementing with ATP can restore the defects induced by Drp1 suppression.

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Hypoxic Preconditioning of Adipose derived Mesenchymal Stem Cells improves Wound Healing in Rats

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Adipose tissue derived mesenchymal stem cells (Ad-MSCs) enhance wound repair via paracrine effect. Because the extent of environmental oxygen affects the characteristics of Ad-MSC, including their stemness and angiogenic factor secretion, the present study was designed to elucidate and compare the impact of normoxic and hypoxic cell-culture conditions on the expression and secretion of Ad-MSC-derived paracrine factors that hypothetically contribute to wound healing. Semi-quantitative reverse transcriptase polymerase chain reaction (RT-PCR), immunocytochemistry (ICC) and western blot analyses of normoxic and hypoxic Ad-MSCs showed that MSCs expressed HIF-1α and secreted significant amounts of angiogenic factors, basic fibroblast growth factor (bFGF), brain derived neurotrophic factor (BDNF), hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF) by hypoxia mimetic agent cobalt chloride. Moreover, hypoxic preconditioning of Ad-MSCs significantly enhanced proliferation, migration and tube formation of endothelial cells (HUVEC). Consistent with these in vitro results, skin wound healing was significantly accelerated in SD Rats treated with hypoxic preconditioned Ad-MSCs relative to normoxic Ad-MSCs. These findings suggest that Ad-MSCs promote skin wound healing via hypoxia-enhanced angiogenic factor secretion.

Keywords: Hypoxia, Aipose tissue mesenchymal stem cells, Wound healing, Angiogenesis, HUVEC

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Role Of CrkII In RANKL-Induced Osteoclastogenesis

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Rac1, a member of small GTPases, is a key regulator of osteoclast differentiation and function. The Crk family adaptor proteins, consisting of Src homology (SH) 2 and SH3 protein-binding domains, regulate cell proliferation, migration, and invasion through Rac1 activation. In this study, we examined the role of CrkII in osteoclast differentiation and function. Retroviral overexpression of CrkII in osteoclast precursors enhanced osteoclast differentiation and resorptive function through Rac1 activation. The knockdown of CrkII in osteoclast precursors using small interfering RNA inhibited osteoclast differentiation and its resorption activity. Unlike wild-type CrkII, overexpression of the three SH domains in mutant forms of CrkII did not enhance either osteoclast differentiation or function. Phosphorylation of p130 Crk-associated substrate (p130Cas) by osteoclastogenic cytokines in preosteoclasts increased the interaction between p130Cas and CrkII, which is known to be involved in Rac1 activation. Furthermore, transgenic mice overexpressing CrkII under control of a tartrate-resistant acid phosphatase promoter exhibited a low bone mass phenotype, associated with increased resorptive function of osteoclasts in vivo. Taken together, our data suggest that the p130Cas/CrkII/Rac1 signaling pathway plays an important role in osteoclast differentiation and function, both in vitro and in vivo.

Keywords: Crk-Associated Substrate Protein, Osteoclasts, RANK Ligand, RNA Small Interfering, Signal Transduction

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STAT5 Is A Key Transcription Factor For IL-3-Mediated Inhibition Of RANKL-Induced Osteoclastogenesis

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Among the diverse cytokines involved in osteoclast differentiation, interleukin (IL)-3 inhibits RANKL-induced osteoclastogenesis. However, the mechanism underlying IL-3-mediated inhibition of osteoclast differentiation is not fully understood. Here we demonstrate that the activation of signal transducers and activators of transcription 5 (STAT5) by IL-3 inhibits RANKL-induced osteoclastogenesis through the induction of the expression of Id genes. We found that STAT5 overexpression inhibited RANKL-induced osteoclastogenesis. However, RANKL did not regulate the expression or activation of STAT5 during osteoclast differentiation. STAT5 deficiency prevented IL-3-mediated inhibition of osteoclastogenesis, suggesting a key role of STAT5 in IL-3-mediated inhibition of osteoclast differentiation. In addition, IL-3-induced STAT5 activation upregulated the expression of Id1 and Id2, which are negative regulators of osteoclastogenesis. Overexpression of ID1 or ID2 in STAT5-deficient cells reversed osteoclast development recovered from IL-3-mediated inhibition. Importantly, microcomputed tomography and histomorphometric analysis revealed that STAT5 conditional knockout mice showed reduced bone mass, with an increased number of osteoclasts. Furthermore, IL-3 inhibited RANKL-induced osteoclast differentiation less effectively in the STAT5 conditional knockout mice than in the wild-type mice after RANKL injection. Taken together, our findings indicate that STAT5 contributes to the remarkable IL-3-mediated inhibition of RANKL-induced osteoclastogenesis by activating Id genes and their associated pathways.

Keywords: Cell Signalling, Transcription, Osteoclast, STAT5, IL-3

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Developmental regulation of mesenchymal signalings in epithelial differentiation during mice palatogenesis

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During palatogenesis, the anterior hard palate is covered with thick ortho or parakeratinized epithelium meanwhile, posterior soft palate is covered with thin non keratinized epithelium with taste buds. To elucidate the developmental mechanisms underlying these region specific differentiation patterns of palatal epithelium along with anteroposterior axis, we employed the tissue recombination assay during in vitro organ cultivation of developing palate at E16 for 2 days. The recombination assay results revealed that epithelial differentiation with specific localization patterns of Cytokeratin 10 and Ki67 would be modulated by mesenchymal tissues. Based on these fundamental morphological results, we examined the underlying signaling regulations, which would regulate the epithelial differentiation, using laser microdissection and genome wide screening methods. After screening the data, we selected and confirmed the region specific enriched genes using RT-qPCR and in situ hybridization. After the precise evaluations of expression patterns of candidate genes, we selected the Meox2 (Mesenchyme homeobox 2) as a key regulator in mesenchymal tissue, which would control the epithelial differentiation. To examine the developmental function of Meox2, we employed in vitro organ cultivation method with the knocking down and overexpression of Meox2 using siRNA and electroporation methods respectively at E14.5 for 2 and 4 days. After 2 days cultivations, we firstly examined the altered expression patterns of related signaling molecules, such as Shh, Bmps, Fgfs, and Wnts using in situ hybridization and RT-qPCR. In addition, after 4 days cultivations, we examined the altered histogenesis and localization patterns of Cytokeratin10 and Ki67. Overall, we found that mesenchymal Meox2 would play crucial roles in non-keratinized epithelial differentiation through complex signaling regulations in mice palatogenesis.

Keywords: Palatal development, Epithelial-mesenchymal interactions, Keratinization, Laser-microdissection, Genome wide screening

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Grhl3 modulates epithelial structure formation of the circumvallate papilla during mouse development

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Grainyhead-like 3 (Grhl3) is a transcription factor involved in epithelial morphogenesis. In the present study, we evaluated the developmental role of Grhl3 in structural formation of the circumvallate papilla (CVP), which undergoes dynamic morphological changes during organogenesis. The specific expression pattern of Grhl3 was examined in the CVP-forming region, specifically in the apex and epithelial stalk from E13.5 to E15.5 using in situ hybridization. To determine the role of Grhl3 in epithelial morphogenesis of the CVP, we employed an in vitro tongue culture method, wherein E13.5 tongue were isolated and cultured for 2 days after knocking down of Grhl3. Knockdown of Grhl3 resulted in significant changes to the epithelial structure of the CVP, such that the apical region of the CVP was smaller in size, and the epithelial stalks were more deeply invaginated. To define the mechanisms underlying these morphological alterations, we examined cell migration, proliferation, and apoptosis using phalloidin staining, immunohistochemistry against Ki67, ROCK1, and E-cadherin, and a TUNEL assay, respectively. These results revealed an increase in proliferation, a reduction in apoptosis, and an altered pattern of cytoskeletal formation in the CVP-forming epithelium, following Grhl3 knockdown. In addition, there were changes in the specific expression patterns of signaling and apoptosis-related molecules such as *Axin2, Bak1, Bcl2, Casp3, Casp8, Ctnnb1, Cnnd1, Gli3, Lef1, Ptch1, Rock1, Shh,* and *Wnt11*, which could explain the altered cellular and morphological events. Based on these results, we propose that developmental stage-specific *Grhl3* plays a significant role in CVP morphogenesis not by just disruption of epithelial integrity but by regulating epithelial cell proliferation, apoptosis, and migration via *Shh, Wnt*, and apoptosis signaling during mouse embryogenesis.

Keywords: Epithelial morphogenesis, Rearrangement, Cytoskeletal formation, Morphogenesis, Grainyhead-like 3

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In Sufficiency of Vitamin C Induces a Defect on the Fetal Growth and Maintenance of Pregnancy in Gulo(-/-) Mice

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Developing fetus is particularly susceptible to vitamin C deficiency because rapid growth and immature antioxidant system. So, we investigated the effect of vitamin C on the fetal development using Gulo(-/-) mice. When maternal Gulo(-/-) mice was depleted of vitamin C for 2 weeks during pregnancy, the serum level was vitamin C was half of vitamin C-sufficient Gulo(-/-) mice or wild-type (WT) mice. The number and body weight of fetus was reduced, and the concentration of vitamin C in the amniotic fluid was significantly decreased in the vitamin C-insufficient Gulo(-/-) mice. Moreover, Gulo(-/-) mice showed a loose integrity, an increased expression of matrix metalloproteinase 9 (MMP-9), and a decreased vascular permeability in the placenta. Also, the production of progesterone, a hormone for maintaining pregnancy, was considerably reduced. Therefore, vitamin C insufficiency during gestation could disturb the fetal growth and maintenance of pregnancy.

Keywords: Vitamin C, Pregnancy, Gulo(-/-) mice

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ER stress and polyuria in α-galactosidase A deficient mice

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Fabry disease is a lysosomal storage disorder caused by deficiency of the enzyme α-galactosidase A (α-Gal A). Misfolded enzymes are retained in the endoplasmic reticulum (ER) and degraded before sorting into lysosomes resulting in lysosomal accumulation of globotriaosylceramide (Gb3). The purpose of this study was to investigate the effects of ER stress on polyuria, initial renal symptoms, in α-Gal A deficient mice. Kidney tissues were processed for α-Gal A enzyme activity assay, Gb3 level quantification, immunocytochemistry, and immunoblot analysis. α-Gal A deficiency caused significant polyuria that was associated with increased renal Gb3 level. Fabry kidneys showed a significantly increased expression of ER stress proteins, Bip and CHOP. Immunocytochemistry revealed that the expression of Bip and CHOP was induced mainly in glomeruli, outer medullary vascular bundles, and medullary collecting ducts. AQPs are key transport proteins involved in urine concentration in the kidney. Expression of AQP2, 3, and 4 proteins significantly decreased in Fabry kidneys, but the abundance of AQP1 protein remained unchanged. Confocal microscopy demonstrated that AQP2 was abnormally localized in the cytoplasm in medullary collecting ducts. Electron microscopy confirmed the presence of typical lamellar inclusion bodies in collecting duct cells. These findings suggest that ER stress and altered expression of AQPs may play an important role in urinary concentration defect in Fabry disease.

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Keywords: α-Galactosidase A, ER stress, Polyuria, AQP

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Increased Expression of HMGB1 and NFkB after 5/6 nephrectomy in the rat brain

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Pathophysiologic mechanisms of developing cognitive dysfunction in chronic kidney disease (CKD) were not completely understood. We aimed to investigate whether expression of high-mobility group box 1(HMGB1) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), which are related with neuroinflammation, would be changed on brain after 5/6 nephrectomy of rat. Male Sprague–Dawley rats were used in all experiments (control for acute kidney injury (AKI): n = 10, control for CKD: n = 10, AKI (n = 10, CKD: n = 10). For AKI model, bilateral renal artery clamping during 45 minutes and reperfusion was performed. For CKD model, the method regarding 5/6 nephrectomy of rat kidney was applied. The brain/blood tissues for AKI and CKD were harvested in 6 hours and 4 weeks, respectively, after last operation. The immunohistochemical stain and Western blot for HMGB1 and NF-kB at brain were undertaken. Moreover, TdT-mediated dUTP nick end-labeling staining was performed for evaluating apoptosis. In IHC stain and Western blot, increased expression for both HMGB1 and NF-kB were noted in CKD group at frontal cortex and hippocampus but not in AKI and control group. In TUNEL stain, cell death was noted in only CKD at frontal cortex and hippocampus but no AKI and control. Our study showed that CKD, even though in early stage, is associated with increased expression of HMGB1 and NF-kB on brain. These results suggested that CKD would be related with inflammatory reaction and cognitive dysfunction on brain via pathway of HMGB1 and NF-kB.

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Keywords: Chronic kidney disease, inflammation, brain

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Expression of FGF5 and Its Related Molecules in Hair Growth Cycle

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FGF5 (Fibroblast Growth Factor 5), one of the hair cyle regulator, is a catagen inducer in hair cycle. The mutation of FGF5 causes abnormal hair length in human, mouse, dog, etc. FGF5 is known to be expressed in the outer root sheath (ORS) in the hair follicle and macrophage-like cells around the hair follicle, however, exact localization of FGF5 is not clear in the hair follicle. Furthermore, FGF5 isoforms, long and short forms, was found in various tissues. FGF5 short form may have opposite role contrast to FGF5 long form, inhibiting FGF5 long form. Signaling pathway of FGF5 also was not identified in the hair follicle. To investigate expression and localization of FGF5 and its related molecules, RT-PCR and immunohistochemistry for FGF5 long form, axin2 and keratin 15, stem cells markers in the hair follicle, were performed in the mouse hair follicle. We founded that mRNA of FGF5 long and short forms was founded in the hair follicle with RT-PCR. Immunoreactivity for FGF5 long form was found in the ORS and the hair bulge, however, in the only hair bulge in telogen. Immunoreactivity for axin2 and keratin 15 was also founded with same location in the hair follicle. Further study for FGF5 short form should be done including interaction with FGF5 long form with using antibody detecting both FGF5 long form and short form and overexpression of FGF5 isoforms in ORS cells. Taken together, FGF5 in the ORS and hair bulge may have important role in hair growth cycle, especially bulge stem cell regulation.

