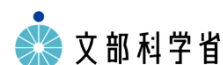


Book of Abstracts



文部科学省 私立大学研究ブランディング事業
A MEXT Private University Research Branding Project



顎骨疾患の集学的研究拠点形成

Tokyo Dental College, Multidisciplinary Research Center for Jaw
Disease (MRCJD)

Asian Rising Sun Symposium at Tokyo Dental College 2019

2019.6.29 (Sat) 13:00-17:30

会場：東京歯科大学水道橋校舎西棟ラウンジ

ARSS 2019 Jun. 29, Sat.

(Honorifics omitted)

13:00 : Open Remarks:

Tatsuya Ichinohe (Vice-President, Tokyo Dental College)

Akira Yamaguchi (Project Leader, Tokyo Dental College Research Branding Project)

Session I

Moderator: Satoru Matsunaga (Department of Anatomy, Tokyo Dental College)

Keisuke Sugahara (Department of Oral Pathobiological Science and Surgery, Tokyo Dental College)

13:05 : Lecture I: Outcomes of oral squamous cell carcinoma correlated with imaging feature: perineural encasement and bone destruction pattern

Chena Lee (Department of Oral & Maxillofacial Radiology, College of Dentistry, Yonsei University)

13:35 : Lecture II: Normalizing tumor microenvironment for cancer treatment

Ming-Heng Wu (Graduate Institute of Translational Medicine, College of Medical Sciences and Technology, Taipei Medical University)

Session II

Moderator: Yuichiro Kikuchi (Department of Microbiology, Tokyo Dental College)

Ryouichi Satou (Department of Epidemiology and Public Health, Tokyo Dental College)

14:05 : Lecture III: *Treponema denticola* TDE_0344, an AbrB-like transcriptional regulator, is involved in switching of the flagellar motor

Keiko Yamashita (Department of Periodontology, Tokyo Dental College)

14:35 : Lecture IV: Analysis of phototoxin taste correlates nucleophilicity to Type-1 phototoxicity

Eun Jo Du (Department of Anatomy and Cell Biology School of Medicine, Sungkyunkwan University)

15:05 : Coffee Break (15 min)

Session III

Moderator: Toshihide Mizoguchi (Oral Health Science Center, Tokyo Dental College)

Kento Odaka (Department of Oral and Maxillofacial Radiology, Tokyo Dental College)

15:20 : Keynote Lecture: HIV-mediated cellular signaling and bone pathophysiology

Tadahiro Iimura (Department of Pharmacology, Graduate School of Dental Medicine, Hokkaido University)

16:00 : Lecture V: Chemosensory perception in human brain -The interaction of taste and smell as a simplified flavour model-

Suen Long Kiu (Novus Life Sciences Limited)

Session IV

Moderator: Takenobu Ishii (Department of Orthodontics, Tokyo Dental College)
Takashi Nakamura (Department of Biochemistry, Tokyo Dental College)

16:30 : Lecture VI: Odontogenic keratocyst - The role of PTCH1 and Hedgehog signaling in its pathogenesis

Zhang Jianyun (Department of Oral Pathology, Peking University School of Stomatology)

17:00 : Lecture VII: Multi-layered mutation in hedgehog-related gene in patient with Gorlin syndrome
Shoko Onodera (Department of Biochemistry, Tokyo Dental College)

17:30 : Closing Remarks:

Masatsugu Hashimoto (Vice-President, Tokyo Dental College)

18:30 : Post Symposium Reception

[Keynote Lecture]

HIV-mediated cellular signaling and bone pathophysiology

Tadahiro Iimura, D.D.S., Ph. D.

Department of Pharmacology, Graduate School of Dental Medicine,
Hokkaido University

The lifespan of patients who have HIV infection has increased significantly with global HIV epidemic treatment in last few decades, and simultaneously low bone mass has emerged as a significant comorbidity. C-C chemokine receptor 5 (CCR5) is a co-receptor of macrophage-tropic viruses including HIV. Epidemiological and pathological findings have suggested that functional loss in CCR5 correlates with lower incidences of HIV transmission and bone destruction diseases. However, physiological roles of CCR5 in bone metabolism have not been well documented. We first observed that blockades of human CCR5 by anti-hCCR5 neutralizing antibody obviously inhibited human osteoclastogenesis in dose-dependent manner, without affect to osteoblast differentiation. Ccr5-deficient mice had significantly increased number and size of osteoclasts, although they did not show significant difference in BMD compared to their wild-type littermates. Interestingly, Ccr5-deficient mice were less susceptible to RANKL-induced bone loss, suggesting functional impairment of osteoclasts. Live imaging and super-resolution microscopy analyses revealed that Ccr5-deficient osteoclasts showed larger in size and disorganized their motility, cytoskeletal rearrangement and cell-attachment machineries including integrins, thus leading decreased bone resorption activity. Our further molecular and cellular analyses suggested that CCR5-mediated signal was associated with c-src and small GTPase activation that was required for proper osteoclasts function. These data unveil unique and essential roles of CCR5 in bone metabolism and bone destruction diseases, which has experimentally provided an evidence for skeletal merits of HIV-infected patients with anti-CCR5 therapy. Our finding also has implications for novel drug development against bone-destructive diseases with targeting CCR5-mediated signaling.

