

Tokyo Dental College

Research Project

Asian Rising Stars Symposium 2024 July 27, 2024

Well-being Society Achieved by Maintaining and Improving

Oral-Maxillofacial Function at Every Stage of Life

(Well-being Project)

Program and Abstracts

Program

13:00-13:05: Opening Remarks

Tatsuya Ichinohe (Dean, Tokyo Dental College)

Session I Moderator : Takehito Ouchi (Department of Physiology, Tokyo Dental College) Tatsukuni Ohno (Oral Health Science Center, Tokyo Dental College)

13:05-13:35:Lecture I

Calvarial stem cells : guardians of cranial bone homeostasis and injury repair

Bo Li (State Key Laboratory of Oral Diseases, National Center for Stomatology, National Clinical Research Center for Oral Diseases, Department of Orthodontics, West China Hospital of Stomatology, Sichuan University)

13:35-14:05:Lecture II

PDLSC-conditioned medium reduces root resorption in delayed replantation of avulsed teeth

Lu Jia (Department of Physiology, School of Basic Medicine, Emergency Comprehensive Department, School of Stomatology, Hebei Medical University)

Session II Moderator : Masahide Koyachi (Department of Oral Pathobiological Science and Surgery, Tokyo Dental College)

Hitomi Sato (Department of Oral and Maxillofacial Radiology, Tokyo Dental College)

14 : 05-14 : 35 : Lecture Ⅲ

The volumetric medical image for accurate and reliable guided dentistry

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

14:35-15:05: Lecture IV

Content evaluation of dental radiology videos on YouTube

Wai Kan Andy Yeung (Oral and Maxillofacial Radiology, Applied Oral Sciences and Community Dental Care, Faculty of Dentistry, University of Hong Kong)

15:05-15:20:Coffee Break (15 min)

Session III Moderator : Takayuki Ueda (Department of Removable Prosthodontics and Gerodontology, Tokyo Dental College)

15: **20–16**: **00**: Keynote Lecture

The importance of oral function in older adults from the viewpoint of healthy Longevity

Masanori Iwasaki (Division of Preventive Dentistry, Department of Oral Health Science, Graduate School of Dental Medicine, Hokkaido University)

Session IV Moderator : Mamoru Yotsuya (Department of Fixed Prosthodontics, Tokyo Dental College)

Hideo Yonezawa (Department of Microbiology, Tokyo Dental College)

16 : 00-16 : 30 : Lecture V

A Morphological Approach to Understanding Swallowing Mechanisms \sim The genioglossus muscle is the only muscle that attaches to the epiglottis. \sim

Kei Kitamura (Department of Histology and Developmental Biology, Tokyo Dental College)

16:30-17:00:Lecture VI

Inhibiting symbiotic bacterial-fungal interaction alters in vitro biofilm formation and its cariogenic potential

Jian-Na Cai (School of Oral Stomatology, Binzhou Medical University)

17:00-17:05: Closing Remarks

Akira Yamaguchi (Well-being Project advisor, Tokyo Dental College)

[Lecture I]

Calvarial stem cells : guardians of cranial bone homeostasis and injury repair

Bo Li, DDS, DMD, PhD

Research Associate, Attending Physician State Key Laboratory of Oral Diseases, National Center for Stomatology, National Clinical Research Center for Oral Diseases, Department of Orthodontics, West China Hospital of Stomatology, Sichuan University.



Abstract :

