

令和元年度 島根大学医学部研究交流会

日時：2019年10月18日（金） 18:00 - 19:30

場所：ラパン

日時：2019年10月23日（水） 18:00 - 19:30

場所：国際交流ラウンジ

日時：2019年10月18日（金） 18:00 - 19:30 場所：ラパン

ポスター番号：発表・討議時間（8分）

座長：飯笹久 先生（微生物学）

18-1 18:00 - 18:08

大腸がんに対する複合的抗がん化学免疫療法（Combined anti-cancer chemoimmunotherapy against colon cancer）：谷浦隆仁：消化器・総合外科

18-2 18:08 - 18:16

Application of a Bioactive/Bioresorbable Three-Dimensional Porous Uncalcined and Unsintered Hydroxyapatite/Poly-D/L-lactide Composite with Human Mesenchymal Stem Cells for Bone Regeneration in Maxillofacial Surgery: A Pilot Animal Study : SHA JING JING : Department of Oral and Maxillofacial Surgery

18-3 18:16 - 18:24

Bone Regeneration Potential of Uncalcined and Unsintered Hydroxyapatite/Poly L-lactide Bioactive/Osteoconductive Sheet Used for Maxillofacial Reconstructive Surgery: An In Vivo Study : Dong Ngoc Quang : artment of Oral and Maxillofacial Surgery

18-4 18:24 - 18:32

Feasibility of a Three-Dimensional Porous Uncalcined and Unsintered Hydroxyapatite/poly-D/L-lactide Composite as a Regenerative Biomaterial in Maxillofacial Surgery : BAI YUNPENG : Department of Oral and Maxillofacial Surgery

座長：岡本貴行 先生（薬理学）

18-5 18:32 - 18:40

EBV 陽性頭頸部腫瘍細胞において miR-BART-X は VHL を標的とし HIF-1 α を介して解糖経路を活性化する：飯笹久：微生物学講座

18-6 18:40 - 18:48

非アルコール性脂肪性肝疾患の病態形成に関与する miRNA の同定：
岡本貴行：薬理学講座

18-7 18:48 - 18:56

血管内皮細胞の硬さとその役割：岡本貴行：薬理学講座

18-12 18:56 - 19:04

The role of *Helicobacter pylori* infection in the development of Epstein-Barr virus-associated gastric cancer : Sintayehu Fekadu Kebede : Department of Microbiology 微生物学講座

<10月研究紹介ポスター>

18-8 19:04 - 19:12

Ubiquitin-like protein MNSF β is disaggregated and regulates cell proliferation : .
野津香織：地域医学共同研究部門

<Shimane Journal of Medical Science 2017 優秀学術論文>

18-9

(最優秀学術論文) Effects of Kampo Formulas on Differentiation and Proinflammatory Cytokines Expression of 3T3-L1 Cells (発生生物学) Qing YAN (顔青), Noriko OGAWA, Akihiro MATSUMOTO, Yuqi DANG, Hiroki OTANI

18-10

(優秀学術論文) Protection of Rat Retina against Light-induced Damage by Intraperitoneal and Oral Administration of a Polyphenol Fraction from Seed Shells of Japanese Horse Chestnuts (*Aesculus turbinata* BLUME) (眼科学) Tomoe ISHIHARA (石原朋恵), Sachiko KAIDZU, Hideto KIMURA, Yasuro KOYAMA, Yotaro MATSUOKA, Akihiro OHIRA

18-11

(優秀学術論文) Neuro-otological examinations in Patients with Spinocerebellar Degeneration (耳鼻咽喉科学) Michiko SHIBATA (柴田美智子), Ryoji HAMAMURA, Noriaki AOI, Mitsuhiro KIMURA, Shuhei YAMAGUCHI, Hideyuki KAWAUCHI

日時：2019年10月23日 18:00 - 19:30 場所：国際交流ラウンジ

(グループ1) 座長：桑子賢一郎 先生 (神経・筋肉生理学)

ポスター番号：発表・討議時間 (8分)

23-1 18:00 - 18:08

Evaluation of the functional effects of genetic variants—missense and nonsense SNPs, indels and copy number variations—in the gene encoding human deoxyribonuclease I potentially implicated in autoimmunity : Akari Kusaka : Department of Legal Medicine

23-2 18:08 - 18:16

Establishment of wheat peroxidase I-specific IgE test to identify wheat-dependent exercise-induced anaphylaxis developed by sensitization to grass pollen : Ryohei Ogino : Department of Dermatology

23-3 18:16 - 18:24

Prevalence of sensitization to galactose-a-1,3-galactose in Tokyo is comparable to that in Shimane : Yusei Nakagawa : Department of Dermatology

23-4 18:24 - 18:32

A case of macropapular exanthema with pancytopenia showing undetectable serum TARC level : Yasuyuki Ochi : Department of Dermatology

23-5 18:32 - 18:40

Electrical Impedance Tomography を用いて体位による換気分布の変化を観察した心臓血管外科術後の一例 : 佐藤 慎也 : 島根大学医学部附属病院リハビリテーション部

23-6 18:40 - 18:48

The Assessments of the Effects of NinjinYoeito (Herbal Medicine) on Gunn rats: a possible hyperbilirubinemia-induced animal model of schizophrenia : Muhammad Alim Jaya : Department of Psychiatry

23-7 18:48 - 19:04

L-アルギニン補充は抗がん剤と免疫チェックポイント阻害による複合免疫療法の抗がん効果を増強する (Supplementation of L-arginine augments antitumor effects induced by chemotherapy and immune checkpoint blockade therapy) : 佐藤悠介 Yusuke Sato : 免疫学 Department of Immunology

(グループ2) 座長：宮城聡 先生 (生命科学 生物学)

ポスター番号：発表時間 (8分)