Tadahiro Iimura, D.D.S., Ph.D

2019 - Present Professor, Hokkaido University, Graduate School of Dental Medicine
2016 - 2019 Professor, Ehime University, Graduate School of Medicine
2015 - 2019 Professor, Ehime University, Proteo-Science Center (PROS)
2013 - 2014 Associate Professor, Ehime University, Proteo-Science Center (PROS)
2009 - 2013 Associate Professor, Tokyo Medical and Dental University, Global COE
2002 - 2008 Senior Research Associate, Stowers Institute for Medical Research (Kansas City)
2000 - 2002 Researcher, Institute for Developmental Biology in Marseille (France)
1995 Ph.D. Tokyo Medical and Dental University, Graduate School
1991 Dentist, Hokkaido University, School of Dental Medicine

Publications

- [1] J.W. Lee, A. Hoshino, K. Inoue, T. Saitou, S. Uehara, Y. Kobayashi, S. Ueha, K. Matsushima, A. Yamaguchi, Y. Imai, T. Iimura, The HIV co-receptor CCR5 regulates osteoclast function, *Nat Commun*, 8 (2017) 2226.
- [2] H. Yamane, A. Takakura, Y. Shimadzu, T. Kodama, J.W. Lee, Y. Isogai, T. Ishizuya, R. Takao-Kawabata, T. Iimura, Acute development of cortical porosity and endosteal bone formation from the daily but not weekly short-term administration of PTH in rabbit, *PLoS One*, 12 (2017) e0175329.
- [3] A. Takakura, J.W. Lee, K. Hirano, Y. Isogai, T. Ishizuya, R. Takao-Kawabata, T. Iimura, Administration frequency as well as dosage of PTH are associated with development of cortical porosity in ovariectomized rats, *Bone Res*, 5 (2017) 17002.
- [4] M. Sugiyama, T. Saitou, H. Kurokawa, A. Sakaue-Sawano, T. Imamura, A. Miyawaki, T. Iimura, Live imaging-based model selection reveals periodic regulation of the stochastic G1/S phase transition in vertebrate axial development, *PLoS Comput Biol*, 10 (2014) e1003957.
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- [7] A. Hoshino, S. Ueha, S. Hanada, T. Imai, M. Ito, K. Yamamoto, K. Matsushima, A. Yamaguchi, T. Iimura, Roles of chemokine receptor CX3CR1 in maintaining murine bone homeostasis through the regulation of both osteoblasts and osteoclasts, *J Cell Sci*, 126 (2013) 1032-1045.
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- [9] T. Iimura, X. Yang, C.J. Weijer, O. Pourquie, Dual mode of paraxial mesoderm formation during chick gastrulation, *Proc Natl Acad Sci U S A*, 104 (2007) 2744-2749.
- [10] T. Iimura, O. Pourquie, Collinear activation of Hoxb genes during gastrulation is linked to mesoderm cell ingression, *Nature*, 442 (2006) 568-571.

[Lecture I]

Outcomes of oral squamous cell carcinoma correlated with imaging feature: perineural encasement and bone destruction pattern

Department of Oral & Maxillofacial Radiology, College of Dentistry, Yonsei University
Chena Lee

Background: Up-to-date, the prognosis of oral squamous cell carcinoma has not been improved dramatically even though advancement in diagnostic and treatment modalities were made. Tumor cell differentiation and perineural invasion (PNI) are known as intermediate risk factors affecting early locoregional recurrence. However, the relationship between PNI and recurrence has yet to reach consensus, and the degree of differentiation is somewhat subjective. With the substantial development in imaging technology, it is necessary to provide imaging feature as supplementary information for expecting prognosis of OSCC patient.

Objective: The primary aim of this study was to identify diagnostic imaging findings associated with poor outcomes in oral squamous cell carcinoma of mandible.