Cranial bones constitute a protective shield for the vulnerable brain tissue. Unlike long bones, cranial bones possess unique properties in terms of developmental origin, osteogenesis progress, and anatomical structure. The major stem cell population for cranial bone resides in the suture mesenchyme, termed calvarial stem cells (CSCs). However, how CSCs contribute to cranial bone homeostasis and injury repair away from the suture remains elusive. Gli1+ cells have been identified as CSCs in vivo, and our short- and long-term lineage tracing demonstrates that Gli1+ CSCs can self-renew and display a suture-specific distribution pattern under physiological conditions. Upon calvaria injury, Gli1+ CSCs are activated and expanded, participating in injury repair and tissue regeneration by long-range migration along the dura mater. In addition, we found that the CXCL12-CXCR4 axis plays a pivotal role in guiding Gli1+ CSC migration during the healing process. Blocking the CXCL12-CXCR4 axis hampers injury repair and results in non-unions, further confirmed via genetic knockout(cKO) of Cxcr4 in Gli1-lineage cells. Of note, CXCR4 is a G protein-coupled receptor (GPCR) coupled to Gai, which inhibits Gas in activating protein kinase A(PKA). Intriguingly, mice expressing gain-of-function Gas mutant phenocopy Cxcr4 cKO mice with fewer Gli1+ CSCs recruited to the injury site and impaired healing. Conversely, mice expressing Gas loss-of-function mutant exhibit accelerated bone regeneration with increased Gli1+ CSC activation, aberrant Hedgehog signaling, and enhanced osteogenic differentiation. Dysregulated Hedgehog signaling is concomitantly amplified by injury through induced sonic hedgehog(SHH) expression. Furthermore, anti-SHH monoclonal antibody (mAb) treatment partially rescues the phenotype of Gas loss-of-function mutant mice. Altogether, our data indicate that CSCs are guardians of cranial bone homeostasis and injury repair, and the CX-CL12-Hedgehog signaling axis plays a critical role in regulating CSCs, shedding light on stem cell-based therapy.

2011-2016 Undergraduate, West China School of Stomatology, Sichuan University (SCU)
2014-2014 Visiting Undergraduate, Medical Center of Hamburg University (UKE)
2015-2015 Visiting Undergraduate, Osaka Dental University (ODU)
2016-2021 Postgraduate, West China School of Stomatology, Sichuan University (SCU)
2019-2021 Visiting Postgraduate, Harvard School of Dental Medicine (HSDM)
2021-Present Research Associate/Attending Physician, West China School of Stomatology, Sichuan University (SCU)

Research Fields of Interest

- 1. Craniofacial Bone and Suture Biology
- 2. Mesenchymal Stem and Progenitor Cells
- 3. Cellular Senescence and Aging
- 4. Head and Neck Oncology

Selected Honors

- 1. SAKURA Exchange Program in Science, Japan Science and Technology Agency(2015)
- 2. Keystone Symposia Scholarship, Keystone Symposia (2020&2020)
- 3. Postdoctoral Fellowship Award, China Postdoctoral Science Foundation (2022)
- 4. Excellent Paper Award, Sichuan Stomatological Association (2023)
- 5. First Prize for Poster, Chinese Stomatological Association (2023)
- 6. International Orthodontics Foundation (IOF) Young Research Grant Award (2024)

- Li B.*, Li J., Fan Y., Zhao Z., Li L., Okano H.*, Ouchi T*. Dissecting calvarial bones and sutures at single-cell resolution. *Biol Rev Camb Philos Soc.* 2023; 98(5): 1749-1767.(*: Co-corresponding)
- 2. <u>Li B.</u>*, Li J., Li B., Ouchi T., Li L., Li Y.*, Zhao Z*. A single-cell transcriptomic atlas characterizes age-related changes of murine cranial stem cell niches. *Aging Cell*. 2023; 22(11):e13980.(*: Co-corresponding)
- 3. Li J., Zhang Z., Tang J., Hou Z., Li L.*, <u>Li B</u>*. Emerging roles of nerve-bone axis in modulating skeletal system. *Med Res Rev.* 2024 ; 44(4) : 1867-1903.(* : Co-corresponding)
- 4. Weng Z., Wang Y., Ouchi T., Liu H., Qiao X., Wu C., Zhao Z., Li L., <u>Li B</u>*. Mesenchymal Stem/ Stromal Cell Senescence : Hallmarks, Mechanisms, and Combating Strategies. *Stem Cells Transl Med.* 2022 ; 11(4) : 356-371.(* : Corresponding)
- 5. Liu Y., Huang N., Qiao X., Gu Z., Wu Y., Li J., Wu C., <u>Li B.</u>*, Li L*. Knockdown of PGC1*a* suppresses dysplastic oral keratinocytes proliferation through reprogramming energy metabolism. *Int J Oral Sci.* 2023 ; 15(1) : 37.(* : Co-corresponding)
- 6. Weng Z., Zhang B., Wu C., Yu F., Han B., <u>Li B.</u>*, Li L*. Therapeutic roles of mesenchymal stem cell-derived extracellular vesicles in cancer. *J Hematol Oncol.* 2021 ; 14(1) : 136.(* : Co-corresponding)