23-8 18:00 - 18:08

抗がん剤により老化に陥った乳がん細胞の免疫細胞による細胞傷害に対する異なる感受性 (Different sensitivities of chemotherapy-induced senescent breast cancer cells to immune cell-mediated cytotoxicity) : 小谷仁司 : 免疫学

23-9 18:08 - 18:16

CCL19 発現間葉系細胞の局所投与による新規抗がん免疫療法の確立 (A novel immunotherapy by local injection of CCL19-expressing mesenchymal stem cells using mouse model) : 飯田 雄一 : 免疫学

23-10 18:16 - 18:24

Primary Study on the Role of Nna1 Mutation in the Cerebellar Development of Mouse with Ataxia and Male Sterility : Pang Bo : Pathology

23-11 18:24 - 18:32

Interkinetic nuclear migration in the trachea and esophageal epithelia of the mouse embryo.
: Regassa Dereje Getachew : Department of Developmental Biology, 発生生物学

23-12 18:32 - 18:40

Histological analysis of the epithelial lumen, mesenchyme and muscle cell layer in the mouse developing duodenum. : Jahan Nusrat : 発生生物学

23-13 18:40 - 18:48

医学研究における「Public Health」の重要性と必要性：研究費の取り方、留学の仕方：そのコツをお教えします。： 廣瀬 昌博 : 医学部地域医療政策学講座 (附属病院医療安全管理部)

23-14 18:48 - 18:56

Maternal nutritional status during pregnancy in Shimane Prefecture : Fourth report
- A comparison by meal skipping - : 籠橋有紀子 : 島根県立大学看護栄養学部

23-15 18:56 - 19:04

Maternal nutritional status during pregnancy in Shimane Prefecture : Second report
- Comparison among early, middle and late pregnancy - : 中谷陽子 : 島根県立大学看護栄養学部

<発表者へ>

- ・ ポスターサイズ：縦 1.3 m X 幅 1.0 m 以内
A poster size must be within 1.3 m high X 1.0 m wide.
- ・ 17:30-17:55 の間にポスターを貼ってください。この時間帯に貼ることができない者は前もって免疫学講座にポスターを預けておいてください。
Please put up a poster during 17:30 – 17:55. Unless, deposit your poster to the Department of Immunology in advance.
- ・ 発表形式：指定された時間（8 分）のポスター前で発表・討議
Each presentation/discussion has 8 min.
- ・ この研究交流会への出席は大学院講義への出席とみなされます。出席した大学院生は教官にサインをもらってください。
Attending to this meeting can be regarded as that to a lecture for post-graduate students. Have a sign of teachers.

2019年10月18日（金曜日）

18-1

発表者： 大学院生 大学院生以外

タイトル (title) : 大腸がんに対する複合的抗がん化学免疫療法 Combined anti-cancer chemoimmunotherapy against colon cancer

発表者 (presenters) : 谷浦隆仁 Takahito Taniura

所属 (affiliation) : 島根大学医学部 消化器・総合外科

Department of Digestive and General Surgery

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抄録 (abstract)

ある種の抗がん化学療法剤は直接的な殺細胞効果だけでなく、担がん宿主の抗がん免疫を賦活・修飾することが知られている。今回、マウス CT26 大腸がんを皮下接種した同系腫瘍モデルを用いて、臨床で大腸がんに対する標準的化学療法剤として使用されている 5-FU と L-OHP を併用投与した場合の抗がん免疫応答に及ぼす影響、また、調節性 T (Treg) 細胞を抑制することが知られている抗がん化学療法剤 cyclophosphamide (CP) と 3 剤を併用した場合の治療効果を検証した。担がん 10 日目と 18 日目に抗がん剤を投与した場合、5-FU/L-OHP 2 剤併用または CP 単剤の群と比較し、3 剤を併用した群で有意な CT26 の増殖抑制が観察され、半数のマウスで CT26 が完全退縮した。しかし、ヌードマウスではこのような併用効果を認めなかった。複合的抗がん化学免疫療法で CT26 が治癒したマウスでは CT26 の再接種に対して防御免疫が誘導され、また、脾細胞から CT26 特異的細胞傷害性 T 細胞 (CTL) を誘導できた。さらに、3 剤を併用した群ではがん局所において CTL の浸潤促進と単球系骨髄由来抑制性細胞 (MDSC) の減少が観察された。以上の結果から、3 種の抗がん化学療法剤による複合的抗がん化学免疫療法は、大腸がんに対して有効な免疫療法になる可能性が示された。

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Application of a Bioactive/Bioresorbable Three-Dimensional Porous Uncalcined and Unsintered Hydroxyapatite/Poly-D/L-lactide Composite with Human Mesenchymal Stem Cells for Bone Regeneration in Maxillofacial Surgery: A Pilot Animal Study

発表者 (presenters) : SHA JING JING

所属 (affiliation) : Department of Oral and Maxillofacial Surgery

メールアドレス (address) : 396318296@qq.com

抄録 (abstract)