Keywords: FGF5, Hair cycle, Hair growth, Hair bulge

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P77

Rescue of cleft palate with therapeutic hedgehog target chemical in Endocrine-cerebro-ostedysplasia (ECO) syndrome mouse model

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

Keywords: Hedgehog, Endocrine-cerebro-ostedysplasia (ECO) syndrome, Rescue, Therapeutic chemical

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P78

Tempo-spatial Requirements of Hedgehog and BMP Signaling During Middle Ear Development

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The mammalian middle ear (ME), responsible for transmitting mechanical vibrations from the outer ear to the inner ear, is comprised of a chain of three ossicles: malleus, incus, and stapes. Any failure of ME function can lead to conductive hearing loss. ME ossicles are derived from neural crest cells (NCCs). Malleus and incus are derived from neural crest cells (NCCs) migrated into branchial arch (BA)1, while stapes is from NCCs migrated into BA2. However, it is still unclear about the molecular mechanisms involved in the NCC migration in forming ME ossicles. Here, we investigated the roles of Hedgehog (Hh) and Bmp4 in mediating ossicle formation. In order to elucidate the mechanisms by which NCCs migrate and differentiate into specific ME ossicles, we generated mouse mutants by using Cre/loxp technology to specifically manipulate Hh (*Wnt1-Cre;Smo*$^{lox/lox}$, *Wnt1-Cre;Smo*$^{M2/+}$) and TGF-β (*Wnt1-Cre;Smad4*$^{lox/lox}$) signaling in NCCs. Additionally, we also generated *Foxg1-Cre;Shh*$^{lox/lox}$ and *Foxg1-Cre;Bmp4*$^{Tm1/lox}$ to knockdown Sonic hedgehog (Shh) and Bone morphogenetic protein 4 (Bmp4) signaling in the pharyngeal endoderm (PE). Previously, Hh signaling has been implicated in the NCC differentiation into ME ossicles. In our *Wnt1-Cre;Smo*$^{lox/lox}$ mutants, in which NCCs failed to respond to Hh signaling, the initial condensation of the three ossicle anlages based on Sox9 expression is observed at E10.5, but this expression disappeared by E11.5. In *Foxg1-Cre;Shh*$^{lox/lox}$ mutants, we observed no condensation in BA1, but a small condensation in BA2 is present. These results suggest that Hh signaling is not required for initial condensation but for subsequent development of ME ossicles. Constitutive activation of Hh signaling in NCCs in *Wnt1-Cre;Smo*$^{M2/+}$ mutants resulted in enlarged condensation in both BA1 and BA2 at E10.5 and in fused ME ossicles displaced from the inner ear at E15.5. Notably, we observed that initial condensation of stapes in BA2, but not in BA1, is closely associated with Bmp4 expression domain in PE. Upon inactivation of TGF-β signaling in NCCs using *Wnt1-Cre;Smad4*$^{lox/lox}$ mutants, NCCs failed to migrate to the prospective stapes region in BA2, but not in BA1. Similar phenotypes were observed in *Foxg1-Cre;Bmp4*$^{lox/lox}$ mutants, in which endodermal Bmp4 expression was abolished, suggesting that Bmp4 signaling emanating from PE dictates migration and initial condensation of NCCs to form stapes in BA2. Our results indicate that Bmp4 and Hh signaling regulate migration and differentiation of NCCs into ME ossicles in a tempo-spatial-dependent manner, such that endodermal Bmp4 signaling guides NCCs into migrate to the prospec-

tive stapes region in BA2, and Hh signaling subsequently plays roles in maintenance and further development of ME ossicles.

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Keywords: Middle ear, initial condensation, hedgehog and Bmp4 signaling, pharyngeal endoderm

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P79

Elucidation of Neural Stem Cell Character of Caudal Cell Mass in Developing Chick Embryo

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The caudal cell mass (CCM) has been known as the main player in secondary neurulation, forming the secondary neural tube. This model suggests that the CCM may have the character of neural stem cells (NSCs). However, evidence of NSC characteristics of the CCM has not been shown.

The neural potential of the CCM was assessed by confirming the in vitro culture of neurospheres from the CCM throughout the stages of secondary neurulation (Hamburger and Hamilton (HH) stages 16 to 32). We further evaluated whether there was spatiotemporal diversity in the neural potential of the developing central nervous system by quantification of the in vitro neurosphere culture results from the brain, upper spinal cord, lower spinal cord, and CCM from various developmental stages.

The CCM was capable of the in vitro formation of neurospheres, which were able to self-renew and differentiate into neurons, astrocytes, and oligodendrocytes. This provided evidence that the CCM had characteristics of NSCs. Quantitative evaluation of the neurosphere formation from the CCM at various stages showed the greatest number of cultured neurospheres at HH stage 28. From brain, the greatest number of neurospheres was formed at stage 16. Considering the trend of increase in the number of neurospheres for brain, spinal cord, and CCM, the neural potential seemed to follow a cephalo-caudal direction as development proceeded.

This study showed that neurospheres can be cultured in vitro from CCM of various stages, supporting its characterization as NSCs. The spatiotemporal diversity of NSC character was also shown, reflecting the dynamic process of neurulation during development.

Keywords: Chick Caudal Cell Mass Secondary Neurulation Development Neural Stem Cells

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P80

ZHX1 Promotes the Proliferation, Migration and Invasion of Cholangiocarcinoma Cells

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Zinc-fingers and homeoboxes 1 (ZHX1) is a transcription repressor that has been associated with the progressions of hepatocellular carcinoma, gastric cancer, and breast cancer. However, the functional roles of ZHX1 in cholangiocarcinoma (CCA) have not been determined. We investigated the expression and roles of ZHX1 during the proliferation, migration, and invasion of CCA cells. *In silico* analysis and immunohistochemical studies showed amplification and overexpression of ZHX1 in CCA tissues. Furthermore, ZHX1 knockdown using specific siRNAs decreased CCA cell proliferation, migration, and invasion, whereas ZHX1 overexpression promoted all three characteristics. In addition, results suggested EGR1 might mediate the effect of ZHX1 on the proliferation of CCA cells. Taken together, these results show ZHX1 promotes CCA cell proliferation, migration, and invasion, and present ZHX1 as a potential target for the treatment of CCA.

Keywords: Zinc-fingers and homeoboxes 1 (ZHX1) cholangiocarcinoma (CCA)

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Combinational treatment of Erlotinib and Ampelopsin overcomes to resistance to Erlotinib through Nox2-ROS-Bim pathway.

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Erlotinib, a tyrosine kinase inhibitor (TKI) of epidermal growth factor receptor (EGFR) has shown dramatic effect for the non-small cell lung cancer (NSCLC) patients with EGFR mutation. However, the presence of primary or the occurrence of acquired resistance to EGFR-TKI is the most common reason that we have to switch to other anti-cancer agents. Even though newer agents that have activity for T790M mutation which is one of the most common resistant mechanism to EGFR-TKI have been developed, identification of potential agents to overcome resistance to EGFR-TKI are still needed for the treatment of NSCLC patients. In this study, we used erlotinib-resistant H1975 NSCLC cell lines to investigate the effect of combinational treatment of erlotinib and ampelopsin which has been known as a flavonoid component from Ampelopsis grossedentata and anti-cancer activity against various cancers. Combined treatment of erlotinib and ampelopsin with non-cytotoxic concentration significantly induced caspase-dependent cell death in erlotinib resistant NSCLC cells. Furthermore, these cell deaths resulted in the accumulation of reactive oxygen species (ROS) through up-regulation of nicotinamide adenine dinucleotide phosphate oxidase 2 (Nox2) expression, a direct source of ROS. The expression level of Bim was increased to the combination treatment but not either alone. These results provided that combination of erlotinib and ampelopsin induced cell death via Nox2-ROS-Bim pathway, and ampelopsin could be used as a novel anti-cancer agent combined with EGFR-TKI to overcome resistance in EGFR-mutant NSCLC.

Keywords: Erlotinib, Ampelopsin, Nox2, ROS, Bim

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GR Mediated-Regulation of GPx3 in Lung Cancer Cells

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Lung cancer is a malignant lung tumor characterized by uncontrolled cell growth in tissues of the lung. Recent reports indicate that glutathione peroxidase 3 (GPx3) could be a useful bio-marker for lung cancer, because GPx3 expression is specifically related to lung cancer. Furthermore, GPx3 has received considerable attention as a tumor suppressor in various cancers during recent years. Glutathione peroxidase 3 (GPx3), one of the antioxidant enzymes, act as a modulator in the redox signaling, immunomodulatory, and detoxification of reactive oxygen species (ROS). GPx3 has been identified as a tumor suppressor in many cancers. Regarding GPx3 expression regulation has been only identified down-regulation mechanism through hyper-methylation of its promoter in many cancers. However, other regulation role on GPx3 expression is still not reported. This study aimed to investigate a novel GPx3 regulation role. GPx3 gene analysis predicted that ten glucocorticoid response elements (GREs) were spread on GPX3 gene. This result prompted us to study regulation of GPx3 expression by glucocorticoid receptor (GR) which is implicated in tumor response to chemotherapy. The dexamethasone (Dex) was used to examine the possible relationship between GR and GPx3 expression. The Dex significantly induced GPx3 expression level in H1299, H1650 and H1975 which cell lines have exhibited a low GPx3 expression. The EMSA and ChIP-PCR results suggested that GR protein directly bind with GRE 6 and 7, both GREs are closely located with GPx3 promoter. When compare influences of GRE wild type (WT) or mutant type (MT) into GPx3 transcription efficiency using luciferase report system, blocking of GR-GRE complex significantly reduced 7-8 folds luciferase activity. Suppression of GR by siRNA transfection in lung cancer cells was immediately reflected to GPx3 down-regulation. These data suggest that GPx3 expression can be actively regulated through the roles of

epigenetic- or GR mediated-regulations in lung cancer cells, independently. GPx3 could potentiate glucocorticoid (GC)-mediated anti-inflammatory signaling in lung cancer cells. This finding provides useful information for developing therapies designed to enhance GPx3 expression by GC and will also be helpful in developing effective treatment strategies.

Keywords: Glutathione Peroxidase-3, Glucocorticoids, Glucocorticoid Receptor, Glucocorticoid Response Element, Dexamethasone, Gene Regulation.

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Discovery of lung cancer serological markers using MRM-MS analysis

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Non-small-cell lung cancer (NSCLC) constitutes approximately 80% of all diagnosed lung cancers, consists of two major subtypes: adenocarcinoma (ADC) and squamous cell carcinoma (SQC). Every year, more than 900,000 deaths from ADC and SQC combined are reported worldwide. Therefore, diagnostic markers detectable in the plasma/serum of NSCLC patients are greatly needed. Omic-based platforms have been promoted for the discovery of disease biomarkers. Enormous efforts have been made to discover biomarkers using plasma samples from NSCLC patients, but unfortunately, clinical use of those markers might be limited. In this study, we hypothesized that if some proteins show quantitative changes in cancer tissues compared to normal tissues and are present in the cell secretome, then there would be a better chance of detecting those proteins in plasma/serum. We established a pipeline for the discovery of markers using 10 transcriptome data sets obtained from the Gene Expression Omnibus (GEO) and profiling of six lung cancer cell secretomes. Seventeen out of 281 proteins that overlapped between ± 15% differentially expressed genes and identified cell secretome proteins were detected in the pooled plasma of lung cancer patients. To quantify the candidates in the serum of NSCLC patients, multiple-reaction-monitoring mass spectrometry (MRM-MS) with stable isotope-labeled standard (SIS) peptides was performed for eight candidate biomarkers. Finally, two potential biomarkers (BCHE and GPx3; AUC = 0.678 and 0.682, respectively) and one two-marker panel (BCHE/GPx3; AUC = 0.743) were identified that effectively differentiated NSCLC patients from healthy controls. In addition, using an ELISA, a validation test was performed to evaluate the reproducibility of GPx3 and BCHE expression in an independent set of samples. In the validation study, levels of GPx3 and BCHE were significantly lower in the NSCLC group (BCHE and GPx3; AUC = 0.676 and 0.732, respectively, BCHE/GPx3 panel; AUC = 0.768). Collectively, these results demonstrate the feasibility of using our pipeline for marker discovery and our MRM-MS platform for verifying potential biomarkers of human diseases.

Keywords: Secretome, Transcriptome, MRM, Serological Marker, Lung Cancer

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Biomimetic 3D Hydrogel for the Study of Malignancy of Human Prostate Cancer Cells

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Conventional 2D prostate cancer cell culture models do not reflect the true biological activities of prostate cancer cells *in vivo*, and thus

drug screening and testing in 3D prostate cancer cell culture models are more effective than conventional 2D monolayer culture system. In the present study, we established a hydrogel-based 3D prostate cancer culture system using various human prostate cancer cell lines (LNCaP, DU145 and PC3). It was found that cells cultured in the hydrogels grow as tumor-like clusters in 3D formation when compared to cells cultured in 2D monolayer culture. Histological examination of all the three types of prostate cancer cells demonstrated the formation of spheroids, whereas none of the cell types in 2D formed any spheroids. RT-PCR, Western blot, drug resistance and immunofluorescence staining analyses revealed that the expression of various genes related with prostate cancer malignancy was significantly up-regulated in all the three types of cells in 3D cell culture when compared to 2D cell culture. Furthermore, increased migration and invasion in all three types of the human prostate cancer cells was observed in cells cultured in 3D compared to those in 2D. Therefore, this study provides a novel hydrogel-based 3D culture technique for human prostate cancer cells that closely mimicked *in vivo* cancer progression. Furthermore, our data may provide a useful platform technology to develop functional, biocompatible, three-dimensional scaffolds for 3D culture of various cancer cells.

Keywords: 3D culture, Hydrogel, Tumor spheroid, Prostate cancer

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P85

MF-1-1 Enhances Proliferation and Thymopoietic Activity of Thymic Epithelial Cells

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Adhesion of thymocytes to thymic epithelial cells (TECs) is considered to be substantially important due to their interdependent relationship for the functional differentiation of thymocytes inside the thymus. Of many factors that influence the behavior of TECs, the immediate cell microenvironment plays a major role. In this context, we studied the effect of MF-1-1, polypeptides derived from marine species, on cell survival, proliferation and adhesion of TECs. The present study clearly shows that MF-1-1 stimulated TEC activities including cell proliferation, thymocyte adhesion to TECs, and the expression of cell adhesion molecules such as ICAM-1 and VCAM-1, and thymopoietic factors including IL-7, pFAK, Troma-1. Furthermore, the expression of cell survival molecules such as Bcl-2 and Bcl-xL upregulated, while that of a pro-apoptotic molecule such as Bax was downregulated. Furthermore, the upregulated expression of E-cadherin and vinculin in TECs after MF-1-1 treatment was found. Taken together, our data demonstrate that MF-1-1 has a promoting effect on TEC activity, and might be useful for development of a therapeutic strategy to enhance thymus function.

Keywords: Thymic Epithelial Cells , Thymocyte, Pro-apoptosis

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A New PLE-based Hydrogel as a Biomimetic Scaffold for 3D Cell Culture

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One of the most crucial problems of the generally used two-dimensional 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 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 two-dimensional cell culture techniques. In the present study, a composite hydrogel containing decellularized PLE-1-1 and MF-1-1 was constructed for use in three-dimensional 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 culture, Hydrogel, Cell spheroid, Decellularized

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Cytoprotective and Anti-inflammatory Effect of MF-1-1 in HaCaT Human Keratinocytes

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The toxicity and inflammatory skin diseases are the most common problem in dermatology. In this study, we report that MF-1-1, polypeptides derived from marine organisms, protects human skin keratinocytes (HaCaT cells) against chemical hypoxia-induced damage and TNF-α induced inflammatory injury. HaCaT cells were treated with cobalt chloride ($CoCl_2$), a well-known hypoxia mimetic agent, and TNF-α, a pro-inflammatory cytokine, to establish a chemical hypoxia-induced as well as inflammatory cell injury model. Our findings showed that co-treatment of HaCaT cells with MF-1-1 and $CoCl_2$ for 24 h significantly attenuated $CoCl_2$-induced cytotoxicity and inflammatory responses, evidenced by increases in cell viability, decreases in ROS generation and inhibition of iNOS and TNF-α expression. In addition, co-treatment with MF-1-1 markedly reduced $CoCl_2$-induced expression of Bax, cleaved caspase-3 expression, cytochrom c and phospho-p38-MAPK level, while MF-1-1 induced Bcl-2 upregulation. The MF-1-1 also depressed TNF-α-induced secretions of IL-1β and IL-8, as well as nuclear translocation of NF-κB p65 subunit. Taken together, the findings of the present study have demonstrated that MF-1-1 protects HaCaT cells against $CoCl_2$-induced cytotoxicity and TNF-α-induced inflammatory responses.