[Lecture II]

PDLSC-conditioned medium reduces root resorption in delayed replantation of avulsed teeth

Lu Jia, DDS

PhD student Department of Physiology, School of Basic Medicine, Emergency Comprehensive Department, School of Stomatology, Hebei Medical University



Abstract :

Tooth avulsion is the most serious dental trauma, defined as the complete displacement of the tooth from its original alveolar. Dental replantation is the standard treatment for tooth avulsion, and periodontal healing is the ideal prognosis. However, root resorption is the most common and serious complication in delayed replantation of avulsed teeth, which may lead to anterior tooth loss in adolescents and affect aesthetics and health in physical and mental. Periodontal ligament stem cells (PDLSC) are considered to be the optimal cell for periodontal tissue repair and regeneration. Its conditioned medium can be used for cell-free therapy, which is convenient to obtain, fully utilizes bioactive factors, and avoids immune rejection and ethical concerns associated with stem cell transplantation. In this study, we collected clinical specimens and found high expression of osteoclast related factors and inflammatory factors in the periapical soft tissue of delayed replantation tooth. PDLSC-CM significantly promoted the healing of the periodontal ligament, reduced root resorption and inflammatory reactions in rats received delayed dental replantation. Moreover, PDLSC-CM inhibited the osteoclast formation and reduced M1 polarization in osteoclast precursors and Raw264.7 macrophages. In addition, proteomics data revealed that HAPLN1 was markedly downregulated in PDLSC-CM treated replantation roots, and overexpression of HAPLN1 cancelled the protective effect of PDLSC-CM on root resorption. In summary, our study uncovers that PDLSC-CM promotes periodontal ligament healing and reduces root resorption by downregulating HAPLN1 in delayed replantation of avulsed teeth. PDLSC-CM can be used as preservation medium for avulsed teeth, which is expected to be widely applied in clinical practice.

2013-2018	Bachelor	School of Stomatology, Hebei Medical University
2018-2021	Master	School of Stomatology, Nanjing Medical University
2021-2022	Dentist	Stomatological Hospital of Hebei Medical University
2022-Preser	nt PhD candidate	School of Basic Medicine, Hebei Medical University

Research Fields of Interest

- 1. The application of stem cells in oral diseases
- 2. The regulation of the nervous/vascular system in bone and dental metabolism

- Jia L.[#], Yang Z.[#], Sun L.[#], Zhang Q., Guo Y., Chen Y., Dai Y., & Xia Y.(2021). A three-dimensional-printed SPION/PLGA scaffold for enhanced palate-bone regeneration and concurrent alteration of the oral microbiota in rats. *Materials science & engineering. C, Materials for biological applications*, 126, 112173. https://doi.org/10.1016/j.msec.2021.112173
- 2. Shi Z., Jia L., Zhang Q., Sun L., Wang X., Qin X., & Xia Y.(2022). An altered oral microbiota induced by injections of superparamagnetic iron oxide nanoparticle-labeled periodontal ligament stem cells helps periodontal bone regeneration in rats. *Bioengineering & translational medicine*, 8(3), e10466. https://doi.org/10.1002/btm2.10466
- 3. Han L.[#], Guo Y.[#], Jia L.[#], Zhang Q., Sun L., Yang Z., Dai Y., Lou Z., & Xia Y.(2021). 3D magnetic nanocomposite scaffolds enhanced the osteogenic capacities of rat bone mesenchymal stem cells in vitro and in a rat calvarial bone defect model by promoting cell adhesion. *Journal of biomedical materials research. Part A*, 109(9), 1670-1680. https://doi.org/10.1002/jbm. a.37162
- 4. Xia Y., Zhao Y., Zhang F., Chen B., Hu X., Weir M. D., Schneider A., <u>Jia L.</u>, Gu N., & Xu H. H. K. (2019). Iron oxide nanoparticles in liquid or powder form enhanced osteogenesis via stem cells on injectable calcium phosphate scaffold. *Nanomedicine* : *nanotechnology, biology, and medicine*, 21, 102069. https://doi.org/10.1016/j.nano.2019.102069
- Guo X., Ma H., Cui Z., Zhao Q., Zhang Y., Jia L., Zhang L., Guo H., Zhang X., Zhang Y., Guan Y., & Ma H.(2024). Chronic Intermittent Hypobaric Hypoxia Reduces Hypothalamic N-Methyl-d-Aspartate Receptor Activity and Sympathetic Outflow in Spontaneously Hypertensive Rats. *High altitude medicine & biology*, 25(1), 77-88. https://doi.org/10.1089/ham.2023.0098