A novel three-dimensional porous uncalcined and unsintered hydroxyapatite/poly-D/L-lactide (3D-HA/PDLLA) composite demonstrated superior biocompatibility, osteoconductivity, and plasticity, thereby enabling complex maxillofacial defect reconstruction. Mesenchymal stem cells (MSCs)—a type of adult stem cell—have a multipotent ability to differentiate into chondrocytes, adipocytes, and osteocytes. We previously found that CD90 and CD271 double-positive cell populations from human bone marrow had high proliferative ability and differentiation capacity in vitro. In the present study, we investigated the utility of bone regeneration therapy using implantation of 3D-HA/PDLLA loaded with human MSCs (hMSCs) in mandibular critical defect rats. Microcomputed tomography (Micro-CT) indicated that implantation of a 3D-HA/PDLLA-hMSCs composite scaffold improved the ability to achieve bone regeneration compared with 3D-HA/PDLLA alone. Compared to the sufficient blood supply in the mandibular defection superior side, a lack of blood supply in the inferior side caused delayed healing. The use of Villanueva Goldner staining (VG staining) revealed the gradual progression of the nucleated cells and new bone from the scaffold border into the central pores, indicating that 3D-HA/PDLLA loaded with hMSCs had good osteoconductivity and an adequate blood supply. These results further demonstrated that the 3D-HA/PDLLA-hMSCs composite scaffold was an effective bone regenerative method for maxillofacial boney defect reconstruction.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Bone Regeneration Potential of Uncalcined and Unsintered Hydroxyapatite/Poly L-lactide Bioactive/Osteoconductive Sheet Used for Maxillofacial Reconstructive Surgery: An In Vivo Study

発表者 (presenters) : Dong Ngoc Quang

所属 (affiliation) : Department of Oral and Maxillofacial Surgery

メールアドレス (address) : quangbeo87@gmail.com

抄録 (abstract)

Uncalcined and unsintered hydroxyapatite/poly L-lactide (u-HA/PLLA) material has osteoconductive characteristics and is available for use as a maxillofacial osteosynthetic reconstruction device. However, its bone regeneration ability in the maxillofacial region has not been fully investigated. This study is the first to assess the bone regenerative potential of osteoconductive u-HA/PLLA material when it is used for repairing maxillofacial bone defects. A total of 21 Sprague-Dawley male rats were divided into three groups: the u-HA/PLLA, PLLA, or sham control groups. A critical size defect of 4 mm was created in the mandible of each rat. Then, the defect was covered with either a u-HA/PLLA or PLLA sheet on the buccal side. The rats in each group were sacrificed at 2, 4, or 8 weeks. The rats' mandibles were sampled for histological analysis with hematoxylin and eosin staining, histomorphometry, and immunohistochemistry with Runx2 and osteocalcin (OCN) antibody. The amount of bone formed in the u-HA/PLLA group was significantly higher than that of the PLLA group. The expression of Runx2 and OCN in the u-HA/PLLA group was also significantly higher. These results demonstrate that the u-HA/PLLA material has excellent bone regenerative ability and confirm its applicability as a reconstructive device in maxillofacial surgery.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Feasibility of a Three-Dimensional Porous Uncalcined and Unsintered Hydroxyapatite/poly-D/L-lactide Composite as a Regenerative Biomaterial in Maxillofacial Surgery

発表者 (presenters) : BAI YUNPENG

所属 (affiliation) : Department of Oral and Maxillofacial Surgery

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抄録 (abstract)

This study evaluated the feasibility of a novel three-dimensional (3D) porous composite of uncalcined and unsintered hydroxyapatite (u-HA) and poly-D/L-lactide (PDLLA) (3D-HA/PDLLA) for the bony regenerative biomaterial in maxillofacial surgery, focusing on cellular activities and osteoconductivity properties in vitro and in vivo. In the in vitro study, we assessed the proliferation and ingrowth of preosteoblastic cells (MC3T3-E1 cells) in 3D-HA/PDLLA biomaterials using 3D cell culture, and the results indicated enhanced bioactive proliferation. After osteogenic differentiation of those cells on 3D-HA/PDLLA, the osteogenesis marker genes runt-related transcription factor-2 (Runx2), and Sp7 (Osterix) were upregulated. For the in vivo study, we evaluated the utility of 3D-HA/PDLLA biomaterials compared to the conventional bone substitute of beta-tricalcium phosphate (β -TCP) in rats with critical mandibular bony defects. The implantation of 3D-HA/PDLLA biomaterials resulted in enhanced bone regeneration, by inducing high osteoconductivity as well as higher β -TCP levels. Our study thus showed that the novel composite, 3D-HA/PDLLA, is an excellent bioactive/bioresorbable biomaterial for use as a cellular scaffold, both in vitro and in vivo, and has utility in bone regenerative therapy, such as for patients with irregular maxillofacial bone defects.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : EBV 陽性頭頸部腫瘍細胞において miR-BART-X は VHL を標的とし HIF-1 α を介して解糖経路を活性化する

発表者 (presenters) : 飯笹 久

所属 (affiliation) : 微生物学講座

メールアドレス (address) : iizasah@med.shimane-u.ac.jp

抄録 (abstract)

Epstein-Barr ウイルス (EBV) は、上咽頭癌ばかりでなく他の頭頸部腫瘍 (HNSCC) の発生にも関わるという報告が増加している。我々は、EBV が持続感染した扁平上皮細胞株を作製した。EBV 陽性扁平上皮細胞株では解糖系が亢進し、乳酸の産生が増加していた。また糖代謝関連遺伝子群の発現を解析すると、EBV 陽性細胞では HIF-1 α 分解因子である VHL の発現が低下し、HIF-1 α の発現が上昇していた。EBV がコードする miRNA (BART miRNA) は、上皮腫瘍で高発現している。VHL 3' UTR をルシフェラーゼ遺伝子の下流に組み込んだベクターを用いると、EBV 陽性細胞では陰性細胞よりもルシフェラーゼ活性が低下した。次に、VHL を標的とする miRNA を探索し、miR-BART-X に注目した。miR-BART-X 特異的阻害剤を用いると、ルシフェラーゼ活性は上昇し、VHL の発現も上昇した。さらに、HIF-1 α の発現低下と解糖系遺伝子の発現低下も認めた。miR-BART-X は、VHL を標的とすることで HIF-1 α 転写因子のユビキチン分解を抑制し、解糖系の亢進や乳酸産生の増加を導くと考えられた。

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : 非アルコール性脂肪性肝疾患の病態形成に関する miRNA の同定