Material and methods: All mandibular SCC cases (n=66) diagnosed in Dental Hospital, Yonsei University College of Dentistry from 2006 to 2016 were retrospectively reviewed. Cases were excluded if they had not undergone surgery or had pre-operative images with poor quality for evaluation. Pre-operative computed tomography (CT) and magnetic resonance imaging (MRI) were evaluated to classify lesions into 3 grades according to the aggressiveness in bone involvement pattern. Also, inferior alveolar nerve (IAN) encasement was evaluated. Maximum diameter of the tumor was measured. All imaging features were reached consensus under the agreement of two oral and maxillofacial radiologists with 5 and 15 years of experience. The prognosis, locoregional recurrence, node metastasis, distant metastasis, and death or hospice were correlated with imaging findings. Also, histopathologic assessment was correlated with imaging bone involvement pattern and IAN encasement.

Result: Total 52 cases (31 males, 21 females) were reviewed. According to imaging evaluation system, 29, 20 and 3 cases were grouped into grade 1, 2 and 3 respectively. With the histologic examination, 20, 27, and 5 cases were confirmed as well, moderate and poor differentiated state respectively. Imaging grades were different from histologic differentiation. Imaging grade 1 cases presented lower locoregional recurrence rate compared to well differentiated cases. Imaging grade 3 cases presented higher hospice/death rate compared to the poorly differentiated cases. When combined imaging grade 2-3 and well-poor differentiation group, locoregional recurrent rate became higher. There were 22 cases showing IAN encasement in image while 13 cases confirmed as perineural invasion in histopathologically. Imaging IAN encasement cases showed slightly higher locoregional recurrence rate compared to perineural invasion cases.

Curriculum Vitae

Chena Lee (D.D.S., Ph.D.)

2008. 3 ~ 2012. 2 Seoul National University, School of Dentistry

2014. 9 ~ 2016. 2 Seoul National University, School of Dentistry, Ph.D

2016. 3 -2017. 2 Fellow, Dept. Oral & Maxillofacial Radiology, Seoul National University Dental hospital

2017. 3 ~ 2019. 2 Fellow, Dept. Oral & Maxillofacial Radiology, Yonsei University College of Dentistry

2013. 3 – 2016. 2 Residency, Dept. Oral & Maxillofacial Radiology, Seoul National University Dental hospital

2019.3 ~ present: Clinical assistant professor, Yonsei University College of Dentistry

Publications

Prognosis in case of nerve disturbance after mandibular implant surgery in relation to computed tomography findings and symptoms.

Na JY, Han SS, Jeon K, Choi YJ, Choi SH, Lee C.

J Periodontal Implant Sci. 2019 Apr 19;49(2):127-135.

Performance of dental pattern analysis system with treatment chronology on panoramic radiography.

Lee C, Lim SH, Huh KH, Han SS, Kim JE, Heo MS, Yi WJ, Lee SS, Choi SC.

Forensic Sci Int. 2019 Apr 18;299:229-234.

Organized hematoma of temporomandibular joint.

Lee C, Yook JI, Han SS.

Imaging Sci Dent. 2018 Mar;48(1):73-77.

Morphological analysis of the lower second premolar for age estimation of Korean adults.

Lee JH, Lee C, Battulga B, Na JY, Hwang JJ, Kim YH, Han SS.

Forensic Sci Int. 2017 Dec;281:186.e1-186.e6.

Therapeutic effect of intraductal irrigation of the salivary gland: A technical report.

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Shin JM, Lee C, Kim JE, Huh KH, Yi WJ, Heo MS, Choi SC, Lee SS.

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Imaging Sci Dent. 2016 Jun;46(2):103-8.

Keratoameloblastoma: a case report and a review of the literature on its radiologic features.

Lee C, Park BJ, Yi WJ, Heo MS, Lee SS, Huh KH.

Oral Surg Oral Med Oral Pathol Oral Radiol. 2015 Nov;120(5):e219-25.

[Lecture II]

Normalizing tumor microenvironment for cancer treatment

Graduate Institute of Translational Medicine, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

Ming-Heng Wu

Abstract

Recent studies on tumor microenvironment have changed the traditional tumor cell-centric view of cancer. This talk will cover two fibrosis-associated cancer types, oral and hepatic carcinoma, in which activated fibroblasts or myofibroblasts are dominant components in tumor stroma and could be potential theranostic targets. We will report that galectin-1 (Gal-1), a β -galactoside binding protein, is up-regulated in fibrotic stroma which regulates fibrotic disease progression and correlates with the poor prognosis of cancer patients. Targeting Gal-1 in activated fibroblasts or carcinoma-associated fibroblasts (CAFs) suppresses multiple pro-inflammatory cytokine production and ameliorates CAF-augmented cancer cell growth and malignancy including stem cell-like properties, invasion and migration abilities. Gal-1 modulates multiple fibrogenic and inflammatory signal pathways for fibroblast activation through glycosylation-dependent mechanisms. Therefore, targeting Gal-1 could be a feasible therapy for fibrosis-related cancers.