Keywords: HaCaT cell, Anti-inflammatory, Cytoprotective

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Clinical and Prognostic Significance of Merkel Cell Polyomavirus in Non-Small Cell Lung Cancer

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Recently, an association between Merkel cell polyomavirus (MCPyV) and epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer (NSCLC) was reported. However, the underlying carcinogenic effects and the prognosis related to MCPyV are still unclear. The aim of this study was to clarify the incidence and prognosis related to MCPyV infections in NSCLC. Tissue samples from 167 NSCLC patients (92 with squamous cell carcinomas (SCCs) and 75 with adenocarcinomas) were analyzed for the presence of MCPyV and EGFR mutations. Clinicopathological characteristics, disease-free survival rate, and overall survival rate were assessed with respect to MCPyV. MCPyV DNA was detected in 30 patients (18.0%), and EGFR mutations were found in 31 out of 127 patients (24.4%). EGFR mutations were more frequently detected in MCPyV-positive patients than in MCPyV-negative patients; however, this did not reach statistical significance (p = 0.075). There was no difference in overall survival between patients with and without MCPyV infections. The disease-free survival rate of patients with pN0 stage, SCC, or EGFR mutations was lower for patients with MCPyV than without MCPyV (p = 0.036, 0.042, and 0.050, respectively). Although the prevalence of MCPyV infection was relatively low, the presence of MCPyV DNA was significantly correlated with cancer prognosis in subgroups of NSCLC patients. These results suggest that MCPyV may be partly associated with pathogenesis and prognosis in some cases of NSCLC.

Keywords: Merkel cell polyomavirus, EGFR mutations, Non-small cell lung cancer, Prognosis

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Trifluoperazine, a Well-known Antipsychotic, Inhibits Glioblastoma Invasion by Binding to Calmodulin, and Disinhibiting Calcium Release Channel IP3R

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Calcium (Ca^{2+}) signaling is an important signaling process, implicated in cancer cell proliferation and motility of the deadly glioblastomas that aggressively invade neighboring brain tissue. We have previously demonstrated that caffeine blocks glioblastoma invasion and extends survival by inhibiting Ca^{2+} release channel Inositol 1,4,5-Trisphosphate Receptor (IP3R) Subtype 3. Trifluoperazine (TFP) is an FDA-approved antipsychotic drug for schizophrenia. Interestingly, TFP has been recently reported to show a strong anticancer effect on lung cancer, hepatocellular carcinoma and T-cell lymphoma. However, the possible anticancer effect of TFP on glioblastoma has not been tested. Here, we report that TFP potently suppresses proliferation, motility and invasion of glioblastoma cells in vitro, and tumor growth in in vivo xenograft mouse model. Unlike caffeine, TFP triggers massive and irreversible release of Ca^{2+} from intracellular stores by IP3R subtype 1 and 2 by directly interacting at the TFP binding site of a Ca^{2+} binding protein, Calmodulin subtype 2 (CaM2). TFP binding to CaM2 causes a dissociation of CaM2 from IP3R and subsequent opening of IP3R. Based on these findings we propose TFP as a potential therapeutic drug for glioblastoma by aberrantly and irreversibly increasing Ca^{2+} in glioblastoma cells.

Keywords: Glioblastoma, Trifluoperazine (TFP), Inositol 1,4,5-triphosphate receptor (IP3R), Calmodulin, Calcium

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Hinokitiol Induces DNA Demethylation via DNMT1 and UHRF1 Inhibition in Colon Cancer Cells

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Background: DNA hypermethylation is a key epigenetic mechanism for the silencing of many genes in cancer. Hinokitiol, a tropolone-related natural compound, is known to induce apoptosis and cell cycle arrest and has anti-inflammatory and anti-tumor activities. However, the relationship between hinokitiol and DNA methylation is not clear. The aim of our study was to explore whether hinokitiol has an inhibitory ability on the DNA methylation in colon cancer cells.
Results: MTT data showed that hinokitiol had higher sensitivity in colon cancer cells, HCT-116 and SW480, than in normal colon cells, CCD18Co. Hinokitiol reduced DNA methyltransferase 1(*DNMT1*) and ubiquitin-like plant homeodomain and RING finger domain 1(*UHRF1*) expression in HCT-116 cells. In addition, the expression of ten-eleven translocation protein 1(*TET1*), a known DNA demethylation initiator, was increased by hinokitiol treatment. ELISA and FACS data showed that hinokitiol increased the 5-hydroxymethylcytosine (5hmC) level in the both colon cancer cells, but 5-methylcytosine (5mC) level was not changed. Furthermore, hinokitiol significantly restored mRNA expression of O^6-methylguanine DNA methyltransferase (*MGMT*), carbohydrate sulfotransferase 10 (*CHST10*), and B-cell translocation gene 4 (*BTG4*) concomitant with reduction of methylation status in HCT-116 cells.
Conclusions: These results indicate that hinokitiol may exert DNA demethylation by inhibiting the expression of *DNMT1* and *UHRF1* in colon cancer cells.

Keywords: Hinokitiol, DNA methylation, Anti-tumor activities, DNA methylation inhibitor, Colonic neoplasm.

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

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

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

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The Effect of Interleukin-22 on Skin Keratinocytes Irradiated by UVB

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IL-22 is produced by activated $CD4^+$ T cells and NK cells, but IL-22Rα expression is restricted to nonhematopoietic cells in the skin, pancreas and so on. It has recently been reported that IL-22 plays a critical role in the maintenance of epidermal homeostasis by controlling cell cycle of keratinocytes. In addition, it is already known that UVB induces skin inflammation. However, there are no reports regarding the role of UVB on the production of IL-22 and its receptor expression. Therefore, we investigated the role of IL-22 on the proliferation of UVB-irradiated HaCaT and the induction of skin inflammation in terms of IL-22Rα expression. The expression of IL-22Rα in HaCaT was increased by UVB irradiation. Interestingly, the translocation of IL-22Rα from cytosol to membrane was increased by UVB. It is generally known that UVB suppresses the proliferation of HaCaT, but the suppressed proliferation of UVB-irradiated HaCaT was recovered by the treatment of rIL-22 and culture supernatant of activated PBMCs. Finally, the production of pro-inflammatory cytokines was increased from UVB-irradiated HaCaT and primary keratinocytes by the treatment of rIL-22. Taken together, IL-22 increases skin inflammation and the proliferation of HaCaT through the interaction with up-regulated IL-22Rα on HaCaT by UVB irradiation.

Keywords: Interleukin-22, Skin Inflammation, UVB, HaCaT

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Red Ginseng and Vitamin C Increase

Immune Cell Activity and Decrease Lung Inflammation Induced by Influenza A Virus/H1N1 Infection.

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Because red ginseng and vitamin C have immunomodulatory function and anti-viral effect, we investigated whether red ginseng and vitamin C synergistically regulate immune cell function and suppress viral infection. Red ginseng and vitamin C were treated to human peripheral blood mononuclear cells (PBMCs) or sarcoma-associated herpesvirus (KSHV)-infected BCBL-1, and administrated to Gulo(-/-) mice, which are incapable of synthesizing vitamin C, with or without influenza A virus/H1N1 infection. Red ginseng and vitamin C increased the expression of CD25 and CD69 of PBMCs and natural killer (NK) cells. Co-treatment of them decreased cell viability and lytic gene expression in BCBL-1. In Gulo(-/-) mice, red ginseng and vitamin C increased the expression of NKp46, a natural cytotoxic receptor of NK cells and interferon (IFN)-γ production. Influenza infection decreased the survival rate, and increased inflammation and viral plaque accumulation in the lungs of vitamin C-depleted Gulo(-/-) mice, which were remarkably reduced by red ginseng and vitamin C supplementation. Administration of red ginseng and vitamin C enhanced the activation of immune cells like T and NK cells, and repressed the progress of viral lytic cycle. It also reduced lung inflammation caused by viral infection, which consequently increased the survival rate.

Keywords: H1N1, Influenza A virus, Red Ginseng, Vitamin C

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Expression of CD46 in Bladder Cancer to Mediated Adenoviral Gene Therapy

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CD46 is a complement inhibitor membrane cofactor which also acts as a receptor for various microbes, including species B adenoviruses (Ads). While most Ad gene therapy vectors are derived from species C and infect cells through coxsackie-adenovirus receptor (CAR), CAR expression is down regulated in many cancer cells, resulting inefficient Ad-based therapeutics. Despite a limited knowledge on the expression status of many cancer cells, an increasing number of cancer gene therapy studies include fiber-modified Ad vectors redirected to the more ubiquitously expressed CD46. Several bladder cancer cell lines were tested upon modified adenoviral targeting CD46 by FACScan analysis, cell killing assay, immunofluorescence, and Western blot. Further in vivo studies were performed to demonstrate xenograft cancer growth using syngeneic mouse models. Our data indicated that, most bladder cancer cell lines showed high expression of CD46 and have a significantly higher response to Ad5/35-GFP and to Ad5/35-tk/GCV. CD46 expression was positively correlated with Ad5/35-mediated GFP fluorescence and accordingly its cell killing. Injection of Ad5/35-tk/GCV caused much greater tumor-suppression in mice bearing CD46-overexpressed cancer xenograft compared to mock group. Analysis of bladder cancer patients samples revealed that patients with positive CD46 expression had a higher survival rate. Taken together, our study demonstrated that species B-based adenoviral gene therapy is a suitable approach for generally CD46-overexpressed bladder cancer but would require careful consideration preceding CD46 analysis and categorizing cancer patients.

Keywords: Adenovirus, CD46, Bladder cancer, Gene therapy

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The Effect of Alloferon on the Enhancement of NK Cell Cytotoxicity against Cancer via Up-Regulation of Perforin/Granzyme B Secretion

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Alloferon is a novel immunomodulatory peptide originally isolated from infected insects. It has anti-viral and anti-tumor effects via the activation of NK cells. However, specific mechanisms leading to NK cell activation and anti-tumor responses yet to be clarified. In this study, we demonstrate that alloferon increases killing activity of NK cells to cancer cells via the up-regulation of the expression of NK-activating receptors, 2B4. In addition, the production of IFN-γ and TNF-α and granule exocytosis from NK cells against cancer cell were increased by alloferon. Lastly, the anti-tumor effect of alloferon was confirmed in vivo to demonstrate effective retardation of tumor growth in the human-to-mouse xenograft model. All taken together, these results suggest that alloferon has anti-tumor effects through up-regulation of NK-activating receptor 2B4 and the enhancement of granule exocytosis from NK cells.

Keywords: Alloferon, NK cell, anti-tumor effect, 2B4

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α-Enolase Stimulates the Cancer Cell Proliferation via TGF-β Production

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It has been recently reported that α-Enolase (ENO1) is involved in multiple functions such as glycolysis, cancer metastasis and tumor growth. ENO1 is ubiquitously is expressed both in the cytosol and on the cell surface in cancer. However, it remains to be elucidated the function of ENO1 expressed on cancer cells. Thus, we investigated the role of ENO1 in the various cancer cells. First, it was examined the expression of ENO1 on the cell surface in gastric carcinoma cell line, SNU16, colon cancer cell line, HCT116 and lymphoma cell line, U937. As a result, HCT116 and SNU16 slightly expressed ENO1 on their surface, and ENO1 was highly expressed on the U937 cell surface. To identify whether ENO1 is related to cancer cell proliferation of viability, we performed CCK-8 assay after ENO1 stimulation. ENO1 stimulation by anti-ENO1 antibody induced the proliferation of all cancer cells. Since tumor growth factor (TGF)-β is known to regulate cellular proliferation and differentiation in cancer, the level of TGH-β was measured, and its level were increased by ENO1 stimulation. These results suggest that ENO1 on the cancer cell surface is involved in the up-regulation of TGF-β production and cell proliferation.

Keywords: α-Enolase, tumor growth factor (TGF)-β, SNU16, HCT116, U937

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IL-22 Producing NKp46^{+}Cells has a Critical Role on the Prevention of IL-6-Dependent DSS-Induced Colitis in Vitamin C-Insufficient *Gulo (-/-)* Mice

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Intestinal mucosal damage in the inflammatory bowel disease (IBD) involves the dysfunctional immunoregulation of the gut. Among the immunoregulatory factors, reactive oxygen species (ROS) are produced in abnorally high levels in IBD, and their destructive effects may contribute to the initiation or propagation of the disease. Vitamin C not only scavenges free radicals as an antioxidant but also has anti-inflammatory effects. Therefore, we investigated the effect of vitamin C on dextran sulfate sodium (DSS)-induced colitis in *gulo (-/-)* mice which cannot synthesize vitamin C. Vitamin C-insufficient *gulo (-/-)* mice showed decreased survival and lowered recovery efficacy. It was accompanied with more severe colitis such as epithelial erosion, infiltration of inflammatory cells and contraction of colon. The production of pro-inflammatory cytokine, interleukin (IL)-6, and signal transducer and activator of transcription 3 (STAT-3) phosphorylation was remarkably increased in DSS-treated vitamin C-insufficient *gulo (-/-)* mice compared to vitamin C-sufficient *gulo (-/-)* mice and wild type mice after DSS treatment. In contrast, the level of anti-inflammatory cytokine, IL-22, was significantly decreased in the serum and colonic tissue lysates of vitamin C-insufficient *gulo (-/-)* mice. in addition, the number of NKp46^{+}cells, which are known to secret IL-22, were decreased in the DSS-treated colonic tissues of

to vitamin C- sufficient *gulo (-/-)* mice. To summarize, vitamin C insufficiency was associated with more severe DSS-induced colitis, and was related to increase of pro-inflammatory IL-6 production and oxidative stress, resulting in activated STAT3 signaling, and decrease of anti-inflammatory IL-22 production and IL-22-secreting $NKp46^+$ cells. Taken together, it suggests that vitamin C represents a protective effect on DSS-induced colitis by regulating the production of cytokine and the induction of inflammation.

Keywords: Inflammatory bowel disease (IBD), Vitamin C, gulo (-/-) mice , NKp46+cell

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The Regulation of the Pathogenesis of Pancreatic Cancer, Effect of IL-22 and α-Enolase on Human Pancreatic Cancer Cell Line, Panc1

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IL-22 is a member of IL-10 family, produced by activated DC, T cells, Th17 cells and NK cells. Binding of IL-22 to it's receptors IL22R1 and IL-10R2 influences variety of immune responses. The receptors are found in non-immune cells such as liver, colon, skin and pancreas. Also the tumors originated from these sites have over-expressed IL-22R. Although acinal population of Pancreas has the highest expression of IL22R, regulation of IL-22 and activation of IL-22 receptor in the pancreatic cancer are poorly understood. In pancreatic cancer cell line, Panc1, introduction of rIL-22 suppressed cell proliferation and induces G2/M phase cell cycle arrest. However IL-22 influenced cytokine TGH-β was increased upon rIL-22 treatment. On the other hand, pro-inflammatory cytokine IL-22 played dual role of anti-tumor effect as well as pro-tumor effect. We have also found the involvement of α-Enolase in the regulation of IL-22 and IL-22 activation in Panc1 cell line. α-Enolase is known to be highly expressed in cell surfaces of inflammation and cancer and according to clinical research, α-Enolase is up-regulated pancreatic cancer patients. Thus it can be suggested that the regulation of IL-22 in Panc1 is under the influence of α-Enolase and the mechanisms involved need to be further investigated.