発表者 (presenters) : 岡本貴行

所属 (affiliation) : 薬理学講座

メールアドレス (address) : okamoto@med.shimane-u.ac.jp

抄録 (abstract)

肥満やメタボリックシンドロームを原因として非アルコール性脂肪性肝疾患 (NAFLD) は発症する。わが国でも検診等の受診者の 30% に脂肪肝がみられ、将来、NAFLD は国民病になりうると予測される。NAFLD 患者は心血管イベントの発症リスクが高く、さらに非アルコール性脂肪肝炎 (NASH) に至ると肝硬変や肝癌など肝関連死が高率となる。これまで NAFLD およびその関連疾患において発現異常をきたす miRNA の存在が多数報告され、NAFLD の治療標的分子、または診断分子としての応用が期待されている。

われわれはこれまで NAFLD 患者の肝組織で発現する miRNA の発現解析を行い、正常肝と比較して著しく発現が変動する miRNA を複数見出した。われわれは、NAFLD 肝組織で特に顕著な発現増加がみられる miR-27b に着目し、miR-27b が NAFLD の基礎病態である脂肪蓄積に及ぼす影響を解析した。その結果、miR-27b はマウス 3T3-L1 細胞における脂肪蓄積を促進した。また、miR-27b はミトコンドリアでの脂肪酸代謝に関わるアシル CoA チオエステラーゼ 2 (ACOT2) の発現を誘導した。ACOT2 を siRNA で発現低下させると 3T3-L1 細胞における脂肪蓄積は抑制された。

以上の結果から、NAFLD 患者で増加する miR-27b は ACOT2 の発現誘導を介して脂肪蓄積を促進していることを明らかにした。

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : 血管内皮細胞の硬さとその役割

発表者 (presenters) : 岡本貴行

所属 (affiliation) : 薬理学講座

メールアドレス (address) : okamoto@med.shimane-u.ac.jp

抄録 (abstract)

動脈硬化病変では血管組織の線維化や石灰化によって血管硬化（弾性率の増加）が生じる。血管硬化は心血管イベント発生リスクと相関を示し、これらは血管の硬さが血管機能に及ぼす可能性を示唆する。一方で、細胞そのものも固有の硬さを呈するが、細胞の硬さ変化と血管機能の関連については不明な点が多い。本研究で我々は、血管内皮細胞に着目し、炎症時における血管内皮細胞の硬さ変化とその役割を解析した。

細胞の硬さは原子間力顕微鏡を用いて測定した。ヒト臍帯静脈内皮細胞を腫瘍壊死因子で刺激した。刺激4時間後に細胞は著しく硬化し、24時間後には未刺激時と同程度まで軟化した。細胞の硬さは細胞骨格と細胞間相互作用の影響を受ける。細胞の硬化部位でのアクチンの重合を観察し、硬化部位でアクチンの重合が亢進することを明らかにした。また、細胞間ギャップ結合を阻害した細胞は著しく硬くなることを明らかにした。さらに硬化した血管内皮細胞上への単球の接着を評価した結果、血管内皮細胞の硬さ依存的な単球接着の亢進がみられた。

以上の結果から、炎症時における血管内皮細胞硬化は白血球の接着を亢進し、血管病変形成を促進する可能性が示唆された。

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : The role of *Helicobacter pylori* infection in the development of Epstein-Barr virus-associated gastric cancer

発表者 (presenters) : Sintayehu Fekadu Kebede

所属 (affiliation) : 微生物学講座 Department of Microbiology

メールアドレス (address) : serkalem@med.shimane-u.ac.jp

抄録 (abstract)

Most of gastric cancer (GC) cases are associated with infection of *Helicobacter pylori* (*H. pylori*). On the other hand, 10% of GC cases detect Epstein-Barr virus (EBV) infection in cancer cells. However, it is unclear that pathophysiological involvement of *H. pylori* infection in the development of EBV associated cancer (EBVaGC). To clarify this, gastric epithelial AGS cells were infected with *H. pylori* CPY6271 strain. After 7 hours, *H. pylori* was removed by washing cells with saline and adding antibiotics to the culture. AGS cells exposed with *H. pylori* were infected with recombinant EBV having eGFP gene in its BXLFl gene (eGFP-EBV). Establishment of infection was confirmed by fluorescence microscopy and efficiency of infection was quantified by FACS analysis. AGS cells exposed with *H. pylori* was induced with hummingbird phenotype, but viability of cells was not affected. AGS cells infected with *H. pylori* were slightly increased with EBV infectivity by microscopic observation. I am going to quantify change in EBV gene expression by *H. pylori* infection. I have also established a protocol to recover high tittered EBV during the course of my research, which is worth to be reported.

18-8

Ubiquitin-like protein MNSF β is disaggregated and regulates cell proliferation.

地域医学共同研究部門 野津香織

Shimane Journal of Medical Science 2017 優秀学術論文

18-9

(最優秀学術論文) Effects of Kampo Formulas on Differentiation and Proinflammatory Cytokines Expression of 3T3-L1 Cells. (発生生物学) Qing YAN (顔 青) , Noriko OGAWA, Akihiro MATSUMOTO, Yuqi DANG, Hiroki OTANI

18-10

(優秀学術論文) Protection of Rat Retina against Light-induced Damage by Intraperitoneal and Oral Administration of a Polyphenol Fraction from Seed Shells of Japanese Horse Chestnuts (*Aesculus turbinata* BLUME) (眼科学)
石原 朋恵 Tomoe ISHIHARA, Sachiko KAIDZU, Hideto KIMURA, Yasuro KOYAMA, Yotaro MATSUOKA, Akihiro OHIRA