[Lecture III]

The volumetric medical image for accurate and reliable guided dentistry

Kento Odaka, DDS, PhD

Senior Assistant Professor Department of Oral and Maxillofacial Radiology, Tokyo Dental College



Abstract :

Imaging modalities such as CT and MRI are commonly employed in the oral and maxillofacial field for diagnostic and treatment planning purposes. These modalities can provide both qualitative and quantitative data, including information on the boundary and content of lesions, as well as volumetric data on the morphology of the patient's anatomical structures. The main theme of my research is to improve the precision and reliability of guided diagnosis and dental treatment through an interdisciplinary approach. This entails extracting any area from the data obtained, reconstructing it in three dimensions and using it as a basis for computer-aided design (CAD) for additive manufacturing (AM), extended reality (XR) and radiomics.

AM is the fabrication technique for a three-dimensional object from a CAD model with the material being added layer by layer. In our projects, the additive manufactured devices were used to physically guide the manipulation of the instruments in surgery and endodontic treatment as designed before the treatment. Furthermore, we have assessed the directly fabricated prostheses such as denture bases or clasps by AM with the aim of optimal designing for individual patients before manufacturing. XR is an umbrella term to refer to augmented reality (AR), virtual reality (VR), and mixed reality (MR). The advent of XR technology has enabled the realisation of simultaneous bidirectional communication including visual information, with the potential to revolutionise the field of education, clinical conferencing, and real-time guided surgery. Radiomics is a method that extracts a vast array of features from medical images through the utilisation of data-characterisation algorithms. Deep learning technology has a profound affinity with image recognition, including medical images, and is expected invaluable in the field of segmentation and diagnosis, with an understanding of its limitations.

In this presentation, I will showcase our work in the domains of oral and maxillofacial surgery, endodontics, and prosthodontics.

2012 DDS, Tokyo Dental College, Tokyo, Japan

- 2017 PhD, Graduate School of Dentistry, Tokyo Dental College, Tokyo, Japan
- 2017-2018 Assistant Professor, Department of Anatomy, Tokyo Dental College, Tokyo, Japan
- 2018-2021 Assistant Professor, Department of Oral and Maxillofacial Radiology, Tokyo Dental College, Tokyo, Japan
- 2021-Present Senior Assistant Professor, Department of Oral and Maxillofacial Radiology, Tokyo Dental College, Tokyo, Japan
- 2023-2024 Visiting Researcher, Department of Oral and Maxillofacial Surgery, Charité-Universitätsmedizin Berlin, Berlin, Germany