Keywords: IL-22, NK cell, α-Enolase, Panc1

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Preventive Effect of GV1001 on Gemcitabine-induced Pancreatic Cancer Cachexia

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GV1001 derived from the human telomerase reverse transcriptase (hTERT) sequence is a peptide vaccine for the treatment of pancreatic cancer. The preclinical data clearly showed immunogenicity of GV1001 in patients with pancreatic cancer supported by the synergy of gemcitabine with cancer vaccines and the other positive immunomodulatory effects of gemcitabine. Even though it is reported that GV1001 may block weight loss of cancer patients and improve general condition after treatment of gemcitabine, but there are insufficient evidences so far. For this reason, we evaluate the preventive effect of GV1001 on gemcitabine-induced weight loss in xenograft animal model. There was definite weight loss of tumor-bearing mice by the treatment of gemcitabine. However, it was recovered by the treatment of gemcitabine with GV1001. Interestingly, we found that leptin, the satiety hormone, is decreased in tumor-bearing mice by treatment of GV1001, but ghrelin, the hunger hormone, is increased. In addition, we compared skeletal muscle integrity between tumor-bearing mice upon the treatment of gemcitabine with or without GV1001. When tumor-bearing mice were treated with gemcitabine only, the decrease of skeletal muscle integrity was observed. The decrease is ameliorated by the co-treatment of GV1001. Taken together, GV1001 effectively prevents the loss of weight and skeletal muscle integrity by gemcitabine.

Keywords: GV1001, Gemcitabine, Cachexia

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

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

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

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Anti-inflammatory Effect of Alloferon on Ovalbumin-induced Asthma

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Asthma is a well-known inflammatory lung disease; however, the specific underlying mechanism is largely unknown. We previously demonstrated that alloferon effectively downregulates pulmonary inflammation. In this study, we examined whether alloferon has a therapeutic effect on asthma. Alloferon remarkably decreased the number of eosinophils, macrophages, and neutrophils in the bronchoalveolar lavage fluid (BALF) from ovalbumin (OVA)-induced asthma mice. It was synergistically decreased with 2.5 mg/kg prednisolone (PDA). Inflammatory cell infiltration around the bronchioles and in the alveolus of OVA-induced asthma mice was effectively prevented by alloferon alone and combined treatment with alloferon and PDS. The production of IL-5 and IL-17 was decreased by alloferon alone and combined treatment with alloferon and PDS. There was no change the level of total immunoglobulin (Ig) following alloferon administration; however, total Ig was decreased by PDS. IgG2a levels were not changed by either alloferon alone or alloferon in combination with PDS. However, the levels of OVA-specific IgG1 and IgE were decreased by alloferon and PDS. In conclusion, our results suggest that a combination of alloferon and prednisolone is effective for the treatment of asthma, as it prevents inflammatory cell infiltration via the downregulation of IL-5 and IL-17 production and decreases IgG1 and IgE production via the suppression of T helper type 2 immune response.

Keywords: Alloferon; Asthma; Interleukin-17

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The Role and Regulation Mechanism of HOXB5 in human Breaset cancer cells

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HOX genes are transcription factors that play important roles in body patterning and cell fate specification during normal development. Among of these, HOXB5, is involved in a variety of developmental processes, particularly during the enteric nervous system (ENS) development, and thus, abnormalities in HOXB5 function during embryo stages lead to Hirschsprung's disease. Importantly, many HOX genes, including HOXB5, are expressed not only during embryogenesis but also in adults and are dysregulated in various cancers. In a previous study, we found aberrant overexpression of HOXB5 in breast cancer tissues and cell lines and demonstrated that HOXB5 is important in the regulation of cell proliferation in breast cancer cells. Also, HOXB5 induces invasive potential through epithelial-mesenchymal transition (EMT). The relationship between HOXB5 and phenotypic changes in MCF7 breast cancer cells has been studied, however, HOXB5 functions as a transcription factor and its involvement in signaling pathways remain unclear. In this study, we selected putative downstream target genes of HOXB5, such as interleukin (IL)-6, Snail2 and epidermal growth factor receptor (EGFR) by PCR array analysis. These genes have been reported to be involved in cacner progression, which is characterised by increased growth speed and invasiveness of the tumor cells. Here, we discovered that HOXB5 transcriptionally upregulates the promoter activity of these genes. Chromatin immunoprecipitation (ChIP) analysis to confirm direct binding of HOXB5 to the promoter region is now ongoing. Since we found that HOXB5 induces EGFR protein expression and SRC phosphorylation, we will further investigate signaling pathway components to understand the underlying molecular mechanisms of HOXB5 action in breast cancer.

Keywords: Breast cancer, HOXB5

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The crucial role of IL-22 and its receptor on TARC production and T cell migration by HDM extract

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House dust mite (HDM) is known as one of the factors that causes atopic dermatitis (AD). Interleukin (IL)-22 and thymus and activation regulated chemokine (TARC) are related to skin inflammatory disease and highly expressed in AD lesions. However, the effects of HDM on IL-22 production in T cells and on TARC production and IL-22Rα receptor expression in keratinocytes are unknown. To identify the role of HDM in keratinocytes and T cells, we investigated IL-22Rα expression and TARC production in the human keratinocyte cell line HaCaT and IL-22 production in T cells treated with HDM extract as well as their roles in HDM-induced skin inflammation. HDM extract not only increased IL-22Rα expression and TARC production in HaCaT but also enhanced IL-22, tumor necrosis factor (TNF)-α and interferon (IFN)-γ production in T cells. The HDM extract-induced IL-22 from T cells significantly increased the production of IL-1α, IL-6 and TARC in HaCaT cells. In addition, we found that TARC produced in HDM extract-treated HaCaT induced T cell recruitment. These results suggest that there is a direct involvement of HDM extract-induced IL-22 in TARC production and T cell migration. Taken together, TARC production in HaCaT through the interaction between IL-22 and IL-22Rα facilitates T cell migration. These data show one of the reasons for inflammation in the skin lesions of AD patients.

Keywords: Inflammation, House dust mite, Atopic dermatitis, Interleukin-22, Thymus and activation regulated chemokine

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Zinc Functions as Androgen Receptor Inhibitor to Suppress

Prostate Cancer Growth

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Background: Compared to normal human prostate, prostate cancers diminished level of zinc, lead to the progression from benign to malignant tumors. However, the role of zinc still remained unclear. This study goal is to clarify the ability of zinc supplementation to suppress prostate cancers (PCa) development.

Materials and methods: Several prostate cancer cell lines were grown, and applied to cell proliferation assay, Western blot, and reporter assay, treated with or without presence of Zinc chloride. In vivo study were further performed to support for in vitro studies by using syngeneic animals

Results: Prostate malignant cell lines were incubated with physiological does of zinc chloride exhibited remarkably inhibition of cell proliferation. Associating with this result, a reporter-mediated transactivation revealed a dramatic decrease of androgen expression and several androgen target proteins, such as PSA and p21, accordingly with zinc chloride treatment. We further showed that, incubation with zinc strikingly downregulated androgen receptor (AR) protein levels after 4 hours up to 24 hours in both human LNCaP and murine TRAMP C2 prostate cancer cell lines. We also demonstrated that peritoneal injection of zinc chloride dramatically reduced tumor growth in mice, which is bearing C2 subcutaneous tumors. Analysis from tumor tissues lysis revealed that there were a reduced of AR expression while increased apoptosis.

Conclusion: These results above demonstrated that the supplement of zinc chloride downregulated AR expression, suggesting that zinc may play a major role to prevent PCa growth. While AR functions as a major effector in prostate cancer development, zinc may be a considerable target for further prostate cancer treatment.

Keywords: zinc, prostate cancer, androgen receptor

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P105

Anti-angiogenic activities of zingerone in tumor progression

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Ginger is widely used as a natural treatment for numerous diseases. Zingerone, which is a phenolic compound isolated from ginger, has varied pharmacological activities, including anti-oxidant, anti-inflammatory, and antidiabetic properties. Because tumor angiogenesis is an essential step for tumor progression, suppression of angiogenesis is a good strategy for tumor therapeutics. In this study, we investigated the anti-tumor and anti-angiogenic effects of zingerone in a mouse tumor model and explored the related molecular mechanism. Zingerone significantly inhibited the angiogenic activities of endothelial cells by both direct and indirect manners. Moreover, zingerone suppressed the function of MMP-2 and MMP-9 through the JNK signaling pathway. In conclusion, we suggest that zingerone may be a potential therapeutic drug for human cancers.

Keywords: Zingerone; Angiogenesis; Cancer; Matrix Metalloproteinases; JNK

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P106

Metformin enhances cisplatin-induced cytotoxicity through down-regulating of Rad51 expression in breast cancer cellsMetformin enhances cisplatin-induced cytotoxicity through down-regulating of Rad51 expression in breast cancer cells

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Metformin has been used as first-line treatment in patients with type 2 diabetes, and is reported to reduce cancer risk and progression in a number of cancers, including breast cancer. Cisplatin remains the main drug for treating advanced triple breast cancer. However, drug resistance often develops through several mechanisms during the treatment course, including one mechanism mediated by the increase of DNA repair, related to the upregulation of DNA recombination. The aim of this study was to investigate whether metformin sensitizes triple breast cancer cells to cisplatin and the sensitivity mechanism. This study demonstrated that cisplatin increases the expression of RAD51, DNA homologous recombinase, whereas metformin decreased RAD51 protein and RNA levels. The treatment of MDA-MB-231 breast cancer cells with the proteasome inhibitor MG132 blocks metformin-mediated downregulation of RAD51. Furthermore, metformin increases the ubiquitination of RAD51 in a time dependent manner, suggesting that metformin decreases the expression of RAD51 by ubiquitination. Cisplatin increased the phosphorylation of ERK1/2, whereas metformin decreases the phosphorylation of ERK1/2. In addition, the inhibition of ERK1/2 blocks cisplatin-mediate expression of RAD51, suggesting that cisplatin increases the expression of RAD51 by activation of ERK1/2. Furthermore, we found that metformin increases cisplatin-induced phosphorylation of gamma-H2AX, a hallmark of DNA double-strand breaks, suggesting that metformin can increase the sensitivity of MDA-MB-231 cells to cisplatin through up-regulation of DNA-strand breaks. Knock-down of RAD51 enhances the cisplatin-induced breast cancer cell invasion and migration. These results suggest that metformin increase the sensitivity of cisplatin and prevent cisplatin –resistance.

Keywords: Metformin, Cisplatin, Triple-negative breast cancer cells. Rad51

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P107

Comparison of Characteristics of Three Kind of Mesenchymal Stem Cells

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Mesenchymal stem cells (MSCs) are multipotent cells that can differentiate into mesodermal lineage, such as adipocytes, osteoblasts, and chondrocytes. In addition, MSCs have been reported to be immunomodulatory, and be immunoprivileged owing to the lack of HLA-DR. These characteristics enable these cells, most frequently bone marrow-derived MSCs (BM-MSCs) since now, to be considered as a therapeutic modality in inflammatory diseases.

Different types of MSCs were derived from different places in adult body. Among them, umbilical cord-derived MSCs (UC-MSCs), periodontal ligament stem cells (PDLSCs), and adipose tissue-derived MSCs (Ad-MSCs) have been taken a lot of attention as possible clinical alternatives for BM-MSCs because of their better accessibility.

In this study, we compared the characteristics of the three kinds of MSCs comprising immunophenotypes, pluripotency, and immunologic properties. Evaluated parameters are as follows; 1) positive surface expression of CD73, CD90, CD105 and negative expression of CD34, CD45, HLA-DR, 2) differentiation into mesodermal cell lineages, 3) suppression of *in vitro* T cell proliferation, 4) expression of immunosuppressive molecules after activation, 5) used mechanisms for T cell inhibition using indoleamine 2,3-dioxygenase and cyclooxygenase 2. The MSCs did not reveal any remarkable differences in all aspects of these parameters. However, UC-MSCs proliferated most rapidly among the three MSCs, approximately 2.7 times to Ad-MSCs and 1.4 times to PDLSCs on they 6 when the proliferation of UC-MSCs reached its maximum. This should be an advantage in the mass use of the cells in clinical fields.

Considering their proliferating capacity and more easily obtainability, UC-MSCs are thought to be more desirable for practical purpose than the other two MSCs.

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Keywords: Immunomodulatory property, Differentiation, Mesenchymal stem cells

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P108

Expression And Functions Of MED30 in Hepatocellular Carcinoma

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Hepatocellular carcinoma(HCC) is the third leading cause of death in the world. Also, its late diagnosis and chemoresistance increase death rate. Hence, it is necessary to find new diagnostic and therapeutic targets in HCC. MED30 is one of the Mediator complex subunits, which connects between the Mediator complex and RNA Polymerase II. However, the expression and functions of MED30 in cancer have been rarely understood. Therefore, we tried to figure out the expression and functions of MED30 in HCC. The analysis of TCGA database showed MED30 was frequently amplified in HCC. Moreover, immunohistochemistry also showed its overexpression in HCC tissues compared to the surrounding normal liver tissue. To examine roles of MED30, we knock-downed MED30 in several HCC cell lines using siRNA. MED30 Knock-down decreased proliferation in Hep3B, HepG2 and SK-Hep1 cells, and decreased migration rate in SK-Hep1 cells. For gain-of-function study, we overexpressed MED30 in SK-Hep1 and HepG2 cells using cDNA and its overexpression showed increased proliferation of SK-Hep1 and migration of HepG2 cells. Unexpectedly, MED30 overexpression decreased proliferation in HepG2 cells and migration in SK-Hep1 cells. These results suggest roles of MED30 during the progress of HCC might be context-dependent. To understand complex roles of MED30, further studies are in progress.

Keywords: Hepatocellular Carcinoma Migration Proliferation MED30

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P109

Prognostic Value of TERT-CLPTM1 locus polymorphism (rs401681) in Hepatocellular Carcinoma

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Genetic variants on telomere-maintaining gene complex have been related to various cancers. Telomere length was also known to be associated with carcinogenesis. In present study, SNP in TERT-CLPTM1 locus and telomere length were studied in hepatocellular carcinoma (HCC). TERT-CLPTM1 SNP (rs401681) and telomere length were analyzed 156 patients by using sequencing and real-time PCR, respectively. SNP results showed that 80 (51.3%) were homozygous for CC, 62 (39.7%) heterozygous (CT) and 14 (9.0%) homozygous for TT. CC allele was associated with advanced T stage ($p = 0.003$) and UICC staging($p = 0.008$). Average of telomere length in HCC was 3.97 ± 1.38, and it was not significantly different according to the type of rs401681. Shortening of telomere length was found frequently in younger (66.3%) than older (51.4%) without statistical significance ($p = 0.056$). However, it had a deep relationship with T stage. ($p = 0.048$). Additionally, we observed that rs401681 polymorphism was significantly associated with good prognosis. The median follow-up of patients for survival analysis was 75.1 months. Disease free survival of HCC patients with C/C genotype was significantly shorter than that of those with the C/T or T/T genotypes ($p = 0.006$). Multivariate analysis revealed that rs401681 CC genotype was an independent, significant prognostic factor (harzard ratio = 1.95; 95% confidence interval: 1.21-3.14; $p = 0.006$). Our data suggest that rs401681 polymorphism might predict the clinical outcomes of HCC patients, independently telomere length.

Keywords: Hepatocellular Carcinoma, Telomere, TERT-CLPTM1, Polymorphism

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The Roles Of MED30 In Pancreatic Cancer Cells

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Pancreatic cancer is the fourth leading cause of cancer-related death with highly chemoresistant. Rapid progression and poor prognosis of pancreatic cancer shorten the survival rate after the diagnosis. New diagnosis and therapeutic target need to be developed to improve survival rate. MED30 was described as an essential member of mediator complex which related with transcription. Frequent amplification of MED30 were observed in pancreatic cancer patients of TCGA database. Moreover, the over-expression of MED30 was also revealed in the immunohistochemistry of pancreatic cancer patient tissues. To reveal function roles of MED30 during the progression of pancreatic cancer, we overexpressed or knock-downed MED30 in using cDNA or siRNA. MED30 overexpression increased proliferation, migration, and invasion of pancreatic cancer cells. In contrast, MED30 knock-down showed opposite effects. Furthermore MED30 knock-down inhibited tumorigenicity in SCID mice significantly. In conclusion, MED30 has pathophysiological roles in proliferation, migration, and invasion of pancreatic cancer cells, Thus the MED30 could be a potent diagnosis and therapeutic target in pancreatic cancer.