18-11

(優秀学術論文) Neuro-otological examinations in Patients with Spinocerebellar Degeneration (耳鼻咽喉科学) 柴田 美智子 Michiko SHIBATA, Ryoji HAMAMURA, Noriaki AOI, Mitsuhiro KIMURA, Shuhei YAMAGUCHI, Hideyuki KAWAUCHI

2019年10月23日 (水曜日)

23-1

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title): Evaluation of the functional effects of genetic variants—missense and nonsense SNPs, indels and copy number variations—in the gene encoding human deoxyribonuclease I potentially implicated in autoimmunity

発表者 (presenters) : Akari Kusaka

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抄録 (abstract)

Genetic variants, such as single nucleotide polymorphisms (SNPs), in the deoxyribonuclease I (DNase I) gene which remarkably reduce or abolish the activity are assumed to be substantially responsible for the genetic backgrounds determining susceptibility to autoimmune dysfunction. Here, we exhaustively evaluated many genetic variants, including missense and nonsense SNPs and indel (inframe) variants in the gene, potentially implicated in autoimmune diseases as functional variants resulting in altered activity levels. Accordingly, a total of 60 genetic variants in the DNase 1 gene (DNASE1) inducing abolishment or marked reduction of the DNase I activity could be identified as genetic risk factors for autoimmunity, irrespective of how sparsely they were distributed in the population. It was noteworthy that SNP p.Gln244Arg, reportedly associated with autoimmunity and reducing the activity to about half of that of the wild type, and SNP p.Arg107Gly, abolishing the activity completely, were distributed worldwide and in African populations at the polymorphic level, respectively. On the other hand, with regard to copy number variations in DNASE1 where loss of copy leads to a reduction of the in vivo enzyme activity, only 2 diploid copy numbers were distributed in Japanese and German populations, demonstrating no loss of copy.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Establishment of wheat peroxidase I-specific IgE test to identify wheat-dependent exercise-induced anaphylaxis developed by sensitization to grass pollen

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抄録 (abstract)

We have identified peroxidase I as a causative allergen for wheat-dependent exercise-induced anaphylaxis developed as pollen food allergy syndrome (PFAS-WDEIA) due to cross-reaction between wheat proteins and grass pollen allergens. The purpose of this study is to establish peroxidase I-specific IgE test and test its sensitivity and specificity to identify PFAS-WDEIA.

Serum were obtained from 6 patients with PFAS-WDEIA, 18 patients with conventional WDEIA, 11 patients with hydrolyzed wheat protein allergy, 17 patients with hay fever, and 22 patients with red meat/crustacean allergy. Peroxidase I was purified upon chromatography steps, and peroxidase I-specific IgE test was established by CAP-FEIA system.

Positive of peroxidase I-specific IgE test were 3 of 6 PFAS-WDEIA patients and 2 of 17 hay fever patients, but none of 18 conventional WDEIA, 11 hydrolyzed wheat allergy, nor 22 red meat/crustacean allergy patients. Sensitivity and specificity of peroxidase I- and existing allergen-specific IgE tests to identify PFAS-WDEIA patients were calculated as follows; 50% and 97% for peroxidase I, 83% and 79% for wheat, 50% and 79% for gluten, 0% and 79% for ω -5 gliadin.

Wheat peroxidase I-specific IgE test is useful to identify patients with wheat-dependent exercise-induced anaphylaxis developed by sensitization to grass pollen.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Prevalence of sensitization to galactose- α -1,3-galactose in Tokyo is comparable to that in Shimane

発表者 (presenters) : Yusei Nakagawa

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抄録 (abstract)

Principal cause of cetuximab-induced anaphylaxis is IgE antibodies against galactose- α -1,3-galactose (α -Gal) present on mouse-derived Fab portion of cetuximab heavy chain. Cetuximab allergy patients often develop allergic reaction to mammalian meat by reacting α -Gal. In this study, we aimed to clarify sensitization rate in Tokyo, the largest city in Japan and to compare with that in Shimane. We enrolled 50 subjects in Tokyo Medical and Dental University (TMDU) Hospital, and 100 subjects in Shimane University Hospital, both of whom were consulted with complaining anything except food allergy. Serum α -Gal-specific and beef-specific IgE were measured using ImmunoCAP. Specific IgE to cetuximab was detected by immunoblotting. As a result, the α -Gal-specific IgE were detected (≥ 0.10 kUa/L) in 16 out of 100 (16%) subjects in Shimane University Hospital and 8 of 50 (16%) subjects in TMDU Hospital. Moreover, among them, 11 of the 16 in Shimane University Hospital and 5 of the 8 in TMDU Hospital were positive (≥ 0.35 kUa/L) for the beef-specific-IgE test. Additionally, immunoblotting showed 5 of 100 subjects (5%) in Shimane University Hospital and 2 subjects (4%) in TMDU Hospital have IgE antibody to cetuximab. Thus, there is almost no difference of α -Gal sensitization rate between Shimane and Tokyo.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : A case of macropapular exanthema with pancytopenia showing undetectable serum TARC level

発表者 (presenters) : Yasuyuki Ochi

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抄録 (abstract)

We have already reported that serum thymus and activation-regulated chemokine (TARC) level is extremely high in early stages of drug-induced hypersensitivity syndrome and a good marker to differentiate other drug eruptions, especially macropapular exanthema (MPE). We experienced a case of MPE complicated with pancytopenia which shows undetectable serum TARC level.

A 54-year-old woman with myelofibrosis consulted our hospital complaining high fever and cough. Levofloxacin was started for high fever, and the patient developed systemic erythema four days after the levofloxacin treatment. Her physical examination revealed multiple papular erythema with itch on almost her entire body. MPE was diagnosed, levofloxacin was discontinued, and topical steroid therapy was initiated. Her blood examination showed pancytopenia, including WBC count 1990, RBC count 236,000, and platelet count 15,000. Her serum TARC was under detection limit of 100 pg/ml on Day 3, 6, and 13 after onset of her eruptions. The skin rashes disappeared two weeks after the onset.