Research Fields of Interest

Image Segmentation, CAD, Additive Manufacturing, Biomechanics, Radiomics

- <u>Odaka K.</u>, Steffen C., Wagendorf O., Geißler S., Ebker T., Rubarth K., Nguyen T.T., Bortel E.L., Sarasaen C., Duda G.N., Heiland M., Voß J.O. Volumetric Evaluation of Osteotomy Gap Following Mandibular Bilateral Sagittal Split Osteotomy Using a Novel Semi-Automated Approach : A Pilot Study. *Clinical Oral Investigations* 28 : 358, 2024
- 2. Koyachi M., Sugahara K., Tachizawa K., Nishiyama A., <u>Odaka K.</u>, Matsunaga S., Sugimoto M., Tachiki C., Nishii Y., Katakura A. Enhanced Precision in Genioplasty : A Novel Intraoperative Spatial Repositioning Using Computer-Aided Design and Manufacturing Technology and a Holographic Mixed Reality Application. *Journal of Clinical Medicine* 12(23)7408, 2023
- Noguchi T., <u>Odaka K.</u>, Fukuda K. Clinical Application of Inferior Alveolar Nerve Block Device for Safe and Secure IANB by Any Operator. *Pain Research and Management* 2023 : 1-7, 2023
- 4. <u>Odaka K.</u>, Kamiyama S., Takizawa H., Takano N., Matsunaga S. Comparison of the fatigue life of pure titanium and titanium alloy clasps manufactured by laser powder bed fusion and its prediction before manufacturing. *Journal of Prosthodontic Research* 67(4): 626-32, 2023
- 5. Yamada M., <u>Odaka K.</u>, Kasahara N., Matsunaga S., Tamiya Y., Sako R., Furusawa M. A Case of Non-surgical Root Canal Treatment Using an Operating Microscope on Type III-b Dens Invaginatus. *Operative Dentistry, Endodontology and Periodontology* 1(1) : 97-104, 2021

[Lecture IV]

Content evaluation of dental radiology videos on YouTube

Wai Kan Andy YEUNG, BDS, PhD

Tutor in Radiography Oral and Maxillofacial Radiology, Applied Oral Sciences and Community Dental Care, Faculty of Dentistry, University of Hong Kong



Abstract :

In this era of digital learning, dental students, clinicians, and patients often seek online information on health topics, including dental health. YouTube is a very popular online platform that hosts many free-to-watch, user-generated videos. Many videos related to dental radiology are available on YouTube, but the quality of their contents was not thoroughly evaluated before. A series of YouTube video evaluations were performed with the following foci : instructional videos that demonstrated the procedures to take periapical and panoramic radiography, videos that explained the radiographic anatomy on panoramic images, and videos that discussed radiation safety concerning dental radiology. Overall, the videos were informative and useful, but with the following areas for improvement. For videos on how to take periapicals, common issues included not removing the metallic objects from the patient's head and neck region, not showing the selection of radiation dose, and not placing the orientation dot on the film or phosphor plate on the occlusal side. For videos on how to take panoramics, none of them clearly showed that the operator was pressing the exposure button outside the radiographic room with its door closed, as most of them either showed an open door, with no door, or without enough information. For panoramic radiographic anatomy videos, each video described 26 landmarks on average. The maxillary sinus was the structure mostly involved in wrong information, particularly the wrong delineation of its posterior wall. For videos on radiation safety, some of the analogies and the claimed radiation dose were questionable. One video even wrongly stated that dental x-rays are nonionizing radiation.

2012 BDS, HKU Dentistry2017 PhD, HKU Dentistry

2015-present Tutor in Radiography, HKU Dentistry

2020-present Clinic Manager, Oral Diagnosis Clinic and Diagnostic Imaging, Prince Philip Dental Hospital(associated with HKU Dentistry)

Award

2017 Outstanding Research Postgraduate Student (2016-2017), HKU

- Yeung A. W. K.*, Parvanov E. D., Horbańczuk J. O., Kletecka-Pulker M., Kimberger O., Willschke H., & Atanasov A. G.(2023). Are dental x-rays safe? Content analysis of English and Chinese YouTube videos. *Digital Health*, 9, 20552076231179053.
- Wong N. S. M., <u>Yeung A. W. K.</u>, McGrath C. P., & Leung Y. Y.(2023). Qualitative Evaluation of YouTube Videos on Dental Fear, Anxiety and Phobia. *International Journal of Environmental Research and Public Health*, 20, 750.
- Grillon M., & <u>Yeung A. W. K.</u>*(2022). Content Analysis of YouTube Videos That Demonstrate Periapical Radiography. *Applied Sciences*, 12, 9602.
- Yeung A. W. K.* (2022). Content analysis of YouTube videos on radiographic anatomy on dental panoramic images. *Healthcare*, 10, 1382.
- 5. Grillon M., & <u>Yeung A. W. K.</u>*(2022). Content analysis of YouTube videos that demonstrate panoramic radiography. *Healthcare*, 10, 1093.