Keywords: Pancreatic Cancer Proliferation Migration MED30

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The Regulation of NK cell Susceptibility to Lung Cancer Cells by Celecoxib Treatment

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Lung cancer is one of most common cancers in the world. Many patients of lung cancer result in higher rate of death every year more than patients of colon, breast, prostate cancer combined. Celecoxib is a selective inhibitor of cyclooxygenase-2 (COX-2) that have been shown to affect cell growth and apoptosis on various cancer cells. In this study, we investigated that celecoxib increased expression of ULBP-1 on lung cancer cell lines, A549 and H460, in time- and dose-dependent manners. ULBP-1 is one of the ligand for natural-killer group 2 member D (NKG2D) that is expressed on the surface of NK cells, providing stimulatory signals for activation of NK cells. Also, the expression of other NKG2D ligands including ULBP-2, ULBP-3, MICA and MICB was changed on A549 and H460 after treatment with celecoxib. We observed that SP600125, inhibitor of JNK pathway, blocked expression of ULBP-1 after celecoxib treatment on lung cancer cell lines. In addition, when celecoxib was treated on lung cancer cells, NK cell-mediated lysis was altered. Taken together, celecoxib can regulate NKG2D ligands and modulate the susceptibility to NK cell-mediated lysis of lung cancer cells.

Keywords: Celecoxib, NK cell, NKG2D, Lung cancer

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CD99-derived peptidomimetic Inhibits Tumor Metastasis By Suppressing Epidermal Growth Factor Receptor Dimerization and Activation

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EGFR is known to be overexpressed in 14-91% of breast cancer patients. Epidermal growth factor receptor (EGFR) is a 170 kDa trasmembrane protein, activation of which results in its dimerization and tyrosine autophosphorylation and subsequent recruitment

of downstream signaling molecules that mediate cell proliferation, regeneration, migration, endocytosis and clustering. CD99 protein, a 32 kDa type I transmembrane glycoprotein, is known to be expressed in most tissue of the human body. It plays roles in the regulation of receptor activation, cell adhesion and migration. Dimerization and clustering are the important procedures in receptor tyrosine kinase activation of signaling transduction, which are modulated by actin cytoskeleton remodeling. However, molecular mechanisms underlying dimerization and clustering of receptor molecules are still unclarified. In this study, we investigated whether CD99 inhibits tumor metastasis by suppressing EGFR activation in breast cancer cells and its underlying mechanism. Our study presents that EGF-derived YAC tripeptide induced the physical interaction among EGFR-Grb2-SOS-FAK-cSrc complex, which leads to FAK phosphorylation. In addition, YAC tripeptide enhanced an interaction of RhoA, Rac1 and cdc42 with FAK. Dominant-negative RhoA, Rac1 or cdc42 abrogated YAC tripeptide-induced endocytosis of EGFR. Moreover, it induced FAK-mediated activation of Rac1-Wave2-Arp2 and RhoA-Rock2-Ezrin axis. A CD99-derived peptidomimetic attenuated YAC tripeptide-induced EGFR signaling through FAK dephosphorylation via PTPN12. However, transfection of constitutively active RhoA or Rac1 abrogated the inhibitory effect of CD99-derived peptidomimetic on the EGFR clustering, suggesting that CD99 could inhibit EGFR-FAK-RhoA or Rac1-mediated actin cytoskeleton remodeling and tumor metastasis. In conclusion, these results suggest that CD99-derived peptidomimetics may prevent tumor metastasis by inhibiting EGFR activation through PTPN12-mediated suppression of Rac1-Wave2-Arp2 and RhoA-Rock2-Ezrin signaling axis.

Keywords: CD99, EGFR clustering, actin cytoskeleton remodelining, FAK, PTPN12

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Effects of Oriental Medicine Kyung-Ok-Ko on Uterine Abnormality in Hyperandrogenized Rats

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A traditional herbal prescription Kyung-Ok-Ko (KOK), composed of *Rehmannia glutinosa* Liboschitz var. *purpurae, Lycium chinense, Aquilaria agallocha, Poria cocos, Panax ginseng*, and honey, has been widely used in Oriental medicine as an invigorant for age-related diseases, such as amnesia and stroke. However, the beneficial value of KOK on uterine dysfunction related to hyperandrogenism is largely unknown. We investigated the effect of KOK (2.0 g/kg/day, per os) on endometrial abnormalities in a dehydroepiandrosterone (DHEA, subcutaneous)-induced polycystic ovary syndrome (PCOS) rat model. Preadministration of KOK significantly ($p<0.05$) decreased the elevated body weight, uterus weight, and endometrial thickness by PCOS induction, corresponding to reduced apoptosis and the infiltration of immune cells ($CD4^+$ T cells, CD8D T cells, and macrophages) in the endometrium. These results were associated with reduced mRNA expression of interleukin (IL)-1β, IL-6, IL-8, and matrix metalloproteinase-3 and increased mRNA expression of IGF-β1, transforming growth factor (TGF)-β, TGF-β1, and vascular endothelial growth factor in the uterus after DHEA injection. These multiple effects of KOK may synergistically prevent the development of endometrial abnormalities in DHEA-induced hyperandrogenism via anti-inflammatory action, indicating that KOK has preventive and therapeutic potential for suppressing PCOS.

Keywords: Kyung-Ok-Ko (KOK), Polycystic ovary syndrome (PCOS)

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P114

ABT-263 (Navitoclax) induces cell death in MDA-MB-231 but not in MCF-7 selectively and synergistically induces apoptosis with RAD001 (Everolimus) in MCF-7 human breast cancer cells.

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ABT-263 (Navitoclax), which is a Bcl-2 family protein inhibitor, was tested as an anti-cancer agent in clinic. However, the clinical trials were very limited and the mechanism of action was not fully understood. In present study Navitoclax showed dramatic apoptotic effects in MDA-MB-231 breast cancer cells time- and dose- dependently. Another type of breast cancer cells, MCF-7 has resistant effect to Navitoclax differently. More specially, Bcl-2 family proteins including Bcl-2, Bcl-w, Bcl-xL and Mcl-1 have been shown no changes with treatment of Navitoclax in both breast cancer cells, MDA-MB-231 and MCF-7. But RIF was decreased only in MDA-MB-231 dose-dependently. RIF is a member of ROI and which is controlled by mTOR. The combination treatment to MCF-7 cells with Navitoclax and Everolimus (mTOR inhibitor) and using siRNA-mediated mTOR knockdown showed apoptotic effects by control of RIF stability. Together, these findings suggest that Navitoclax induces apoptosis in MDA-MB-231 breast cancer cells through the inhibition of RIF and combi-treatment with Everolimus make synergic apoptotic effect in MCF-7 by RIF stability.

Keywords: ABT-263, MCF-7, Breast cancer, Cell death

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P115

Combined treatment with vitamin C and sulindac synergistically induces p53- and ROS-dependent apoptosis in human colon cancer cells

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Sulindac has anti-neoplastic properties against colorectal cancers; however, its use as a chemopreventive agent has been limited due to toxicity and efficacy concerns. Combinatorial treatment of colorectal cancers has been attempted to maximize anti-cancer efficacy with minimal side effects by administrating NSAIDs in combination with other inhibitory compounds or drugs such as l-ascorbic acid (vitamin C), which is known to exhibit cytotoxicity towards various cancer cells at high concentrations. In this study, we evaluated a combinatorial strategy utilizing sulindac and vitamin C. The death of HCT116 cells upon combination therapy occurred via a p53-mediated mechanism. The combination therapeutic resistance developed in isogenic p53 null HCT116 cells and siRNA-mediated p53 knockdown HCT116 cells, but the exogenous expression of p53 in p53 null isogenic cells resulted in the induction of cell death. In addition, we investigated an increased level of intracellular ROS (reactive oxygen species), which was preceded by p53 activation. The expression level of PUMA (p53-upregulated modulator of apoptosis), but not Bim, was significantly increased in HCT116 cells in response to the combination treatment. Taken together, our results demonstrate that combination therapy with sulindac and vitamin C could be a novel anti-cancer therapeutic strategy for p53 wild type colon cancers.

Keywords: Colon cancer, ROS, Sulindac, Vitamin C, p53

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P116

SAHA, an HDAC inhibitor, overcomes erlotinib resistance in human pancreatic cancer cells by modulating E-cadherin.

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Pancreatic cancer is one of the most lethal cancers and remains a major unsolved health problem. Less than 20 % of patients are surgical candidates, and the median survival for non-resected patients is approximately 3 to 4 months. Despite the existence of many conventional cancer therapies, few targeted therapies have been developed for pancreatic cancer. Combination therapy using erlotinib and gemcitabine is an approved standard chemotherapy for advanced pancreatic cancer, but it has marginal therapeutic benefit. To try to improve the therapeutic outlook, we studied the efficacy of another combination treatment and the relevance to E-cadherin in human pancreatic cancer cells. We treated two human pancreatic cancer cell lines with the histone deacetylase inhibitor (HDACi) SAHA. Interestingly, in these Panc-1 and Capan1 cells, we observed that the expression levels of E-cadherin and phosphorylated EGFR were gradually upregulated after treatment with SAHA. Furthermore, these cells underwent induced cell death after exposure to the combination treatment of SAHA and erlotinib. In Panc-1 cells, overexpression of E-cadherin activated the phosphorylation of EGFR and increased the cell sensitivity to erlotinib. In Capan1 cells, knocking down E-cadherin decreased the expression of phosphorylated EGFR, and these cells did not respond to erlotinib. Therefore, we demonstrated the efficacy of the combined treatment with SAHA and erlotinib in human pancreatic cancer cells, and we determined that the increased efficacy was due, at least in part, to the effects of SAHA on the expression of E-cadherin. Our studies suggest that E-cadherin may be a potent biomarker for pancreatic cancer.

Keywords: Cell death, E-cadherin; Erlotinib, Human pancreatic cancer cells, SAHA

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P117

Interleukin-7 receptor contributes to increase of wound-healing migration as well as Invasion in the prostate cancer

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IL-7Rα plays a critical role in the development and maintenance of immune cells but no studies suggest a verification of a key factor of bone metastasis. To investigate the role of IL-7Rα on bone metastases from prostate cancer, we evaluate the expression of IL-7Rα, wound healing migration, invasion, and zymography on the prostate cancer cells after IL-7 treatment. As results, the expression of IL-7Rα in PC-3 cells was higher than in other metastatic cell lines. Not only wound-healing but also invasion was increased after IL-7 treatment at the PC-3 cells. And, MMP2, MMP9 was also increased in PC-3 cells upon IL-7 stimulation. Moreover, the invasiveness of cells over-expressing IL-7Rα (PC-3$^{IL\text{-}7R\alpha\ OE}$) was significantly increased compared to control cells. Furthermore, in order to elucidate the role of IL-7Rα in bone metastasis, PC-3$^{IL\text{-}7R\alpha\ OE}$ cells were administered into NSG mouse by intracardiac injection. Metastasis into the bone was markedly increased when PC-3$^{IL\text{-}7R\alpha\ OE}$ were injected compared with control vector expressed PC-3 cells. In conclusion, migration and invasion were increase in PC-3 cells after IL-7 treatment. Metastasis into bone was enhanced by PC-3$^{IL\text{-}7R\alpha\ OE}$, suggesting IL-7Rα might be involved in migration as well as invasion in the bone metastatic prostate cancer.

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Keywords: Interleukin-7 receptor, Invasion, Migration, Prostate cancer, Wound-healing

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Erlotinib leads to differential cell death pathway on 2D and 3D culture system in Non-small cell lung cancer cells

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Non-small cell lung cancer (NSCLC) patients with epidermal growth factor receptor (EGFR) mutation have been shown to good responsiveness to Erlotinib, a receptor tyrosine kinase inhibitor for EGFR. Also, the cell death mechanisms of Erlotinib have been well defined in vitro cell culture system. However, the cell death pathway associated with 3D culture system by Erlotinib was poorly understood in NSCLC cells. In this study, we investigated that Erlotinib induced the cell death both 3D and 2D culture system, but the amount of apoptotic cell death is even better in 3D culture system than 2D that. So we studied to discriminate cell death pathway by Erlotinib both on 2D and 3D culture system in NSCLC cells. As expected, treatment with Erlotinib to 2D and 3D culture system induced a typical caspase-dependent apoptosis. But, interestingly, caspase 8 which is a main initiator caspase in receptor-mediated apoptosis was activated only 3D culture condition but not 2D culture by Erlotinib. These cell deaths in 3D were mediated through upregulation of TNF-related apoptosis-inducing ligand (TRAIL) expression. Furthermore, TRAIL-induced cell death increased the expression of c-Jun N-terminal kinase (JNK) and treatment of SP600125, a chemical inhibitor for JNK, significantly inhibited Erlotinib-induced cell death only in 3D culture. These results suggested that Erlotinib differentially induces apoptotic cell death through TRAIL-JNK pathway in 3D culture system and mitochondria-mediated apoptotic cell death in 2D culture system.

Keywords: Erlotinib, TRAIL, JNK, NSCLC, apoptosis

P119

Tumor associated macrophage provide the survival resistance of tumor cells to hypoxic micro-environmental condition through IL-6 receptor-mediated signals

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In this study, the established tumor tissues showed a dense infiltration of CD206+ TAM at the junctions between the normoxic and hypoxic regions, which indicates a role of M2 phenotype TAM in survival adaptation of tumor cells preparing for an impending hypoxic injury before changes in oxygen availability. Coculture of MCF-7 breast cancer cells and M2 phenotype TAM generated from THP-1 cells significantly decreased the rate of tumor cells undergoing cell death in cultures exposed to hypoxia. The acquisition of survival resistance was attributed to increased IL-6 production by M2 TAM and increased expression of IL-6Rα and gp130 in MCF-7 cells in the coculture system. MCF-7 cells cocultured with M2 TAM showed activated JAK1/STAT3 and Raf/MEK/JNK pathways contributing to tyrosine and serine phophorylation of STAT3, respectively. However, only tyrosine phosphorylated STAT3 was detected in the nucleus, which induced upregulation of Bcl-2 and downregulation of Bax and Bak. Finally, knockdown of IL-6R by small interfering RNA significantly counteracted coculture-induced signals and completely abolished the survival resistance to hypoxic injury. Thus, we present evidence for the role of M2 phenotype TAM in IL-6 receptor-mediated signals, particularly tyrosine phosphorylation of STAT3, responsible for the prosurvival adaptation of tumor cells to hypoxia.

Keywords: Hypoxia, TAM, IL-6, Cancer

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P120

Altered Response to Radiaton Treatment in Gefitinib-Resistant Non-Small Cell Lung Carcinoma Cells

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Gefitinib is an epidermal growth factor receptor (EGFR) inhibitor which has shown a substantial clinical benefit in non-small cell lung cancer (NSCLC). Many NSCLC patients with brain metastasis who already got several anti-cancer drug treatment, for instance gefitinib (even though gefitinib is very effective in controlling the NSCLC), have different response to the radiation treatment. Here, we try to elucidate altered response for radiation in gefitinib-resistant cells. For this, we examined the radiation response of three gefitinib-resistance cell lines (PC9-GR1, PC9-GR2 and PC9-GR3) and compared their response with that of NSCLC cell line, PC9. We first analyzed the radiation-induced DNA damage using comet assay. The result showed that DNA damage was increased in gefitinib-resistance cell lines compared with PC9. Also, there are more H2AX phosphorylation in gefitinib-resistance cell lines compared with PC9. When we examined apoptosis after radiation treatment using Annexin V assay, gefitinib-resistance cell lines shows more apoptosis than PC9. Furthermore, Wound healing assay showed that the healing rate of gefitinib-resistance cell lines was significantly lower than that of PC9. Taken together, these data indicate that gefitinib-resistant cell lines are more sensitive to radiation as compared to PC9. For further study, we will find out the precise mechanism of gefitinib-resistance that modulates radiation treatment effect.