With the findings that serum TARC levels have no correlation to platelet counts in 14 cases with MPE previously examined in our department. Taking this into consider, we concluded that the undetectable serum TARC levels in this case are related to the complication of pancytopenia.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : Electrical Impedance Tomography を用いて体位による換気分布の変化を観察した心臓血管外科術後の一例

発表者 (presenters) : 佐藤 慎也

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抄録 (abstract)

【緒言】

Electrical Impedance Tomography (以下、EIT) は非侵襲的に肺の換気分布をリアルタイムにモニタリングすることが可能である。今回、心大血管術後の患者に対し、EIT を用いて体位による換気分布の変化を観察したため報告する。

【症例】

症例は 70 代男性。人工弁機能不全、右冠動脈狭窄に対し大動脈弁置換術及び冠動脈バイパス術を施行した。既往歴に肺気腫があり、%肺活量 86.1%、一秒率 72.7%であった。術後翌日、人工呼吸器を離脱し、呼吸理学療法や段階的な離床を開始した。術後 3 日目に胸部 X 線画像で右優位に胸水の貯留を認めたため、胸水穿刺が施行された。穿刺後、体位の変化 (ベッド上臥位、頭高位、端座位、立位) が換気分布にどのような影響を与えるかを EIT でモニタリングした。その結果、換気分布割合 (右肺 : 左肺) は、ベッド上仰臥位では 11.7% : 88.3%、頭高位では 4.8% : 95.2%、端座位では 20.8% : 79.2%、立位では 47.0% : 53.0% であった。

【結論】

胸水穿刺後でも換気分布異常は残存し、端座位や立位などの離床は換気分布改善に寄与する可能性がある。

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : The Assessments of the Effects of NinjinYoeito (Herbal medicine) on Gunn rats: a possible hyperbilirubinemia-induced animal model of schizophrenia

発表者 (presenters) : Muhammad Alim Jaya

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抄録 (abstract)

Schizophrenia is one of the crucial psychiatric disorders which severely impact on ADL of patients. The main treatment of schizophrenia has been antipsychotics since 1960. However, the effect of antipsychotics is still limited though versatile types of antipsychotics have been launched. Especially, the effect was limited in the neurocognitive symptoms, rather than positive symptoms, for example, delusion, hallucination, excitement.

One of the herbal medicine-NinjinYoeito (NYT) has been reported to improve the neurocognitive symptoms of patients of Alzheimer's disease, and also in developmental disorder as autistic spectrum disorder. In vitro, It has been reported that NYT has the effect enhancing the remyelination accompanied with the suppression of the oxidative stress and neuroinflammation. Therefore, in the current study, we would like to test the effect of the NYT on Gunn rats (congenital hyperbilirubinemic rats) which have the features of schizophrenia, from the viewpoint of the both sides of histopathological and behavioral assessments. And we would like to find the clue of the an alternative or adjuvant treatment for schizophrenia.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : L-アルギニン補充は抗がん剤と免疫チェックポイント阻害による複合免疫療法の抗がん効果を増強する Supplementation of L-arginine augments antitumor effects induced by chemotherapy and immune checkpoint blockade therapy

発表者 (presenters) : 佐藤悠介 Yusuke Sato

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抄録 (abstract)

Myeloid-derived suppressor cells (MDSCs) express arginase I and indoleamine 2,3-dioxygenase and are known to suppress T cell function in tumor-bearing hosts via downregulation of L-arginine and L-tryptophan, respectively. In this study, we examined effects of supplementation of these amino acids on antitumor effects in CT26 colon carcinoma-bearing mice. Supplementation of L-arginine showed the tendency to suppress the tumor growth, whereas that of L-tryptophan promoted the tumor growth. Although combination therapy with cyclophosphamide (CP) and anti-PD-1 antibody significantly suppressed the tumor growth, no tumor regression was observed. However, additional supplementation of L-arginine induced complete tumor regression in more than half mice. Interestingly, LC/MS analysis on the plasma revealed that, although the plasma levels of L-arginine in CT26-bearing mice were not decreased, CP administration significantly decreased them. Importantly, supplementation of L-arginine recovered their levels to those of naive mice. These results suggest that a chemotherapeutic drug CP, but not tumor-bearing state, decreases the level of L-arginine, and that L-arginine supplementation is effective in anticancer immunotherapy when combined with chemotherapy.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : Different sensitivities of chemotherapy-induced senescent breast cancer cells to immune cell-mediated cytotoxicity 抗がん剤により老化に陥った乳がん細胞の免疫細胞による細胞傷害に対する異なる感受性

発表者 (presenters) : 小谷仁司 Hitoshi Kotani

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抄録 (abstract)

Chemotherapeutic drugs induce apoptosis in cancer cells, whereas some cancer cells survive as a result of DNA damage response with being senescent. Despite growth arrest, senescent cancer cells promote tumor formation and recurrence by producing cytokines and growth factors, designated as the senescence-associated secretory phenotype (SASP). In this study, we examined the susceptibility of senescent human breast cancer cells to immune cell-mediated cytotoxicity. Doxorubicin (DXR) treatment induced senescence in MDA-MB-231 and BT-549 cells: induced expression of γ H2AX and SA β -gal and enhanced production of proinflammatory cytokines. Importantly, DXR-treated senescent MDA-MB-231 cells showed increased sensitivity to two types of immune cell-mediated cytotoxicity: cytotoxicity of activated CD4⁺ T cells and ADCC by NK cells. This increased sensitivity was not observed following treatment with the senescence-inducing CDK4/6 inhibitor, abemaciclib. These results indicated that DXR and CDK4/6 inhibitor induced senescence in breast cancer cells, but that they differed in their sensitivity to immune cell-mediated cytotoxicity.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title) : CCL19 発現間葉系細胞の局所投与による新規抗がん免疫療法の確立 A novel immunotherapy by local injection of CCL19-expressing mesenchymal stem cells using mouse model