References:

1. Wu et al. Scientific Reports 2017(7):11006.
2. Lin et al. The Journal of Investigative Dermatology 2015(135):258-268.
3. Wu et al. Angiogenesis. 2014(17):839–849
4. Wu et al. Clinical Cancer Research 2011(17):1306-1316

Keywords:

Galectin-1, fibrosis, and carcinoma-associated fibroblasts, stem cell-like properties

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Education

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
National Cheng Kung University, Taiwan	Ph.D.	2010	Basic Medical Sciences

Experience

2018~now **Associate professor**, Graduate Institute of Translational Medicine, Taipei Medical University

2012~2018 **Assistant professor**, Graduate Institute of Translational Medicine, Taipei Medical University

2007~2009 **Research scholar**, Department of Pathology, University of Rochester, Rochester, NY, U.S.A.

Honor and awards

2016-2018 **Travel Grant Award**, the 75-77th Annual Meeting of the Japanese Cancer Association, Japan

2015.12 **Outstanding Poster Award**, 2015 Glycoscience Symposium, Taipei, Taiwan

2015.12 **Excellent Poster Award**, Taiwan Genomics and Genetics Society, Taiwan

Research Interest

Fibrosis-associated diseases, galectins, glycobiology, and oral cancer biomarkers

Publications

1. Chiang WF, Cheng TM, Chang CC, Pan SH, Changou CA, Chang TH, Lee KH, Wu SY, Chen YF, Chuang KH, Shieh DB, Chen YL, Tu CC, Tsui WL and **Wu MH***. Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) promotes EGF receptor signaling of oral squamous cell carcinoma metastasis via the complex N-glycosylation. **Oncogene** **2018**, **37**, 116–127 (**corresponding author**)
2. **Wu MH**, Luo JD, Wang WC, Chang TH, Hwang WL, Lee KH, Liu SY, Yang JW, Chiou CT, Chang CH, Chiang WF*. Risk analysis of malignant potential of oral verrucous hyperplasia: a follow-up study of 269 patients and copy number variation analysis. **Head & Neck**. **2018**, **40(5)**, 1046-1056
3. **Wu MH***, Chen YL, Lee KH, Chang CC, Cheng TM, Wu SY, Tu CC, Tsui WL. Glycosylation-dependent galectin-1/neuropilin-1 interactions promote liver fibrosis through activation of TGF- β - and PDGF-like signals in hepatic stellate cells. **Scientific Reports** **2017(7):11006-**. (**corresponding author**)
4. Lin YT, Chen JS, **Wu MH**, Hsieh IS, Liang CH, Hsu CL, Hong TM, Chen YL. Galectin-1 Accelerates wound Healing by Regulating Neuropilin-1 /Smad3/NOX4 Pathway and ROS Production in Myofibroblasts. **The Journal of Investigative Dermatology** **2015(135):258-268**.
5. **Wu MH**, Ying NW, Hong TM, Chiang WF, Lin YT, Chen YL*. Galectin-1 induces vascular permeability through the neuropilin-1/vascular endothelial growth factor receptor-1 complex. **Angiogenesis**. **2014(17):839–849**.
6. **Wu, M.H.**, Hong, H.C., Hong, T.M., Chiang, W.F., Jin, Y.T., and Chen, Y.L. Targeting Galectin-1 in Carcinoma-Associated Fibroblasts Inhibits Oral Squamous Cell Carcinoma Metastasis by Downregulating MCP-1/CCL2 Expression. (2011) **Clinical Cancer Research** **17**, 1306-1316.

[Lecture III]

***Treponema denticola* TDE_0344, an AbrB-like transcriptional regulator, is involved in switching of the flagellar motor**

Department of Periodontology, Tokyo Dental College
Keiko Yamashita

Periodontitis is a prevalent oral infectious disease which causes inflammation of periodontal tissue and tooth loss. Subgingival plaque samples from severe periodontal lesions harbor microflora which are dominated by Gram-negative bacteria and spirochetes. An oral spirochete, *Treponema denticola*, is a major pathogen of periodontitis. *T. denticola* has active motility and reported to penetrate into host tissue. Also, this microorganism has several virulence factors, for instance, Dentilisin and major outer sheath protein (Msp) in outer membrane (outer sheath). Dentilisin and Msp exist as a protein complex. And inactivation of Dentilisin was reported to affect the expression of Msp. Therefore, we hypothesized that their expressions might have some relationship and be regulated at DNA level through unknown regulation mechanism.