[Keynote Lecture]

The importance of oral function in older adults from the viewpoint of healthy longevity

Masanori Iwasaki, DDS, PhD

Professor

Division of Preventive Dentistry, Department of Oral Health Science, Graduate School of Dental Medicine, Hokkaido University



Abstract :

Although older adults retain their teeth for longer, they report complaints concerning oral function. The oral health treatment needs of the older population have changed. In addition to methods focused on the teeth affected by dental caries and periodontal diseases, methods focused on the adequate functioning of oral cavity are now needed. Because individual oral health problems are interrelated and their prevalence increases with age, older adults frequently have coexisting oral health problems. Therefore, poor oral function-related problems are becoming more common as society ages. As further attention is given to the importance of oral function in aging populations, new concepts referred to as oral frailty and oral hypofunction have been introduced as multidimensional concepts describing poor oral function in Japan. In particular, the "Joint Working Committee on Oral Frailty" by three academic societies : the Japan Geriatrics Society, the Japanese Society of Gerodontology, and the Japanese Association on Sarcopenia and Frailty, issues Consensus Statement on Oral Frailty, on April 1st, 2024, with the aim to further public understanding of oral frailty.

In the ARSS 2024, I aim to provide an overview of recent epidemiological evidence of the associations of poor oral function with dietary intake and general health from the perspective of oral frailty and oral hypofunction. Oral frailty and oral hypofunction are novel concepts. Maintaining good oral function may be key to healthy longevity.

- 2023-Present Professor, Division of Preventive Dentistry, Department of Oral Health Science, Graduate School of Dental Medicine, Hokkaido University
- 2023-Present Visiting Researcher, Tokyo Metropolitan Institute for Gerontology and Geriatrics

2022-2023 Vice Research Director, Tokyo Metropolitan Institute for Gerontology and Geriatrics 2020-Present : Visiting Professor, Kyushu Dental University

- 2020-2022 Vice Specialized Director, Tokyo Metropolitan Institute for Gerontology and Geriatrics
- 2014-2020 Associate Professor, Kyushu Dental University
- 2010-2014 Assistant Professor, Graduate School of Medical and Dental Sciences, Niigata University
- 2010 : Clinical Fellow, Graduate School of Medical and Dental Sciences, Niigata University
- 2009-2010 Visiting Scholar, University of Michigan
- 2007-2010 Ph.D. of Dental Medicine, Graduate School of Medical and Dental Sciences, Niigata University
- 2006 Residency, Niigata University Medical & Dental Hospital
- 2000-2006 B.A. of Dental Medicine, School of Dental Medicine, Hokkaido University

Awards

- 2023 Geriatrics & Gerontology International Best Reviewer Award
- 2019 LION Award, Japanese Society of Gerodontology
- 2018 LION Award, Japanese Society for Oral Health
- 2012 Best Paper Award, Japanese Society for Oral Health
- 2010 JADR Young Investigator Award

- Iwasaki M., et al. Prevalence of oral frailty and its association with dietary variety, social engagement, and physical frailty : Results from the Oral Frailty 5-item Checklist. *Geriatrics & Gerontology International*. 2024. 24(4) : 371-377.
- NCD Risk Factor Collaboration. Diminishing benefits of urban living for children and adolescents' growth and development. *Nature*. 2023. 615: 874-883.
- <u>Iwasaki M.</u>, et al. Decline in oral function and its management. *International Dental Journal*. 2022. 72(4S) : S12-S20.
- Iwasaki M., et al. The association of oral function with dietary intake and nutritional status among older adults : latest evidence from epidemiological studies. *Japanese Dental Science Review*. 2021. 57 : 128-137.
- <u>Iwasaki M.</u>, et al. Serum antibody to *porphyromonas gingivalis* in chronic kidney disease. *Journal of Dental Research*. 2012. 91(9): 828-833.