発表者 (presenters) : 飯田 雄一 Yuichi Iida

所属 (affiliation) : 免疫学 Department of Immunology

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抄録 (abstract) Mesenchymal stem/stromal cells (MSC) accumulate and reside in tumor sites. Taking advantage of this feature in anticancer therapy, immortalized murine MSC (iMSC) were genetically altered to produce chemokine (C-C motif) ligand 19 (iMSC/CCL19), which attracts dendritic cells (DC) and T lymphocytes. Co-injection of iMSC/CCL19 into mice significantly suppressed the tumor growth. Co-injected iMSC/CCL19 survived longer than CCL19-expressing fibroblast (iFib/CCL19) in the tumor sites. In a therapeutic model, local injection of iMSC/CCL19 suppressed the tumor growth, and increased IFN- γ ⁺ CD8⁺ T cell and CCR7⁺ DC infiltration in tumor site was observed when treated with iMSC/CCL19, but not with iMSC. This anti-tumor effect was completely negated by depletion of CD4⁺ T cells and partially negated by depletion of CD8⁺ T cells. Furthermore, the anti-tumor effects induced by local injection of iMSC/CCL19 were augmented by additional therapy with anti-programmed death (PD)-ligand 1 (PD-L1) antibody, but not with anti-PD-1 antibody. This combination therapy cured most of the tumors in CT26-bearing mice. These results suggest that local therapy with iMSC/CCL19 can suppress tumor growth via effective recruitment of CCR7⁺ DC into tumor sites and increase IFN- γ ⁺ CD8⁺ T cells, and that combination with anti-PD-L1 antibody therapy can be a powerful anti-cancer therapy.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Primary Study on the Role of Nna1 Mutation in the Cerebellar Development of Mouse with Ataxia and Male Sterility

発表者 (presenters) : Pang Bo

所属 (affiliation) : Pathology

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抄録 (abstract)

Nna1 gene is phylogenetically-preserved and codes for carboxyl peptidase (CCP) 1. Its mutation of different types is known to cause a progressive loss of the Purkinje cells (PC). The ataxia and male sterility (AMS) mouse harboring a point mutation and is the only Nna1-allele model. Thus, we investigate ontogenical Nna1 distribution in the cerebellum of the AMS mice of every genotype from postnatal day P-7 through P-28, mainly before disease-phenotype appears. Provide experimental basis for gene-targeted therapy of cerebellar development-related diseases. We applied immunohistochemistry and immunofluorescence using anti-human Nna1 antibodies to investigate its distribution in the cerebellum of AMS mice of each genotype from postnatal days (P) 7-28. RESULTS: Both the molecular and granular layers were positive for Nna1. The semi-quantification of Nna1's stain-strength revealed in the following order: wild-type, ams-heterozygous, then ams-homozygous. CONCLUSION: The distribution of the Nna1 in the cerebellum, except in the PCs, of wild-type mice varies according to the age of the mice, while that in the PCs is stable from P15. However, the loss of PCs might occur due to a protein shortage because the instability of its 3-dimensional structure, which is caused by the Nna1 point mutation.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Interkinetic nuclear migration in the trachea and esophageal epithelia of the mouse embryo.

発表者 (presenters) : Regassa Dereje Getachew

所属 (affiliation) : Department of Developmental Biology, 発生生物学

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抄録 (abstract)

Interkinetic nuclear migration (INM) is the migration of nuclei of the epithelial cells in synchrony with cell cycle, undergoing cell division at apical side and back to basal side during interphase. We investigated the existence, the inter-organ and regional differences of INM pattern in the epithelia of trachea and esophagus of mouse embryos at E11.5 and E12.5 and the following 12 hrs. The chronological changes in 5-ethynyl-2'- deoxyuridine (EdU) labeled nuclei along the apico-basal axis were analyzed. We ran one-way ANOVA using MorphoJ package to analyze the comparison among the groups. The trachea total vs. esophagus total at E11.5 showed different INM patterns of EdU-labeled nuclei distribution ($P = 0.0001$), while at E12.5 no differences between the two organs ($P = 0.0959$). Trachea at E11.5 showed regional difference (dorsal vs. ventral) ($P = 0.012$), while at E12.5 no regional differences ($P = 0.302$). Esophagus showed no regional differences at either E11.5 or E12.5 ($P = 0.694$, $P = 0.602$, respectively). These findings suggest that the inter-organ INM pattern difference exists at E11.5 between trachea and esophagus, and regional difference exists in trachea at E11.5 but not in esophagus, which may be involved in the later different development of the organs.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Histological analysis of the epithelial lumen, mesenchyme and muscle cell layer in the mouse developing duodenum.

発表者 (presenters) : Jahan Nusrat

所属 (affiliation) : 発生生物学

メールアドレス (address) :

抄録 (abstract)

The mechanism of the development of epithelium, mesenchyme, as well as smooth muscle (SM) layer of the gut during embryogenesis is important to understand whole gut development. Our purpose is to clarify the common features in the regional difference in the development of the epithelium, mesenchyme and SM layers of the duodenum for elucidating their possible relationship with the overall macroscopic morphogenesis of the duodenum. We used C57BL/6 mouse embryos at embryonic day (E) 13.5, 15.5, 17.5 (each day, n=3). By histomorphometric analysis we found that the epithelial lumen is oval and its axis showed a general clockwise rotation against the mesentery at E13.5. Number of inner circular SM layers At E13.5, E15.5 and E17.5 showed a regional difference related to the mesentery, but no clear change along the long axis of the duodenum. We also observed that the epithelial nuclear shape and the adjacent mesenchyme density change along the long axis of the duodenum, and these epithelial-mesenchymal interactions might contribute to the winding of the duodenum resulting the “C” shape curve. However, these are our current hypotheses at this moment but need further research to draw any conclusion.