Keywords: Cancer Non-Small Cell Lung Carcinoma Radiation Gefitinib

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Molecular Study Of Ancient Human DNAs From The Largest Tomb And Its 10 Satellite Tombs Of Elite Xiongnu Cemetery In Mongolia

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The population of Xiongnu Empire are not one simple ethnicity, because the Empire governed a vast territory with various normadic races, for several years. To study the genetic evidences of the human remains from the largest tomb and its 10 satellite tombs of elite Xiongnu cemetery in Mongolia, we have analyzed the mitochondrial haplogroups and Y-chromosomal including autosomal short tandem repeats (STRs) from 10 human skeletons of 2,000 years ago at Duurlig Nars. We are still trying to analyze paternally transmitted Y-haplogroups to the subclade level. We have also determined maternally inherited haplogroups by identifying the polymorphisms of HV1 (hypervariable region 1), HV2, and several coding regions of mitochondrial DNA (mtDNA). Kinship analysis of the ancient 10 human skeletons with autosomal STR from from the largest tomb and its 10 satellite tombs of elite Xiongnu cemetery in Mongolia could help gain some insight into the Xiongnu society.

Keywords: Ancient Human Bone DNA Xiongnu

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P122

PARP1 Contributes To Oxidative Stress Through SIRT3 Downregulation During Cisplatin Nephrotoxicity

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Enhanced oxidative stress is a hallmark of cisplatin nephrotoxicity, and PARP1 inhibition attenuates oxidative stress during cisplatin nephrotoxicity. However, the precise mechanisms remain elusive. Here, using an in vitro model of cisplatin-induced injury to human kidney proximal tubular cells, we demonstrated that the protective effect of PARP1 inhibition on oxidative stress is associated with sirtuin 3 (SIRT3) activation. Exposure of cells to 400 μM cisplatin for 8 hours caused a decrease in the activity and expression of manganese superoxide dismutase (MnSOD), catalase, glutathione peroxidase (GPX), and SIRT3; and an increase in lysine acetylation of these antioxidant enzymes. However, treatment with 1 μM PJ34 hydrochloride, a potent PARP1 inhibitor, restored the activity and/or expression of these antioxidant enzymes, decreased lysine acetylation of these enzymes, and improved SIRT3 expression and activity in cisplatin-injured cells. On performing a transfection with SIRT3 double nickase plasmids, SIRT3-deficient cells treated with cisplatin did not show the ameliorable effect of PARP1 inhibition on lysine acetylation and activity of antioxidant enzymes, including MnSOD, catalase, and GPX. Furthermore, SIRT3 deficiency in cisplatin-injured cells prevented PARP1 inhibition-induced increase in the forkhead box O3a transcriptional activity, and upregulation of MnSOD and catalase. Finally, loss of SIRT3 in cisplatin-exposed cells removed the protective effect of PARP1 inhibition against oxidative stress, as represented by concentrations of lipid hydroperoxide and 8-hydroxy-2'-deoxyguanosine, and necrotic cell death, as represented by the percentage of propidium iodide-positively stained cells. Taken together, these results indicate that PARP1 inhibition protects kidney proximal tubular cells against oxidative stress through SIRT3 activation during cisplatin nephrotoxicity, and suggest that inhibiting PARP1 to enhance SIRT3 has the potential to be a strategy for improving outcomes in nephrotoxicity.

Keywords: Poly(ADP-ribose) polymerase Sirtuin 3 Cisplatin Nephrotoxicity Oxidative stress

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Drug X Alleviates HFD-induced Hepatic Steatosis Through Modulation of Hepatic STAMP2

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

Keywords: Nonalcoholic fatty liver diseasse(NAFLD), Hepatic steatosis, Insulin resistance, STAMP2

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Lipid Enlargement Through Fsp27 Protects Articular Chondrocyte Against High-Fat Diet Induced Apoptosis

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Osteoarthritis (OA) is a chronic degenerative joint disease that is characterized by the erosion of articular cartilage and osteophyte formation. Obesity is a major risk factor for the development of OA that is associated with a state of low-grade inflammation, and increased circulating adipokines and free fatty acids (FFA). In obese persons, body fluid level of FFAs is higher compared to control persons. However, it is not certain yet that elevated levels of FFA may contribute to OA pathogenesis. In the present study using cultured rat articular chondrocytes, we demonstrated that oleic acid at high dose exerts lipototoxicity through apoptosis. Importantly oleic acid at lower dose, did not exert lipotoxicity. Thus, we further examined the mechanism by which chondrocytes survives oleic acid-induced lipotoxicity. We observed that lipid droplet enlargement through Fsp27 confers articular chondrocytes antiapoptosis against oleic acid induced apoptosis. We further observed the signalling pathway leading to this antiapoptosis. Our study demonstrated that Fsp27 upregulated in the process of lipid droplet enlargement exerts antiapoptosis through sustaining the expression level of PKCK2. In vivo study using high fat diet-induced obesity C57BL/6 mouse model, we observed that the induction of osteoarthritis was accelerated in obesity mouse compared to the control. Noticeably, a PKCK2 augmenting droug cilostazol delayed the onset of osteoarthritis. Taken together, diet fat-associated osteoarthritic chondrocytes survives through PKCK/Fsp27 mediated lipid droplet enlargement. This antiapoptosis mechanism may be explanatory of that all obese persons does not suffer from osteoarthritis.

Keywords: Osteoarthritis, Cilostazol, High-Fat Diet, Apoptosis, PKCK2

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의과대학생들의 SNS 이용형태 분석 및 고찰

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대학생들은 여러 도전에 직면하여 다양한 스트레스 상황에 처하게 된다. 그중에서 특히 의과대학생들의 스트레스는 매우 높은 것으로 알려져 있다. 이러한 의과대학생들에게 스트레스를 해소하고 사회와 소통할 수 있게 해주는 통로 중 하나가 바로 SNS이다. 이에 우리는 의과대학 학생들의 SNS 이용 실태와 이용 행태를 분석하여 SNS 이용이 의과대학 학생들에게 어떠한 영향을 끼치는지 어떠한 역할을 하는지에 대하여 알아보고자 한다.
본과 1학년의 게시물의 내용을 분석한 결과, 지난 1년 동안 페이스북을 글을 게시한 학생은 51명 (58.6%)이었으며, 총 1,452개 (평균: 28.5개, 1-83)의 글을 게시하였다. 게시한 글을 내용에 따라 분석한 결과로는 생일을 축하하는 글(50%)이나 안부를 확인하는 게시물(18%)이 대부분을 차지하였다. 그다음으로 다른 사람이 올린 게시물을 공유하는 경우(10%)가 많았고, 여행을 가서 올린 게시물(6%)이 그 뒤를 따랐다. 그 외, 프로필 사진 업로드(3%), 학교생활(3%), 연애(2%) 혹은 가족(1%) 등이 있었다. 이를 성별과 나이를 나누어 살펴본 결과, 프로필 사진을 변경하는 횟수는 여학생(16회/17명)에서 남학생(18회/34명)에 비해 높게 나왔다($p = 0.003$). 이를 제외하고는 모든 항목에서 통계학적 유의성은 없었다. 한편 공유를 하는 게시글의 내용을 분석해본 결과, 대부분 유머(42%), 음식(15%), 음악(14%)에 관한 내용을 공유한 것으로 관찰되었다.
앞선 연구와 비슷하게 의과대학생들도 대부분 친교와 교제를 위해 SNS 활동을 하는 것으로 나타났다. 이전 연구에서는 SNS를 통해 업무, 학업, 생활 정보 등과 관련해 도움 주고받는 활동(71.5%)을 하는 것으로 관찰되었지만 의과대학생의 경우는 학업과 관련된 정보를 얻는 경우는 거의 없었다. 전체 게시글의 10%는 타인의 글을 공유하는 경우로 그 내용은 다양하게 나타났다. 대부분은 유머와 관련된 것으로 이러한 게시물을 통해서 의과대학생들은 스트레스를 해소하는 데 중요한 역할을 하는 것으로 생각된다. 의과대학생들의 SNS 이용형태 분석한 본 연구를 바탕으로, 의과대학생들이 향후 의사로서 나아가고 살아가는 데 있어 SNS가 좋은 작용을 할 수 있도록 더욱 많은 연구가 필요할 것으로 생각된다.

Keywords: SNS, 의과대학생, 인터넷, 스마트폰

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Effects of Oxidative Stress and Vitamin C on the Electrolyte Secretion in Mouse Tracheal Epithelium

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We investigated the changes in electrolyte secretion of tracheal epithelium in the mice chronically exposed to normobaric hyperoxia. Also, the effects of vitamin C and H2O2 on the epithelium were tested. In addition, electrolyte transport changes in tracheal epithelium of vitamin C deprived gulonolacton oxidase knockout (gulo[-/-]) mice were observed. The short circuit current (Isc) of the epithelium was measured using a flow-type Ussing chamber technique. Inhibition of Na+ absorption (ΔIsc,amil) was achieved through the luminal application of amiloride. cAMP-dependent Cl- secretion (ΔIsc,Fsk) was evoked by forskolin applied to the basolateral side. Ca2+-dependent Cl- secretion (ΔIsc,ATP) was evoked by luminally applied ATP. In the mice exposed to 98% PO2 for more than 24 hours, Isc,Fsk was markedly decreased while neither Isc,amil nor Isc,ATP was affected. However, a direct application of H2O2 (100 uM) induced a slight increase of Isc, which was considered not significant due to small amplitude. Also the application of ascorbate (100 uM) showed a small increase in the Isc of the airway epithelium. In gulo(-/-) mice, both ΔIsc,Fsk and ΔIsc,ATP decreased from three weeks after vitamin C deprivation, while both were unchanged with vitamin C supplementation. At the fourth week, tissue resistance and all electrolyte transport activities were decreased. These results suggest that the Cl- secretion mechanism of airway epithelium is susceptible to chronic oxidative stress, which indicates that supplementation of the antioxidant might be beneficial for the maintenance of airway surface liquid.

Keywords: Electrolyte secretion, vitamin C, H2O2, Tracheal Epithelium

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해부실습에서 3년간 '교대실습' 경험

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지난 수십 년 간 의학교육의 전반적인 흐름에 따라 해부학 교육에 투자되는 시간이 과거에 비해 많이 줄어들어 충분한 해부학 교육에 장애가 되고 있다. 또한 해부용 시신이 충분하지 않은 점, 해부 실습실의 물리적 환경 등은 특히 해부실습에 어려움을 주고 있다.

우리 대학에서는 시신 1구 당 학생 8명이 배정되어 실습을 하는데, 머리목 부위를 실습할 때는 비록 양쪽에 4명씩 배정되더라도 좁은 실습 부위의 특성 상 실습현장은 매우 붐빌 수밖에 없고, 일부 학생들은 의도치 않게 실습에서 배제되는 일이 발생한다. 이에 대한 방안으로 2014년부터 머리목 부위에 한해서 '교대실습'을 시행해 왔다.

교대실습(rotational dissection)이란 한 조 8명 중 4명 한 팀이 먼저 실습을 하고, 다음 실습에 다른 팀이 이어서 실습을 진행하는 방식을 말한다. 실습 시작 전에 앞서 실습 된 내용을 앞 팀이 뒤 팀에게 설명하는 시간을 15분 동안 가진 후 그날의 실습을 시작한다. 실습 순번이 아닌 팀 학생들은 주어진 시간을 자유롭게 활용하도록 하였다. 2016년에는 교대실습 범위를 팔다리 부위까지 확대하였고, 이에 대한 학생들의 반응과, 이러한 실습방식이 학생들의 실기시험과 필기시험 성적에 미치는 영향을 알아보았다.

교대실습 전반에 대한 반응은 2014~2016년에 각각 65.4%, 68.6%, 81.0% 학생이 긍정적인 반응을 보였다. 반면 부정적인 입장을 보인 학생은 17.7%, 16.6%, 9.5%로 해가 갈수록 학생들은 점차 긍정적이 되었다. 학생들은 여러 장점(*효율적, 집중도, 책임감, 관찰과 접근의 용이성, 직접 할 수 있어서. 능동적 참여 가능, 공간적 여유로움, 열외자가 생기지 않음, 보다 협력적, 휴식을 취할 수 있음*)을 언급하였으며, 반면에 단점으로는 대부분 직접 해보지 못한 부분에 대한 이해의 어려움과 파손된 부분을 보지 못했다는 아쉬움 등을 표현하였다. 앞 조의 실습 내용 설명에 대해서는 56.9%, 72.8%, 82.6%가 긍정적으로 반응하였다. 교차실습 추천 여부를 물었을 때 팔다리와 머리목 부위는 90% 가까운 학생이 교차실습에 찬성했으나, 몸통 부위에 대해서는 반반 가량으로 찬반이 엇갈렸다.

실제 성적에 미치는 영향을 알아보기 위해서 교대실습 전 3년간

(2011~2013년)과 이후 3년간(2014~2016년)의 실기와 필기성적을 비교하여 보았다. 교차실습 첫 해(2014년) 실습성적은 [100점 만점으로 환산 시] 66.0±13.9점으로 조사 기간 중 가장 낮았다. 그러나 이듬해에는 76.9±14.5점, 73.1±13.0점으로 다시 상승하였다. 제도 시행 후 필기성적은 84.9±11.3점(2015년)과 85.3±11.6점(2016년)으로 이전 성적에 비해 높은 성향을 보였다. 2016년에 새롭게 교대실습을 시행한 팔다리 부위 실기성적은 이전과 비교하여 별 차이가 없었지만 필기성적은 89.7±72.4점으로 비교대상인 4년간의 성적들에 비해 현저히 높았다.
학생들은 교대실습으로 인해서 직접 해부하지 않은 부분에 대한 학습 측면의 우려를 나타냈지만 실제 실습성적은 이전과 별 차이가 없었다. 반면 필기성적은 오히려 오른 경향을 보였다. 물론 교대실습만이 필기성적 상승의 유일한 이유라고 할 수는 없지만, 적어도 교대실습으로 인해서 필기나 실기 성적이 하락하지는 않았다고 볼 수 있다. 따라서 이 방법은 향후 해부실습의 새로운 한 형태로 활용될 수 있을 것으로 판단한다.

