Tokyo Dental College
Research Project

Asian Rising Stars Symposium 2023

July 29, 2023

Well-being Society Achieved by Maintaining and
Improving Oral-Maxillofacial Function at Every Stage of Life
(Well-being Project)

Program and Abstracts

Saturday, July 29
Tokyo Dental College Research Project
Asian Rising Stars Symposium 2023

Program

13:00-13:05：Opening Remarks
Tatsuya Ichinohe (Dean, Tokyo Dental College)

Session I Moderator: Masahito Yamamoto (Department of Anatomy, Tokyo Dental College)
Toshihide Mizoguchi (Oral Health Science Center, Tokyo Dental College)

13:05-13:35：Lecture I
Regenerative potentials of the dental pulp stem cells-derived small extracellular vesicles
Sheng-Wei Feng (School of Dentistry, College of Oral Medicine, Taipei Medical University)

13:35-14:05：Lecture II
Schnurri-3: an osteogenesis-plus regulator
Ren Xu (School of Medicine, Xiamen University)

Session II Moderator: Tomoko Someya (Department of Dental Materials Science, Tokyo Dental College)
Natsuko Aida (Department of Biochemistry, Tokyo Dental College)

14:05-14:35：Lecture III
Improved enamel acid resistance by acidulated phosphate sodium monofluorophosphate solution
Ryouichi Satou (Department of Epidemiology and Public Health, Tokyo Dental College)

14:35-15:05：Lecture IV
Cell-laden microspheres and oxygenation materials applied in endodontic regeneration
Li Xie (State Key Laboratory of Oral Disease, West China College of Stomatology, Sichuan University)

15:05-15:20：Coffee Break (15 min)

Session III Moderator: Yoshiyuki Shibukawa (Department of Physiology, Tokyo Dental College)

15:20-16:00：Keynote Lecture
Pathophysiology of sleep bruxism
Takafumi Kato (Department of Oral Physiology, Osaka University Graduate School of Dentistry)

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

16:00-16:30：Lecture V
The effect of cigarette smoke on interaction of host cells with periodontal pathogen and periodontal healing
Kentaro Imamura (Department of Periodontology, Tokyo Dental College)

16:30-17:00 : Lecture VI
POMC neuron targeting peptide regulates energy homeostasis
Ki Woo Kim (Division of Physiology, Department of Oral Biology, Yonsei University College of Dentistry)

17:00-17:05 : Closing Remarks
Akira Yamaguchi (Advisor, Tokyo Dental College Research Well-being Project)

[Lecture I]

Regenerative potentials of the dental pulp stem cells-derived small extracellular vesicles

Sheng-Wei Feng, DDS, MS, PhD

Director & Professor
School of Dentistry,
College of Oral Medicine, Taipei Medical University

Accumulating evidence indicates that the therapeutic effect of mesenchymal stem cells (MSCs) mainly depends on their paracrine action. MSCs-derived small extracellular vesicles (exosomes, Exo) are key mediators in intercellular communications and microenvironment maintenance by delivering therapeutic protein and miRNA. However, the research field suffers from inconsistencies regarding Exo's purification, characterization, and bioactivity at the molecular, cellular, and tissue levels. Moreover, the underlying mechanisms by which Exo regenerates tissues and modulates immune response have not been fully elucidated. There are several methods for the isolation of exosome samples now. Ultracentrifugation is the most used technique, but repeated ultracentrifugation can destroy exosome structure and biological integrity. We evaluated the isolation of exosomes from dental pulp mesenchymal stem cells using ultracentrifugation and ultrafiltration combined with size exclusion chromatography. We directly compared the ability of the two methods to isolate exosomes, comparing and analyzing their exosome characterization, standard quantification, characterization, and proteomic analysis in an integrated and systematic manner. Both ultracentrifugation and ultrafiltration combined with size exclusion chromatography successfully isolated exosomes. Ultrafiltration combined with size exclusion chromatography isolates exosome yields higher, and the sample distribution particles have more average size, making it more suitable for large-scale research applications. We also further evaluate and compare the two different isolation methods of exosomes for periodontal ligament stem cells (PDLSCs) morphology, growth, cell growth cycle, various differentiation abilities, various gene expression, and possible discussion of message transmission paths.

Curriculum Vitae

2004 DDS, Dentistry, Taipei Medical University, Taipei, Taiwan

2007 MS, Dentistry, Taipei Medical University, Taipei, Taiwan

2014 PhD, Dentistry, Taipei Medical University, Taipei, Taiwan

2016-2019 Assistant Professor, School of Oral Hygiene, College of Oral Medicine, Taipei Medical University

2019-2022 Associate Professor, School of Dentistry, College of Oral Medicine, Taipei Medical University

2020.08- Director, School of Dentistry, College of Oral Medicine, Taipei Medical University

2022.08- Professor, School of Dentistry, College of Oral Medicine, Taipei Medical University

Honors

2021 Taiwan Association for Dental Sciences Academic Award

Research Fields of Interest

Oral tissue-derived mesenchymal stem cells, regenerative medicine, tissue engineering