発表者： 大学院生 □ 大学院生以外 ■

タイトル (title)： 医学研究における「Public Health」の重要性と必要性：研究費の取り方、留学の仕方：そのコツお教えします。

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抄録 (abstract)

地域医療政策学講座は、疫学・統計学などの社会医学と経済学・経営学などの社会科学を基盤とし、問題提起・解決志向型で、学際的他領域統合的分野であり、医療の有効性、経済性、標準化や質的評価を追求する医療経済学を基盤とし、地域医療、地域包括ケアを研究フィールドとする学問である。このようなことから、地域医療政策学は広義では「Public Health」の一分野である。

しかしながら、わが国では戦後、GHQによりすべての医学部に「公衆衛生学講座」が設置されたが、「Public Health」の本質が理解されないまま、衛生学講座とともにその姿が医学部から失われつつある。

その一方で、「Public Health」の本質をみなそうとする動きが2000年に始まった。京都大学にわが国初の公衆衛生大学院 (School of Public Health) が新設され、2007年には東京大学、その後帝京大学、聖路加国際大学に設置された。これらは米国 Council on Education for Public Health に認定されるための基本科目「生物統計学」、「疫学」「医療管理学」「社会・行動科学」および「環境保健科学」を置く必要があり、その数は米国の30大学に比べわが国ははるかに少ない。このことはわが国が「Public Health」を重視してこなかった証でもある。

発表会ではPublic Healthの必要性とともに研究費の取り方、留学の仕方をお話しします。

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Maternal nutritional status during pregnancy in Shimane Prefecture :
Fourth report - A comparison by meal skipping -

発表者 (presenters) : 籠橋有紀子

所属 (affiliation) : 島根県立大学看護栄養学部

抄録 (abstract)

【Background】 It is reported that the birth rate of low birth weight babies in Shimane prefecture is the third largest nationwide, and the average of birth weight is reported to be about 30 g less than the national average, and there is a possibility of various risks in the future of the babies.

【Purpose】 We investigate nutritional intake situation, dietary behavior, and food consciousness of pregnant women in Shimane Prefecture and we are studying the relevance to birth weight of babies.

【Methods】 In this study, we examined the frequency of food intake in 26 pregnant women from 10 to 12 weeks (early), around 26 weeks (middle) and 36 weeks (late), and compared the nutrient intake by the difference in the state of meal skipping (skipped vs non-skipped) during pregnancy and birth weight of babies.

【Results & Discussion】 In the early pregnancy group, 38.4% of pregnant women skipped meals more than once a week, and it was suggested that many of the nutrients were less than the amount recommended by the Ministry of Health, Labour and Welfare, Japan. In the middle and late pregnancy groups, 23.0% and 30.7% of pregnant women skipped meals more than once a week, respectively. The average of birth weight of babies were 2993.3 ± 384.1 grams in the non-skipped group and 3102.7 ± 273.8 grams in the skipped group at the early pregnancy and there were no significant differences. We are currently increasing the case number and investigating nutritional situation during pregnancy. This study was approved by the institutional Ethics Committee.

発表者： 大学院生 ■ 大学院生以外 □

タイトル (title) : Maternal nutritional status during pregnancy in Shimane Prefecture :

Second report - Comparison among early, middle and late pregnancy -

発表者 (presenters) : 中谷陽子

所属 (affiliation) : : 島根県立大学看護栄養学部

抄録 (abstract)

【Background】 In Shimane prefecture, the birth rate of low birth weight infants is higher than the national average, and the incidence of future non-communicable disease may increase.

【Purpose】 To investigate relationship between nutritional intake and birth weight of offspring in pregnant women in Shimane prefecture.

【Methods】 In this study, we examined the food intake, We examined food intake, dietary and health consciousness in 26 pregnant women (average age, 29.8 ± 4.6 years) from 10 to 12 weeks (early), around 26 weeks (middle) and 36 weeks (late) of gestation. We then analyzed the relationship between nutrient intake in each pregnancy period and birth weight.

【Results & Discussion】 Among 26, 14 were primiparas (53.8%) and 12 were multiparas (46.2%). Twenty-three (88.5%) had occupation, and three (11.5%) did not. Four (15.4%), 21 (80.8%), and one (3.8%) women had pre-pregnancy BMI in the "low body weight (≤ 18.5)", "normal ($18.5 \leq < 25.0$)", and "obese ($25.0 \leq < 30.0$)" range, respectively. The average hemoglobin values were 12.5 ± 0.6 g/dl, and 11.2 ± 0.7 g/dl in early and late pregnancy, respectively. The average increase in body weight during pregnancy was 10.4 ± 3.2 kg, and the average birth weight of the offspring was 3035.4 ± 344.2 g. The average birth weight of boys (15, 57.7%) and girls (11, 42.3%) was 3112.7 ± 346.1 g and 2929.9 ± 327.5 g, respectively. One (3.8%) was less than 2500 g. There was no correlation between the birth weight and pre-pregnancy BMI or weight gain during pregnancy. The amount of nutrient intake in most of the pregnant women in each pregnancy period is less than that recommended by the Ministry of Health, Labor and Welfare. Among 26, twenty-two (84.6%, early), 20 (76.9%, middle), and 16 (61.5%, late), respectively, reported having stress and fatigue. The average birth weight tended to be heavier in the non-stressed group than in the stressed group. The total scores for dietary behavior and food consciousness were not different at each pregnancy period. We are currently investigating the nutritional status at the one-month checkup. This study was approved by the institutional Ethics Committee.