[Lecture V]

A Morphological Approach to Understanding Swallowing Mechanisms \sim The genioglossus muscle is the only muscle that attaches to the epiglottis. \sim

Kei Kitamura, DDS, PhD

Senior Assistant Professor Department of Histology and Developmental Biology, Tokyo Dental College



Abstract :

Epiglottic retroversion is difficult to explain anatomically. One reason is inadequate structural identification of the ligaments in the submucosal tissue anterior to the epiglottis (pre-epiglottic space, PES). Although studies have shown that tongue root movement plays a role in epiglottic retroversion, few morphological reports have investigated the attachment of the lingual muscles to the epiglottis. This study reconstructed the fiber structure of the PES by comprehensively analyzing fiber alignment in the PES focusing on the hypepiglottic ligament, which runs between the lingual muscles and the epiglottis. Gross and microscopic observations of the submucosal structures from the tongue to the larynx of 20 cadavers (10 men, 10 women; mean age 79 years) were performed. A tendon continuing from the posterior part of the genioglossus muscle and attaching to the center of the epiglottic cartilage was identified in the midline area of the epiglottis. We named this tendon the glossoepiglottic tendon. In contrast, the hyoepiglottic ligament is found between the hyoid bone and the epiglottis and is attached from the lateral margin of the epiglottic cartilage to its base. Furthermore, the glossoepiglottic tendon consists of a high-density fiber bundle that is thicker than the hyoepiglottic ligament. These results show that the conventional hyperpiglottic ligament has a two-layer structure consisting of an upper fiber bundle connected to the genioglossus muscle and a lower fiber bundle connected to the hyoid bone. Sustained contraction of the posterior part of the genioglossus muscle therefore places the epiglottis under persistent traction, suggesting that its relaxation may cause epiglottic retroversion.

2012 DDS, Tokyo Dental College, Japan

- 2016 PhD, Department of Anatomy, Tokyo Dental College, Japan
- 2016-2017 Research assistant, Department of Histology and Developmental Biology, Tokyo Dental College, Japan
- 2017-2021 Assistant Professor, Department of Histology and Developmental Biology, Tokyo Dental College, Japan
- 2021-2024 Senior Assistant Professor, Department of Histology and Developmental Biology, Tokyo Dental College, Japan

Honor

2019 The Japanese Society of Dysphagia Rehabilitation "encouragement award"

Research Fields of Interest

Human Histology, Human embryology, Lingual muscle, Dysphagia, Age-related change in oral soft tissues

- <u>Kitamura K.</u>, Suzuki R., Ishizuka S., Murakami G., odríguez-Vázquez JF., Yamamoto H., Abe S. Growing stylohyoideus muscle insertion to the hyoid bone with special reference to Its topographical relation to the intermediate tendon of digastricus muscle : a histological study using human fetuses. *Ann Anat* (in press), 2024.
- <u>Kitamura K.</u>, Ishizuka S., Ji Hyun Kim., Yamamoto H., Murakami G., Rodríguez-Vázquez JF., Abe S. Development and growth of the temporal fascia : a histological study using human fetuses. *Anat Cell Biol* (in press), 2024.
- <u>Kitamura K.</u>, Watanabe T., Yamamoto M., Ishikawa N., Kasahara N., Abe S., Yamamoto H. A Newly Discovered Tendon Between the Genioglossus Muscle and Epiglottic Cartilage Identified by Histological Observation of the Pre-Epiglottic Space. *Dysphagia*, 38(1): 315-329, 2023.
- <u>Kitamura K.</u>, Kim JH., Cho KH., Murakami G., Rodríguez-Vázquez JF., Yamamoto H. Regional differences in zygapophysial joint cavities : A histological study of human fetuses. *Anat Rec* (Hoboken), 304(5) : 979-990, 2021.