First, we analyzed DNA expression profile of Msp-deficient *T. denticola* with DNA microarray. We found some genes upregulated in the mutant, including potential DNA binding protein. Among these genes, we focused on TDE_0344, which encodes an AbrB-like transcriptional regulator. To investigate the role of TDE_0344 in the virulence of *T. denticola*, we constructed TDE_0344 deficient mutant by homologous recombination. Using the mutant, we first examined the growth rate and colony morphology. The diameters of the colonies formed by the mutant were significantly smaller than those of wild type, while the growth rate of the mutant was same as that of wild type. To investigate this phenotypic change, DNA microarray and real-time PCR were carried out. Contrary to our expectations, deletion of TDE_0344 did not affect the expressions of Dentilisin and Msp genes. However, interestingly, the gene expression analysis revealed that genes related to flagellar assembly and flagellar motor components were significantly upregulated in the mutant. Therefore, we carried out further experiments on the motility of the mutant. Microscopic observation using time-lapse imaging method revealed that deletion of TDE_0344 affected the moving pattern of *T. denticola*.

These findings suggest that TDE_0344 plays a certain role in the virulence of *T. denticola* via regulation of genes involved in the regulation of motility.

Keiko Yamashita, DDS, PhD

2013	D.D.S, Tokyo Dental College, Tokyo Japan
2013-2015	Student of Postgraduate Specialty Track (Full-time)
2015-2019	PhD, Tokyo Dental College Graduate School of Dental Science (Department of Periodontology)
2019-	Resident, Tokyo Dental College Suidobashi Hospital (Department of Periodontology)

AWARD

2019	Alumni Association President Award, Tokyo Dental College Graduate School of Dental Science
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[Lecture IV]

Analysis of Phototoxin Taste Closely Correlates Nucleophilicity to Type-I Phototoxicity

Eun Jo Du^{1,3}, Tae Jung Ahn¹, Hwajin Sung¹, HyunJi Jo¹, Hyung-Wook Kim⁴, Seong-Tae Kim², KyeongJin Kang^{1,3*}

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Abstract

Pigments often inflict tissue-damaging and pro-aging toxicity upon light illumination by generating free radicals and reactive oxygen species (ROS). However, the molecular mechanism by which organisms sense phototoxic pigments is unknown. Here, we discover that Transient Receptor Potential Ankyrin 1-A isoform (TRPA1(A)), previously shown to serve as a receptor for free radicals and ROS induced by photochemical reactions, enables *Drosophila melanogaster* to aphotically sense phototoxic pigments for feeding deterrence. Thus, TRPA1(A) detects both cause (phototoxins) and effect (free radicals and ROS) of photochemical reactions. A group of pigment molecules not only activate TRPA1(A) in darkness, but also generate free radicals upon light illumination. Such aphotic detection of phototoxins harboring the type-I (radical-generating) photochemical potential requires the nucleophile-sensing ability of TRPA1. Besides, agTRPA1(A) from malaria-transmitting mosquitoes *Anopheles gambiae* heterologously produces larger current responses to phototoxins than *Drosophila* TRPA1(A), similar to their disparate nucleophile responsiveness. Along with TRPA1(A)-stimulating capabilities, type-I phototoxins exhibit relatively strong photo-absorbance and low energy gaps between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). Therefore, TRPA1(A) activation is highly concordant to type-I phototoxicity compared to those photochemical parameters. Collectively, nucleophile sensitivity of TRPA1(A) allows flies to taste potential phototoxins for feeding deterrence, preventing post-ingestive photo-injury. Conversely, pigments need to bear high nucleophilicity (electron-donating propensity) to act as type-I phototoxins, which is consistent with the fact that transferring photo-excited electrons from phototoxins to other molecules causes free radicals. Thus, identification of a novel sensory mechanism in *Drosophila* reveals a property fundamental to type-I phototoxins.