Keywords: rotational dissection, 해부실습, 해부학교육

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C/EBP homologous protein (CHOP) Deficiency Attenuates Renal Fibrosis in Unilateral Ureteral Obstructive Kidney

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CCAAT/enhancer-binding protein (C/EBP) homologous protein (CHOP) is an important transcription factor that contributes to endoplasmic reticulum (ER) stress-induced apoptosis which is associated with the pathogenesis of chronic kidney disease (CKD). Herein, we investigated the role of CHOP in the ER stress-induced renal cell apoptosis and fibrosis which is a typical characteristic of CKD. CHOP wild type ($CHOP^{+/+}$) mice and CHOP knock-out ($CHOP^{-/-}$) mice were performed unilateral ureteral obstruction (UUO), which results in apoptosis and fibrosis in the kidney. UUO increased the expression of binding immunoglobulin protein (BiP/GRP78, an ER stress protein) and CHOP in both $CHOP^{+/+}$ mice and $CHOP^{-/-}$ mice. UUO increased collagen deposition and the expression of α-smooth muscle actin (α-SMA), TGF-β, Ly6G, a marker of neutrophil, and F4/80, a marker of macrophage in both $CHOP^{+/+}$ mice and $CHOP^{-/-}$ mouse kidneys. These increases were lower in the $CHOP^{-/-}$ mouse than in the $CHOP^{+/+}$ mice. UUO increased the cleavage of procaspase-3, the induction of pro-apoptotic Bax protein and the number of apoptotic cells. In contrast, the expression levels of anti-apoptotic protein Bcl-2 decreased after UUO. These UUO-induced changes were less in $CHOP^{-/-}$ mice than in $CHOP^{+/+}$ mice. UUO increased the expressions of Beclin1, a regulator of autophagy, and LC3-II, a marker of autophagy. The expressions of Beclin1 and LC3-II after UUO in the $CHOP^{-/-}$ mouse kidney were greater than those in the $CHOP^{+/+}$ mouse kidney. Together, our data have demonstrated that ablation of CHOP attenuates the progression of fibrosis following UUO through mitigation of ER stress-mediated apoptosis and increase of ER stress-induced autophagy.

Keywords: C/EBP homologous protein, apoptosis, autophagy, unilateral ureteral obstruction, renal fibrosis

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Immunotherapy with Methyl gallate, an Inhibitor of Receptor Activator of Nuclear Factor KappaB Ligand-Mediated Osteoclast Differentiation and Inflammation-Induced Bone Loss

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Methyl gallate (MG) is a kind of phenolic acid mainly derived from

the bark of Acer barbinerve. In the field of herbal medicine, MG has been reported to exert remarkable biological actions, such as antitumor, oxidant, and microbial activities. In addition to these beneficial values, MG plays a therapeutic role in experimental arthritis induced by zymosan through acting as a negative regulator against inflammatory response. Despite of the description of the association between MG and skeletal system, there is no evidence for pharmacological effects of MG on major metabolic bone disorders, such as osteoporosis. In the current study, we showed that MG inhibited tartrate-resistant acid phosphatase (TRAP)-positive osteoclast formation from bone marrow macrophages (BMMs) and RAW 264.7 cells. This events arose from down-regulation of c-Fos and nuclear factor of activated T-cells c1 (NFATc1) expression without altering any early signaling pathways. Furthermore, MG suppressed filamentous actin (F-actin) ring formation, which, in turn, impaired bone resorption activity of mature osteoclasts. In agreement with these in vitro effects, at a dose of 20 mg kg^{-1} daily for 9 days, oral administration of MG recovered bone loss and its several micro-CT parameters in a mouse model under pathological condition in response to intraperitoneal injection of lipopolysaccharide (LPS). At this dose, MG also prevented degradation of trabecular bone matrix and osteoclast formation in bone tissues. Collectively, our findings strongly suggest the therapeutic potential of MG for treating pathologic bone loss in osteoporosis.

Keywords: Methyl gallate Osteoclast Osteoporosis

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Harpagoside Sppresses Iflammatory Responses and Bone Destruction in Collagen-Induced Arthritic Mice

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Harpagoside that is an iridoid glycoside constituent isolated from *harpagophytum procumbens* has been known to have various pharmacological effects on pain, arthritis, fever, ulcer, tumor, and inflammation. Specifically, harpagoside is proved to have therapeutic effects on degenerative arthritis and rheumatoid arthritis. However, the molecular mechanisms underlying the beneficial effects of harpagoside on arthritic diseases remain unclear. Thus, this study aimed at investigating the local and systemic effect of harpagoside on rheumatoid arthritis and its intracellular mechanisms by using type 2 collagen-induced arthritis (CIA) mice model. Mice model was divided into two groups, including prevention and therapy group to figure out the potential clinical application of harpagoside as an anti-arthritic agent. As a result, harpagoside reduced clinical score and incidence rate of CIA in both prevention and therapy group. Through histological staining of ankle joint, it was demonstrated that harpagoside locally ameliorated the destruction of bone and cartilage, as well as, the formation of pannus. In this process, harpagoside decreased the expression of inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin (IL)-6, and IL-1β in serum level of CIA mice. Also, harpagoside down-regulated the expression of receptor activator of nuclear factor κB ligand (RANKL), while up-regulated osteoprotegerin (OPG). Next, the effect of harpagoside on systemic bone loss induced by inflammatory arthritis was studied. In the results, harpagoside inhibited trabecular bone loss and tartrate-resistant acid phosphatase (TRAP)-positive osteoclast formation near the growth plate in both prevention and therapy group. This effect of harpagoside was reflected by the inhibitory effects of harpargoside on osteoclast differentiation and function *via* down-regulating not only two types of transcription factors, c-Fos and nuclear factor of activated T cells c1 (NFATc1), but matrix metalloproteinase (MMP)-1 and MMP-3, leading to suppression of osteoclast-specific marker genes, such as *TRAP, osteoclast associated receptor (OSCAR), calcitonin receptor (CTR)*, and *Cathepsin K*. Taken together, these findings show the beneficial effect of harpagoside on local symptoms and systemic bone erosion triggered by inflammatory arthritis and its underlying molecular mechanisms, suggesting that harpagoside is a potential preventive and therapeutic agent against various bone diseases, such as rheumatoid arthritis, osteoporosis, and periodontitis.

Keywords: Bone diseases, Harpagoside, Collagen induced arthritis model, Inflammation, Osteoclast

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P131

실내급배기 장치와 흡입배기형 특수해부실습대를 구축한 해부학실습실 리모델링과 해부학실습 중 유해가스 농도 측정

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육안해부학 실습중 인체는 유해가스인 고농도의 포름알데히드에 노출되고 있음은 잘 알려진 사실이다. 국내외에서는 산업 현장에서 근로자들의 건강을 보호할 목적으로 포름알데히드의 허용농도를 일정수준으로 규정하거나 권고하고 있으나 해부학실습실에 대한 실질적인 규제는 없는 상황으로 이에 대한 안전 대책 마련이 필요한 상황이다. 충북대학교 의과대학은 교육부로부터 2016년도 실험실 안전환경 선도모델 사업에 선정되어 실습실을 리모델링하였고, 실질적인 효과가 있는지를 조사하였다. 리모델링의 주요 내용은 해부실습대의 위쪽 표면에 가스를 흡입할 수 있는 작은 흡입구멍을 갖춘 특수해부실습대를 각 조마다 구비하였다. 특수해부실습대는 흡입한 유해가스를 실습대에 부착된 배기도관을 통하여 배기되도록 하였다. 한편, 실내에 전체적으로 퍼지게 되는 유해가스는 실습실 벽면의 아래 부분을 따라 10군데 설치된 실내 가스 흡입구를 통하여 밖으로 배기되도록 하였다. 또한, 천정에서는 새로운 공기가 아래쪽으로 유입될 수 있도록 18개의 급기구를 설치하였다. 해부학실습 중에 이를 모두 가동시키고, 바닥에서 1.5 m 높이 실내 5부위와 시신 바로 위에서 포름알데히드 농도를 측정하여 그 효과를 조사하였다. 포름알데히드 농도 측정은 이동식 측정기인 Formaldemeter로 측정하였다. 해부실습실 실내 5부위의 포름알데히드 평균농도는 0.31 ppm (0.45 mg/m^3)이었고, 0.21–0.41 ppm (0.26–0.51 mg/m^3)의 분포를 보였다. 시신 바로 위에서의 포름알데히드 평균농도는 0.45 ppm (0.56 mg/m^3)이었고, 0.31–0.64 ppm (0.39–0.80 mg/m^3)의 분포를 보였다. 포름알데히드의 TWA는 5시간 기준으로 해부실습실 실내가 평균 0.19 ppm (0.24 mg/m^3)이었고, 0.13–0.26 ppm의 분포를 보였다. 시신 바로 위의 TWA는 평균 0.28 ppm (0.35 mg/m^3)이었고, 0.19–0.40 ppm의 분포를 보였다. 배기형 해부테이블과 급배기 장치를 설치한 해부실습실은 고용노동부의 포름알데히드 농도 기준을 충족하였고, 대부분의 외국 기준도 충족하는 수준이었다. 이 연구는 국내 의과대학의 해부실습실 환경 개선 선도 모델의 첫 공기 질 평가로서 다른 의과대학 해부실습실의 공기 중 포름알데히드 농도의 기준값으로 활용될 뿐만 아니라 환경 개선 공사를 위한 설계 및 시공의 참고자료로 활용될 것으로 기대된다.

Keywords: 해부학실습실, 흡입배기형 해부실습대, 실내 급배기장치, 포름알데히드 농도

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Renal Mass Reduction Induces the Elongation of Kidney Primary Cilia Length via Increased Production of Reactive Oxygen Species

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Primary cilia play an important role for the maintenance of kidney functions. Recent reports have demonstrated that the length change of primary cilia is highly associated with various kidney diseases including polycystic kidney disease. Here, we investigated whether renal mass reduction affects primary cilia length and, if so, how the renal mass reduction regulates the length of primary cilia. Mice were subjected to either unilateral ureteral nephrectomy (UNx) or sham operations. Some mice were daily administered Mn(III) Tetrakis (1-methyl-4-pyridyl) porphyrin (MnTMPyP, an antioxidant) for 8 days beginning on 1 day after UNx. UNx increased primary cilium length in the kidney epithelial cells located in proximal tubules, distal tubules, Henle's loop, collecting ducts, and parietal cells of the remaining kidney. UNx induced hypertrophy of the remaining kidney with increased reactive oxygen species (ROS) levels. Treatment of MnTMPyP prevented the elongation of primary cilia in tubule cells of remaining kidneys. In addition, MnTMPyP reduced the hypertrophy of remaining kidneys with the inhibition of ROS production in the kidney. In the MDCK cells, a cultured tubular epithelial cell line cells, H_2O_2 induced the elongation of primary cilia. This elongation was prevented by MnTMPyP treatment. In conclusion, renal mass reduction results in the elongation of primary cilia via increased

production of ROS, suggesting that the elongation of primary cilia length may be necessary for the compensation and maintenance of renal function following a reduction in total renal mass

Keywords: Primary cilia, Nephrectomy, Reactive oxidative species

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Protective Effect of *Rhus verniciflua* Stokes Extract against Renal Ischemia-Reperfusion Injury by Enhancement of Nrf2-mediated Induction of Antioxidant Enzymes

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Ischemia-reperfusion injury (IRI) often causes acute kidney disease (AKD) by mediating oxidative stress-induced apoptosis of parenchymal cells. The extract of *Rhus verniciflua* Stokes (RVS) is used as a traditional herbal medicine offering anti-oxidative, anti-apoptotic, and anti-inflammatory properties. Herein, we investigated the therapeutic effect and the underlying mechanism of RVS on IRI-induced AKD by performing *in vivo* and *in vitro* experiments. These experiments encompassed surgical modeling of renal IRI in mice and chemical induction of hypoxia in a human renal tubular epithelial cell line HK-2. We demonstrated that the IRI-induced elevation of blood urea nitrogen, serum creatinine, and lactate dehydrogenase was significantly attenuated by intra-oral (*i.o.*) administration of RVS (20mg/kg/day) for 14 days before surgery. We observed that IRI surgery drastically induced histological damage and cellular apoptosis in renal parenchyma, both of which were attenuated by *i.o.* RVS pretreatment. Furthermore, in HK-2 cells incubated with 300 μM cobalt chloride to induce chemical hypoxia, we found that RVS treatment significantly inhibited cell death and production of reactive oxygen species (ROS). Interestingly, we observed that RVS treatment upregulated the level of endogenous antioxidant enzymes such as heme oxidase-1 and catalase, as well as their upstream regulator nuclear factor erythroid 2–related factor 2, in HK-2 cells. In combination, these results suggested that i.o. intake of RVS has a therapeutic effect on IRI-induced AKD and these effects are at least partly due to the attenuation of ROS production through upregulation of the antioxidant defense system inside renal tubular cells.

Keywords: Ischemia-reperfusion injury, Acute kidney disease, Rhus verniciflua Stokes, Nuclear factor erythroid 2–related factor 2

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에스트로겐 수용체 조절을 통한 천연소재 MS–10의 여성갱년기 개선 효과
Improvement effects of natural substance, MS-10 in menopause via estrogen receptor-mediated regulation.

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In this study, the expression level of estrogen receptor in an ovariectomized rat model was effectively enhanced by MS-10, Cirsium japonicum and Thymus vulgaris extract complex, in a reversible manner. MS-10 plays a positive role in enhancing estrogen activity at low concentrations, leading to improved women's health. In order to determine whether or not MS-10 improves menopausal symptoms clinically, a randomized, double-blinded, and placebo-controlled clinical study was carried out on 62 middle-aged women treated with 500 mg of MS-10 or placebo daily for 12 weeks. Clinical menopausal symptoms were evaluated by Kupperman's index (KI) detecting various menopausal symptoms, including hot flushes, parenthesis, insomnia, nervousness, melancholia, dizziness, fatigue, rheumatic pain, palpitations, formication, and headaches. Total KI score decreased significantly by about 18% upon ingestion of MS-10. Colpoxerosis, a main symptom of menopause, was significantly reduced by about 21% upon ingestion of MS-10 in contrast to placebo. In addition, reduction of insulin-like growth factor-1 with age was improved by over 10% upon ingestion of MS-10, whereas there

were no significant difference with placebo. No side effects appeared after treatment with MS-10. Thus, MS-10 can be suggested as a plausible natural substance for improving women's health.

Keywords: MS-10, menopause, colpoxerosis, Kupperman's index, estrogen receptor

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5-Aminosalicylic Acid Protects Epithelial Tight Junction Thereby Attenuating Intestinal Barrier Defect in Colitic Mice

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Intestinal barrier defects are involved in the pathogenesis of inflammatory bowel disease (IBD). While the oral supplement of 5-Aminosalicylic Acid (5-ASA) is currently used as a first-line therapy for IBD, underlying therapeutic mechanisms are largely unknown. The present study investigated the ameliorative effects of 5-ASA on epithelial tight junction (TJ) barrier defects using a mice model of IBD. For these, mice were divided into 3 groups: the control (the group were administered water for 5 days), the DSS [3.5 % dextran sulfate sodium (DSS) in combination with phosphate buffered saline as a vehicle for 5 days], and the DSS+5-ASA group [3.5 % DSS in combination with 5-ASA (20 mg/kg/day) for 5 days]. DSS group showed severe colon damage, as indicated by colon shortening and increased disease activity index *i.e.*, loss of body weight and increases of fecal occult blood as well as stool consistency. In DSS group, histologic alterations were also evident as demonstrated by goblet cell denudation and diffuse mural thickening with submucosal edema. Furthermore, DSS group showed the functional impairment on intestinal barrier integrity, as demonstrated by marked translocation of fluorescein sodium (F-Na) into the blood at 4 hrs after the oral intake. On the contrary, all these symptoms were significantly attenuated in DSS+5-ASA group. Notably, observation under electron microscopy (EM) revealed that DSS group showed the ultrastructural aberration on the colonic epithelial TJ, which was markedly diminished in DSS+5-ASA group. Immunohistochemical and semi-quantitative analysis for detecting the TJ proteins (zonula occludens-1, occludin, and claudin-5) were corroborated the EM finding well. Finally, it was demonstrated that DSS group exhibited the substantial elevation on colonic gene expressions of matrix metalloproteinase-2 and -9, both enzymes responsible for TJ degradation, which were significantly decreased in DSS+5-ASA group. Taken together, it might suggest that protective effects of 5-ASA on DSS-induced colitis at least partially due to protection of the TJ barrier in colonic epithelium.