[Lecture VI]

Inhibiting symbiotic bacterial-fungal interaction alters in vitro biofilm formation and its cariogenic potential

Jian-Na Cai, PhD

Lecture School of Oral Stomatology, Binzhou Medical University



Abstract :

The emergent property of polymicrobial biofilm is a consequence of intricate microbial interaction that occurs in response to individual cells interactions. Association between Streptococcus mutans and Candida albicans is resulted in a mutually beneficial cross-kingdom cluster, which is structurally complex and displaying enhanced cariogenic potential of biofilm. Given the polymicrobial niche in the oral cavity, both S. mutans and C. albicans are competitive with intrinsic and extrinsic microbes. Here, we hypothesized that applying antagonistic interaction of extrinsic lactic acid bacteria including Lacticaseibacillus rhamnosus towards S. mutans and C. albicans is a feasible strategy to disrupt the virulent cross-kingdom biofilm. Furthermore, combination of collagen peptide(CP) with L. rhamnosus can synergistically inhibit bacterial-fungal biofilm formation and further inhibit its cariogenic properties. Using a dynamic microbial-interaction model, the results showed that L. rhamnosus significantly impaired a dense and complex cariogenic biofilm formation. Although single treatment of CP cannot inhibit the growth of bacterial or bacterial-fungal mixed-species biofilms, it significantly decreased glycolytic acid production of bacterial-bacterial or bacterial-fungal biofilms when co-cultured with L. rhamnosus. Mechanically, L. rhamnosus modulated the virulence potential of this cross-kingdom biofilm via down-regulation of the genes associated with bacterial-fungal interaction, biofilm formation and yeast-to-hyphae transition. Interestingly, in KEGG analysis, combination of L. rhamnosus with CP altered membrane functions of both S. mutans and C. albicans without affecting the membrane/cellular functions of L. rhamnosus, akin to the mechanism of action of F-ATPase inhibitors. The data provide new insights for therapeutic strategies targeting microbial interaction in cross-kingdom biofilms via enhancement of the antagonistic effect of probiotics towards virulent cross-kingdom oral biofilm.

2008-2013	Bachelor	Binzhou Medical University
2013-2015	Master	Jeonbuk National University
2015-2018	PhD	Jeonbuk National University
2021-2023	Postdoc	Jeonbuk National University
2018-Preser	nt Lecture	Binzhou Medical University

Research Fields of Interest

- 1. Dental biofilms
- 2. Microbial ecology in the oral cavity
- 3. Therapeutic approaches targeting cariogenic biofilms

- <u>Cai JN.</u>, Kim D. Biofilm ecology associated with dental caries : understanding of microbial interactions in oral communities leads to development of therapeutic strategies targeting cariogenic biofilms. *Adv Appl Microbiol*. 2023 ; 122 : 27-75.
- <u>Cai JN.</u>, Choi HM., Song KY., Jeon JG. The reciprocal interaction between fluoride release of glass ionomers and acid production of *Streptococcus mutans* biofilm. *J Oral Microbiol*. 2022; 14(1): 2055267.
- 3. <u>Cai JN.</u>, Choi HM., Jeon JG. Relationship between sucrose concentration and bacteria proportion in a multispecies biofilm. *J Oral Microbiol*. 2021 ; 13(1) : 1910443.
- <u>Cai JN.</u>, Jung JE., Lee MH., Choi HM., Jeon JG. Sucrose challenges to *Streptococcus mutans* biofilms and the curve fitting for the biofilm changes. *FEMS Microbiol Ecol.* 2018; 94(7): fiy091.
- <u>Cai JN.</u>, Jung JE., Dang MH., Kim MA., Yi HK., Jeon JG. Functional Relationship between Sucrose and a Cariogenic Biofilm Formation. *PLoS One*. 2016 ; 11(6) : e0157184.
- <u>Cai JN.</u>, Kim MA., Jung JE., Pandit S., Song KY., Jeon JG. Effects of combined oleic acid and fluoride at sub-MIC levels on EPS formation and viability of *Streptococcus mutans* UA159 biofilms. *Biofouling*. 2015; 31(7): 555-563.