Curriculum Vitae (Last updated: 2019-05-29)

Eun Jo Du (Ph.D. candidate)

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Education and Training

B.S.	Life science and environmental technology, The Catholic University of Korea , 2006~2013
M.S. and Ph.D. combined course	School of medicine, Sungkyunkwan University , 2013~Present (Advisor: KyeongJin Kang, Ph. D)

Publications

Du, E. J., Ahn, T. J., Sung, H., Jo, H., Kim, H.-W., Kim, S.-T., & Kang, K. (2019). Analysis of phototoxin taste closely correlates nucleophilicity to type 1 phototoxicity. *Proceedings of the National Academy of Sciences*, 201905998. <https://doi.org/10.1073/pnas.1905998116>

Yeon, J., Kim, J., Kim, D. Y., Kim, H., Kim, J., **Du, E. J.**, ... Kim, K. (2018). A sensory-motor neuron type mediates proprioceptive coordination of steering in *C. elegans* via two TRPC channels. *PLoS Biology*, 16(6), 1–26. <https://doi.org/10.1371/journal.pbio.2004929>

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Du, E. J., Ahn, T. J., Choi, M. S., Kwon, I., Kim, H., Kwon, J. Y., & Kang, K. (2015). *The Mosquito Repellent Citronellal Directly Potentiates Drosophila TRPA1*, Facilitating Feeding Suppression. *Molecules and Cells*, 38(9), 1–7.

Award and patent

Award Best Presentation Award, Korean Society for Drosophila, 2017

Patent Insect repellent comprising hydrogen peroxide, 10-2014-0121050, 2014

Invited Talks

- Korean Society for Drosophila, Summer research presentation, Boryeong, Korea, 2017
 - International Symposium of Korean Society for Chemical Senses and Ingestive Behavior, ERICA Campus, Hanyang University, Ansan, Korea, 2016
-

[Lecture V]

Chemosensory perception in human brain: The interaction of taste and smell as a simplified flavor model

Novus Life Sciences Limited
Long Kiu Suen

Flavor perception with the sensation of taste and smell in a human brain have never been well studied until the establishment of different imaging methods such as functional Magnetic Resonance Imaging (fMRI). Even flavor perception is performed by everyone during food consumption and drug intakes, the full nature is yet to be clarified. In general, flavor is a food-related percept integrating senses from different systems such as taste, smell and vision inside a human brain. As taste and smell constituted the two major elements of the flavor perception, two studies were conducted to investigate the chemosensory perception of taste and smell and their possible neural interaction detectable by fMRI.

In the first study, the brain responses to the stimulations of a sour taste, mango smell and their combined form as a flavor were investigated. The sour taste activated the primary taste cortex, insula, whereas the mango smell delivered in retronasal route activated the primary smell cortices, olfactory tubercle. Mixing the stated agents together, the flavor stimulant activated the insula, frontal operculum and prefrontal cortex which are commonly activated by different flavor stimuli and are suggested to be involved in multisensory integration.

In the second study, the flavor-processing network in terms of the effective connectivity was investigated based on the fMRI result in the first study using dynamic causal modelling. The network was proved to be driven at the anterior insula and modulated by the taste and smell at the connection from frontal operculum to anterior insula. These showed the causal functional relationship (effective connectivity with direction) between frontal operculum and anterior insula during flavor perception.

The results in these studies provided more neuroimaging data for taste, smell and their interactions with some insights to the mechanism of flavor perception, and thereby, improved the understanding to food consumption process in the field of neuroimaging and chemosensory system.

Justin, Suen Long Kiu

BEng (MedE), MPhil

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Working experience

- Feb 2018 – Present
Co-founder, Ossfila Technology Limited, Hong Kong
 - Execution planning and management
 - Business development on 3D-printer filament
- Oct 2018 – Mar 2019
Assistant Director, Novus Life Sciences Limited, Hong Kong
 - Management and work allocation for the team
 - Fund Raising, including preparation of pitch deck and pitching
 - Operations and internal control, including administrative work, bookkeeping and internal audit
 - Business development for biomaterial and diagnostic products
- Jun 2017 – Sep 2018
Senior Manager, Novus Life Sciences Limited, Hong Kong
 - Management and work allocation for the team
 - Research and development of bone-health technologies, including biomaterial product and diagnostic product
 - Operations, including fund raising application, bookkeeping, account management
 - Business development, including shortlisting potential clients
- Sep 2014 – Dec 2016
Teaching and research assistant, HKU & Tokyo Dental College, Japan
 - Fund application, clinical tender review, academic manuscript drafting, academic conference preparation, participant recruitment, teaching material preparation, tutorial for undergraduates