Keywords: 5-Aminosalicylic Acid, Inflammatory bowel disease, Epithelial Tight Junction, Matrix metalloproteinase-2, Matrix metalloproteinase-9

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The Effect of Natural Substance MS-10 on the Improvement of menopausal Symptoms, Including Colpoxerosis, in Clinical Research

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Many natural substances were screened to develop nutraceuticals that reduce menopausal symptoms. A complex of Cirsium japonicum var. maackii and Thymus vulgaris extracts, named MS-10, had significant positive effects. Under a low concentration of estrogen, which represents postmenopausal physiological conditions, MS-10 had beneficial effects on estrogen receptor-expressing MCF-7 cells by reversibly enhancing estrogen activity. In addition, in the ovariectomized rat model, changes in bone-specific alkaline phosphatase activity and osteocalcin, as well as low-density lipoprotein cholesterol and triglyceride levels were significantly decreased by MS-10. These results show that MS-10 protected bone health and reduced metabolic disturbances. Furthermore, in a clinical study, all menopausal symptoms, including hot flushes, parenthesis, insomnia, nervousness, melancholia, vertigo, fatigue, rheumatic pain, palpitations, formication, and headache, as well as colpoxerosis, were significantly

improved by taking MS-10 for 90 days. Therefore, the evidence supports that MS-10 is an effective natural substance that can safely improve menopausal symptoms, including colpoxerosis.

Keywords: Colpoxerosis, Kupperman's Index, MS-10, menopause, ovariectomized rat

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Methionine Sulfoxide Reductase B3 (MsrB3)-Gene Deletion Exacerbates VitaminD3-Induced Kidney Toxicity

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Methionine sulfoxide reductase B_3 ($MsrB_3$) catalyzes the reduction of methionine-S-sulfoxide, scavenging reactive oxygen species (ROS). VitaminD_3 (cholecalciferol), an important factor of calcium and phosphate homeostasis, regulates calcium and phosphate levels in blood. However, high dose vitamin D_3 abnormally increases levels of calcium in the blood (hypercalcemia), leading to damages of organs including kidneys. Here, we investigated the role of $MsrB_3$ in vitaminD_3-induced kidney toxicity. Experiments were conducted using 8-weeks old male $MsrB_3$ wild type ($MsrB_3$ WT) and $MsrB_3$ knock out ($MsrB_3$ KO) mice. To induce hypercalcemia, mice were administered subcutaneously vitaminD_3 for 3 days daily. Kidneys were collected for biochemical and histological studies at 7 days after last administration. After vitaminD_3 injection, calcium levels in the kidney and serum significantly increased when compared with vehicle-injection, and these increases were greater in the $MsrB_3$ KO mice than in $MsrB_3$ WT mice. Phosphate levels in the kidney and serum after vehicle-treatment were not significantly different between $MsrB_3$ KO mice and $MsrB_3$ WT mice. Kidney tubule damages were greater in the $MsrB_3$ KO than $MsrB_3$ WT mice. VitaminD_3 injection decreased Msrs expression, whereas it increased the expression of vitaminD receptor (VDR), oxidative stress-related proteins (CuZnSOD, MnSOD, catalase, and HNE), runt-related transcription factor2 (Runx2), osterix, an osteogenic transcription factor in the kidney. These increases are greater in the $MsrB_3$ KO than $MsrB_3$ WT mice. Taken together, $MsrB_3$ gene-deletion accelerates high dose of vitaminD_3-induced kidney injury. It indicates that $MsrB_3$ protein may play an important role on blood calcium homeostasis, suggesting that $MsrB_3$ protein could be considered as a potential target for the treatment of hypercalcemia.

Keywords: Hypercalcemia, VitaminD3, Oxidative stress, Methionine sulfoxide reductase, Acute kidney injury

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Internet Gaming Addiction and Its Association with Telomere Length

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Background: Internet gaming addiction (IGA) has been associated with many negative health outcomes, especially for youth; however, few studies have examined the biological parameters related to this addiction. In particular, the association between IGA and telomere length (TL) has never been identified. Telomeres are protective chromosomal structures that play a key role in preserving genomic stability.
Purpose: The purpose of this study was to measure and compare the TL of Korean male adolescents with IGA and those without IGA.
Methods: A cross-sectional comparative study was performed with 228 male high school adolescents in a South Korean city (117 IGA group and 111 non-IGA group). Convenience and snowball sampling methods were employed, and data were collected using (1) participant blood samples analyzed for TL and (2) a set of questionnaires to assess sociodemographic characteristics and IGA score of participants. In our study, the TL data were natural log transformed to achieve a normal distribution and were measured using an established and validated qPCR-based technique. The relative TL was calculated as the T/S (telomere/single copy) ratio, which is the ratio between telomere repeat length and copy number of a single-copy

gene (HGB3).

Results: The TL (T/S ratio) was observed to be significantly shorter in the IGA group (mean=149.35, SEM=5.64) than the non-IGA group (mean=188.03, SEM=7.22) (t = 4.222, *P*<.001). The dot plot graph also explained that T/S ratio in the two groups was significantly different. On the contrary, T/S ratio was not significantly associated with adolescent's sociodemographic characteristics, including smoking and alcohol drinking. However, it was negatively correlated with Internet gaming time per day (r=-.246, *P*<.001) and IGA score (r=-.186, *P*=.005).

Conclusion: Results showed that involvement to excessive internet gaming may induce alterations in TL of male adolescents. These biological findings support further understanding of the effects of IGA in health and the need for IGA intervention strategies for male adolescents.

Keywords: Internet addiction, Telomere length

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Mitochondrial DNA Analysis of *Bos taurus* Bones Collected from *Cheonggyecheon* Archaeological Site of Joseon Period

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Although genetic information of *Bos taurus* has been successfully elucidated by a number of studies, there were very few researches on the ancient DNA of the cattle, especially made upon the historical cases that were raised in South Korea. In this study, we tried to analyze the mitochondrial DNA D-loop and coding region sequences of 15th century cattle bone obtained from *Cheonggyecheon* ruins of Joseon period. The consensus sequence was determined by the alignment of individual clone sequences. Consensus mitotype of the *Cheonggyecheon* cattle was 16138C, 106C, 169G, 221+C, 587+C, 2536A, 9682C, 13310C (Haplogroup=T3a). Comparing the current result with the sequences available in GenBank, *Cheonggyecheon* cattle mtDNA was similar to modern *Bos taurus* raised in South Korea, Japan, China (of northern provinces) and a few even in Europe, America and Oceania. Phylogenetic analysis also revealed that *Cheonggyecheon B. taurus* was genetically different from the cattle raised in and around Southern Chinese provinces. Although more studies on aDNA are still needed for enriching our genetic knowledge about the history of genus *Bos*, this report can be an important stepping stone for our future studies on the cattle of historical societies in East Asia.

Acknowledgement: This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (NRF-2016R1A2B4015669).

Keywords: Mitochondrial DNA, D-loop, Korea, Joseon, Bos taurus

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Arctii Lappa Fructus Extract Enhances Lipogenesis by Akt/SREBP-1 pathway in human keratinocyte

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The epidermal lipids of keratinocyte origin play an essential role in the skin barrier function. Disruption of the skin's barrier function results in a rapid and marked increase in epidermal cholesterol and fatty acid synthesis. In this study, we have investigated the signaling pathways involved in lipogenesis of keratinocyte treated with ethanol extract of *Arctii Lappa Fructus* (EAF). In HaCaT cells, the levels of intracellular cholesterol and triglyceride were significantly increased by EAF treatment. EAF stimulated the expression of the transcription factor sterol-regulatory element binding protein-1 (SREBP-1) in dose- and time-dependent manners. The activation of Akt was rapidly induced by EAF in HaCaT cells. Moreover, the induction of

SREBP-1 and activation of Akt were inhibited by PI3K/Akt inhibitor (LY294002) treatment. In this study, we confirmed that EAF stimulated the expression of fatty acid synthase (FAS), a key enzyme involved in lipogenesis. These results suggest that EAF induces lipid synthesis through the PI3K/SREBP-1 signaling pathways in HaCaT cells.

Keywords: *Arctii Lappa Fructus*, Lipogenesis, SREBP-1, Akt, Fatty acid synthase

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Melanogenesis-Promoting Effect of Eclipta prostrata Leaf

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Melanogenesis is a complex biosynthetic process in to the production of pigment, which determines the color of hair, skin, and eye. Melanin can protect skin from the ultraviolet (UV) radiation. The purpose of this study was to investigate the mechanism of ethanol extract of Eclipta prostrata Leaf. (EEP) induced melanogenesis. EEP enhanced tyrosinase activity and melanin contents of B16F10 cells. Moreover, EEP increased the protein expression of tyrosinase and tyrosinase-related protein 1 (TRP-1). But EEP didn't increase the protein expression of tyrosinase-related protein 2 (TRP-2). These results suggest that melanogenesis-promoting effect of EEP was involved in regulation of tyrosinase protein, and EEP may be a potent pigmentation darkening agent in hypo-pigmentation condition.

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Thymol, a Novel phytoncide, shows anti-MRSA effect throught the JNK signaling in A549 lung epithelial cell

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Thymol is a natural monoterpene and is known to have anti-bacterial effects. However, mechanism by which thymol is not clear. Here, we report that thymol has anti-bacterial activities against Methicillin resistance Staphylococcus aureus (MRSA). Thymol inhibits MRSA growth and has the bactericidal effect and inhibits biofilm formation of MRSA. MRSA induced LC3β, a key autophagy gene. MRSA induced LC3β through JNK. MRSA increased phosphorylation of AMPK. Inhibition of AMPK blocked MRSA-induced LC3β induction, suggesting that MRSA induced autophagy via JNK-mediated AMPK pathway. In cell culture system, MRSA suppressed the viability of lung adenocarcinoma A549 cells. Co-treatment of thymol recovered MRSA-induced A549 cells viability inhibition. Moreover, co-treatment of thymol with MRSA suppressed MRSA-mediated LC3β induction as well as phosphorylation of AMPK and JNK. These results demonstrate that thymol has anti-MRSA activity via suppressing autophagy and also suggest that thymol may become a novel drug candidate for MRSA-associated diseases, such as pneumonia.

Keywords: Thymol, MRSA, AMPK, Autophagy

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Irisin, a Novel Myokine, Regulates Glucose Uptake in Skeletal Muscle Cells via AMPK

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Irisin is a novel myokine produced by skeletal muscle. However, its metabolic role is poorly understood. In the present study, irisin induced glucose uptake in differentiated skeletal muscle cells. It

increased AMP-activated protein kinase (AMPK) phosphorylation and the inhibition of AMPK blocked glucose uptake. It also increased reactive oxygen species (ROS) generation. N-acetylcysteine (NAC), a ROS scavenger, blocked irisin-induced AMPK phosphorylation. Moreover, irisin activated p38 mitogen-activated protein kinase (MAPK) in an AMPK-dependent manner. The inhibition and knockdown of p38 MAPK blocked irisin-induced glucose uptake. A colorimetric absorbance assay showed that irisin induced the translocation of GLUT4 to the plasma membrane, and that this effect was suppressed in cells pre-treated with a p38 MAPK inhibitor or p38 MAPK siRNA. In primary cultured myoblast cells, irisin increased the concentration of intracellular calcium. STO-609, a calcium/calmodulin-dependent protein kinase kinase (CaMKK) inhibitor, blocked irisin-induced AMPK phosphorylation, implying that calcium is involved in irisin-mediated signaling. Our results suggest that irisin plays an important role in glucose metabolism via the ROS-mediated AMPK pathway in skeletal muscle cells.

Keywords: AMPK, Myokine, Irisin, Diabetes, glucose uptake

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Insulin derived-peptide ac celerates wound healing in HaCaT keratinocytes by Enhancing the PI3K/Akt and ERK signaling pathways

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Wound healing is a complex process that involves migration and proliferation of keratinocytes, in addition to the production of cytokines and growth factors that affect other cells. Keratinocyte migration and re-epithelialization play the most important roles in wound healing, as they determine the rate of wound healing. Insulin is known to play key roles in skin regeneration and wound-healing. In this study, we investigated whether insulin derived-peptide promotes wound healing through enhanced keratinocyte migration and proliferation. Our findings showed that the treatment of insulin derived-peptide activated PI3K/Akt and ERK signaling pathways through insulin receptor in HaCaT keratinocytes. Furthermore, Insulin derived-peptide promoted cell migration and proliferation by enhancing PI3K/Akt and ERK pathways. These results collectively suggest that insulin derived-peptide may be useful as a therapeutic agent for skin regeneration and wound-healing as an insulin mimetic agonist.

Keywords: Wound healing, Insulin derived-peptide, PI3K/Akt, ERK, HaCaT keratinocyte

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Age and High Fat Diets-related Ac cumulation of Advanced Glycation End-products-albumin, AGE, S100β, HMGB1 and Binding with their Receptor Differ in Subcutaneous, Visceral, and Periaortic Fat

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Periaortic fat and visceral fat induces more inflammation by activating macrophages than subcutaneous fat, and inflammation is an underlying feature of the pathogeneses of various diseases, including cardiovascular disease and diabetes. Advanced glycation end products (AGEs), S100b, and their receptors, the receptor for advanced glycation end products (RAGE), lead to macrophage activation. However, little information is available regarding the differential accumulations of AGE-albumin (serum albumin modified by AGEs), S100b, or expressions of RAGE in different adipocyte types in fat tissues. In this study, the authors investigated whether age or cholesterol-related AGE-albumin accumulations S100b level, and RAGE expressions differ in subcutaneous, visceral and periaortic fat tissues.

It was found that activated macrophage infiltration, AGE-albumin accumulation, and S100b in visceral fat was significantly greater in 28-week-old rats than in 3-week-old rats, but similar in subcutaneous fat. The expression of RAGE in visceral fat was much greater in 28-week-old rats, but its expression in subcutaneous fat was similar in 3- and 28-week-old rats. Furthermore, inflammatory signal pathways (NFkB, TNF-a) and proliferation pathways (FAK) in visceral fat were more activated in 28-week-old rats. These results imply that age-related AGE-albumin accumulation, S100b, and RAGE expression are more prominent in visceral than in subcutaneous fat, suggesting that visceral fat is involved in the pathogenesis of inflammation-induced diseases in the elderly.

We also investigated the changes of subcutaneous, visceral, and periaortic fat in high-fat feeding rats. Sprague Dawley rats were divided into 3 groups as follows: normal-fat diet, high-fat diets, and high-fat diets with pyridoxamine treatment. Subcutaneous, visceral, and periaortic fat were harvested from each diet groups. Body weight and triglyceride levels were increased in high-fat feeding rats. However, pyridoxamine, an AGE inhibitor, treated rats' body weigh t and triglyceride levels were decreased than high-fat only feeding rats. It was found that macrophage activation, RAGE, and RAGE ligand expression of periaortic fat were significantly higher in high-fat feeding rats than subcutaneous and visceral fat in normal-fat and high-fat with pyridoxamine-treated rats. Furthermore, inflammation and RAGE dependent signal pathways in high-fat feeding periaortic fat were more increased than high-fat feeding subcutaneous and visceral fat.

These results imply that age and high-fat diets are related RAGE and RAGE ligand expression are more remarkable in periaortic fat than in subcutaneous and visceral fat. Overall, the results suggest that periaortic fat is related in the pathogenesis of inflammation-induced diseases.

Keywords: Subcutaneous Fat, Visceral Fat, Periaortic Fat, Inflammation, RAGE ligands

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