Qualification

Sep 2014 – Dec 2016

Master of Philosophy, the University of Hong Kong

Sep 2011 – Aug 2014

Bachelor of Biomedical Engineering, the University of Hong Kong

Postgraduate research field

Functional imaging of flavor perception (taste and smell) on human brain

- Designing and modifying stimulation system (both hardware and software) for experiment using MRI
- Fabricating hardware (involving electrical and electronic circuit)
- Preventive and corrective maintenance on stimulation system
- Keeping a mindset of 'safety is the highest priority'
- Analyzing data with different statistical software (Matlab, SPM, SPSS)
- Networking with clinicians, academic experts, and students

Publication

- AWK Yeung, HC Tanabe, JKL Suen, TK Goto. Taste intensity modulates effective connectivity from the insular cortex to the thalamus in humans. *NeuroImage*. 2016;135:214-222. (Impact factor 2015: 5.463)
- TK Goto, AWK Yeung, JKL Suen, BSK Fong, Y Ninomiya. High resolution time-intensity recording with synchronized solution delivery system for the human dynamic taste perception. *Journal of Neuroscience Methods*. 2015;245:147-155. (Impact factor 2015: 2.053)

Achievements

2018

Top 500 DeepTech Startup Worldwide
Hello Tomorrow South-East Asia Top 10 Startup
「招商杯」前海粵港澳青年創新創業大賽香港賽區銅獎
HKU Dreamcatcher Winner
Alibaba Jumpstarter Healthy Aging Group Winner

2017

[Lecture VI]

Odontogenic keratocyst - The role of PTCH1 and Hedgehog signaling in its pathogenesis

Peking University School of Stomatology
Jiayun Zhang, Tiejun Li

Objectives : Mutations in PTCH1 gene, a receptor in the Hedgehog (Hh) signaling, are responsible for Gorlin syndrome (GS) and are related in tumors associated with this syndrome. The aims of this series of studies were to determine the role of PTCH1 mutation and misregulation of the Hh signaling in the pathogenesis of GS-related and sporadic odontogenic keratocysts (OKCs).

Findings: Based on screening 73 sporadic and 30 GS-related OKCs, we identified PTCH1 mutations in 35.6% (somatic, 26/73) of sporadic cases and 83.3% (germ-line, 25/30) of GS-related OKCs. However, a much higher mutation rate (79%, 30/38) in sporadic OKCs was detected by analyzing epithelial samples separated from the fibrous capsules. The previously underestimated mutation rate in sporadic cases might be due to the masking effect of the attached stromal tissues. Mutations in other genes of the Hh signaling such as PTCH2, SUFU, and SMO were rare and their pathologic roles in OKC were uncertain. Using whole-exome sequencing (WES), we further characterized the mutational landscape of 5 OKC samples lacking PTCH1 mutation and revealed 22 novel mutations, among which two significantly altered genes (CDON and MAPK1) were predicted to affect Hh signaling activity in two cases. However no recurrent mutations were identified in the WES samples and validation cohort of 10 OKCs. Functional analysis revealed that PTCH1 mutations activated Hh signaling and resulted in aberrant cell proliferation via both classical and non-canonical Hh pathways.

Conclusions: Our data confirmed the high PTCH1 mutation rate in both GS-related and sporadic OKCs. In PTCH1-negative cases, other genetic alterations were rare, but could also be related to Hh signaling. These results suggested that an inhibitor of the Hh pathway may be effective for the treatment of OKCs.

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Education

- ☐ 2007-2010 Peking University Health Science Center (Beijing, China)
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- ☐ 2004-2007 Tianjin Medical University (Tianjin, China)
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- ☐ 1999-2004 Tianjin Medical University (Tianjin, China)
Major: Bachelor of Oral Science

Work Experience

- ☐ 2010-current Department of Oral Pathology, Peking University School and Hospital of Stomatology
- ☐ resident doctor and assistant research fellow (2010-2016)
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Research Interests

- ☐ odontogenic cyst and tumor
- ☐ Raman imaging application in oral science
- ☐ Digital pathology

Research and Academic Employment

Secretary for Administrative Affairs / Youth member of Society of Oral Pathology, Chinese Stomatological Association

Publications

- (1) Tao Chen, # Chen Cao, # Jianyun Zhang, # Aaron M Streets, Yanyi Huang, * Tiejun Li*. Stimulated Raman Scattering Micro-dissection Sequencing (SMD-Seq) for Morphology-specific Genomic Analysis of Oral Squamous Cell Carcinoma. bioRxiv posted online on March 28, 2017 (2017) . doi: 10.1101/121616
- (2) J.-Y. Zhang, Q. Dong, T.-J. Li*. Differences in collagen fibres in the capsule walls of parakeratinized and orthokeratinized odontogenic cysts, Int. J. Oral Maxillofac. Surg, 2011, 40; 1296–1300
- (3) Guo Y-Y, Zhang J-Y, Li X-F, Luo H-Y, Chen F*, Tie-Jun Li*, PTCH1 Gene Mutations in Keratocystic Odontogenic Tumors: A Study of 43 Chinese Patients and a Systematic Review, PLoS ONE, 2013, 8(10): e77305
- (4) Yingying Hong, Jianyun Zhang, Heyu Zhang, Xuefen Li, Jiafei Qu, Jiemei Zhai, Lei Zhang, Feng Chen*, and Tiejun Li*. Heterozygous PTCH1 Mutations Impact the Bone Metabolism in Patients With Nevroid Basal Cell Carcinoma Syndrome Likely by Regulating SPARC Expression. Journal of Bone and Mineral Research, Vol. 31, No. 7, July 2016, pp 1413–1428
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[Lecture VII]

Multi-layered mutation in hedgehog-related gene in patient with Gorlin syndrome

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Gorlin syndrome is a genetic disease with a variety of symptoms that are attributed largely to heterozygous PTCH1 mutations. Hedgehog pathway encompasses many signaling cascades, however, as mutations other than PTCH1, only the SUFU or PTCH2 mutations have been reported as causes of Gorlin syndrome. We performed next generation sequencing analysis of Gorlin syndrome patient genes and found unexpected multi-layered mutations in hedgehog pathway which might affected development of Gorlin syndrome. We observed PTCH1 gene mutations in every cases we examined as expected, however, three out of four cases have mutations in other Hh receptors genes such as PTCH2 or BOC. There has been no previous reports showing whether single BOC mutation could cause Gorlin syndrome, although PTCH2 gene could be causative. Next we investigated somatic mutations in basal cell carcinoma (BCC) developed in Gorlin syndrome patient. It has been well known that hyper-activation of the Hh pathway either by alteration in PTCH1, SMO or SUFU was major driving force for BCC development in general which explain why Gorlin syndrome patient often have multiple BCCs and other tumors. However, the drivers for BCC development other than PTCH1 has not well elucidated. In Gorlin syndrome patients, BCC arises relatively later year of middle ages suggesting that other drivers for BCC development might exist. Recently, non-syndromic BCC has shown additional somatic mutations in other pathways besides the Hh pathway. We therefore examined the presence of mutations in syndromic BCCs. Multiple BCCs were detected in one Gorlin syndrome patient at 60 year old. This patient had operation to remove these BCCs. We obtained these resected tissues to examine additional mutations in each resected BCC tissues. These resected tissues were histologically confirmed as BCC and we then extracted genomic DNA from each resected BCC separately. 4 out of 10 samples were analyzed to find additional mutation by subtracting from DNA sequence of normal fibroblasts obtained from this patient. We could observe no common additional mutations, however, mutations are enriched in primary cilium related genes. We think that these observation suggested the possibility that abnormal primary cilium functions might contribute development of BCC in Gorlin syndrome patient.

ACADEMIC APPOINTMENT:
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LIST OF PUBLICATIONS:

Targeted reversion of induced pluripotent stem cells from patients with human cleidocranial dysplasia improves bone regeneration in a rat calvarial bone defect model.

Saito A, Ooki A, Nakamura T, Onodera S, Hayashi K, Hasegawa D, Okudaira T, Watanabe K, Kato H, Onda T, Watanabe A, Kosaki K, Nishimura K, Ohtaka M, Nakanishi M, Sakamoto T, Yamaguchi A, Sueishi K, Azuma T.

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Hasegawa D, Shino H, Onodera S, Nakamura T, Saito A, Watanabe K, Onda T, Nishimura K, Ohtaka M, Nakanishi M, Kosaki K, Yamaguchi A, Shibahara T, Azuma T.

PLOS ONE 2017 vol: 12 (10) pp: e0186879

Multi-layered mutation in hedgehog-related genes in Gorlin syndrome may affect the phenotype.

Onodera S, Saito A, Hasegawa D, Morita N, Watanabe K, Nomura T, Shibahara T, Ohba S, Yamaguchi A, Azuma T.

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Transplantation of human-induced pluripotent stem cells carried by self-assembling peptide nanofiber hydrogel improves bone regeneration in rat calvarial bone defects.

Hayashi K, Ochiai-Shino H, Shiga T, Onodera S, Saito A, Shibahara T, Azuma T

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Tsukinowa T, Onodera S, Yoshizawa Y, Saito A, Muramatsu T, Furusawa M, Azuma T.

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The comparison between single vs repeated administration of Wnt3A of HPDL cells

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