Selected Publications

1. Huang WH, Hung CY, Chiang PC, Lee H, Lin IT, Lai PC, Chan YH, **Feng SW*.** Physicochemical Characterization, Biocompatibility, and Antibacterial Properties of CMC/PVA/Calendula officinalis Films for Biomedical Applications. Polymers (Basel). 2023 Mar 14;15(6):1454. (5-Year Impact Factor： 5.063, POLYMER SCIENCE 16/90=17.8%)
2. Chan YH, Ho KN, Lee YC, Chou MJ, Lew WZ, Huang HM, Lai PC, **Feng SW***. Melatonin enhances osteogenic differentiation of dental pulp mesenchymal stem cells by regulating MAPK pathways and promotes the efficiency of bone regeneration in calvarial bone defects. Stem Cell Res Ther. 2022 Feb 19;13(1):73. (5-year IF: **8.393**, CELL & TISSUE ENGINEERING 6/31=17.74 %)
3. Chan YH, Lee YC, Hung CY, Yang PJ, Lai PC, **Feng SW***. Three-dimensional Spheroid Culture Enhances Multipotent Differentiation and Stemness Capacities of Human Dental Pulp-derived Mesenchyma Stem Cells by Modulating MAPK and NF-kB Signaling Pathways. Stem Cell Rev Rep. 2021 Apr 24. Online ahead of print. (IF: **6.692**, MEDICINE, RESEARCH & EXPERIMENTAL 34/139=24.1 %)
4. **Feng SW***, Su YH, Lin YK, Wu YC, Huang YH, Yang FH, Chiang HJ, Yen Y, Wang PD. Small blood stem cells for enhancing early osseointegration formation on dental implants: a human phase I safety study. Stem Cell Res Ther. 2021 Jul 2;12(1):380. (5-year IF: **8.393**, CELL & TISSUE ENGINEERING 6/31=17.74 %)
5. Lew WZ, **Feng SW**, Lee SY, Huang HM. The Review of Bioeffects of Static Magnetic Fields on the Oral Tissue-Derived Cells and Its Application in Regenerative Medicine. Cells. 2021 Oct 5;10(10):2662. (5-year IF: **7.677**, CELL BIOLOGY 51/194=26.03%)
6. Shiu ST, Lee WF, Chen SM, Hao LT, Hung YT, Lai PC, **Feng SW***. Effect of Different Bone Grafting Materials and Mesenchymal Stem Cells on Bone Regeneration: A Micro-Computed Tomography and Histomorphometric Study in a Rabbit Calvarial Defect Model. Int J Mol Sci. 2021 Jul 28;22(15):8101. (5-year IF: **6.132**, BIOCHEMISTRY & MOLECULAR BIOLOGY 67/297=22.6%)

[Lecture II]

Schnurri-3: an osteogenesis-plus regulator

Ren Xu, PhD

Professor of School of Medicine, Xiamen University
Director of Fujian Provincial Key Laboratory of Organ and Tissue Regeneration
Director of the First Affiliated Hospital of
Xiamen University-ICMRS (International Chinese Musculoskeletal
Research Society) Collaborating Center

Abstract:
The skeleton has been suggested to function as an endocrine organ controlling whole organism energy balance, however the regulators of this effect and their potential clinical utility remain unclear. Here, we utilize mice with augmented osteoblast activity, Schnurri-3$^{-/-}$ (*Shn3*$^{-/-}$ mice), to probe general relationships between osteogenesis and metabolic syndrome. At overnutrition condition, *Shn3*$^{-/-}$ mice display obesity resistance with improved glucose homeostasis and insulin sensitivity regulated by browning of white adipose tissue (WAT). Conditional deletion of *Shn3* in osteoblasts (*Shn3*^{Osx} mice) but not adipocytes (*Shn3*^{Adq} mice) not only recapitulated the phenotype against obesity seen in *Shn3*$^{-/-}$ mice but also activated browning of perivascular adipose tissue (PVAT) to alleviate cardiovascular pathological features in the atherosclerosis model, indicating that the role of Shn3 in regulating metabolic syndrome is driven by the skeleton. Through in vitro co-culture assay and in vivo fat-pad transplantation assay, we confirmed that the "osteokines" secreted by activated osteoblasts lacking Shn3 expression indeed promoted WAT browning. Among them, we identified that SLIT2 is a Shn3-regulated factor secreted by osteoblasts that enhances WAT browning, with osteoblasts serving as the major source of systemic circulating SLIT2. Therapeutically, a bone-targeting AAV treatment suppressing Shn3 expression not only increased bone mass but also rescued both obesity and atherosclerosis phenotypes at pathological conditions, which potentially avoided the cardiovascular risk of anti-sclerostin antibodies utilized in osteoporosis. Collectively, our findings established a novel link in bone-fat axis through SHN3 regulated production of SLIT2 in osteoblasts, offering a plausible strategy in treating both bone loss and metabolic syndrome.

Curriculum Vitae

2019-Present	Professor	School of Medicine, Xiamen University, China
2014-2019	Postdoc	Weill Cornell Medicine, Cornell University, US
2013-2014	Research Fellow	Department of Orthopaedic Surgery, Tokyo Medical and Dental University, Japan
2008-2013	PhD	Tokyo Medical and Dental University, Japan

Research Fields of Interest

1. The role of nerve/vascular system in bone degenerative diseases
2. Identification of skeletal stem cell/precursor cell subtypes
3. The endocrine function of bone forming cells

Selected Honors

1. 2019: AIMM-ASBMR John Haddad Young Investigator Award
2. 2018: ASBMR Annual Meeting Young Investigator Award
3. 2017: Webster Jee Young Investigator Award (ICMRS)

Selected Publications

1. **Xu R**, Yallowitz A, Qin A, Wu Z, Shin D, Kim J, Debnath S, Ji G, Bostrom M, Yang X, Zhang C, Dong H, Kermani P, Lalani S, Li N, Liu Y, Poulos M, Wach A, Zhang Y, Inoue K, Lorenzo A, Zhao B, Butler J, Shim J, Glimcher L***** and Greenblatt MB*****. Targeting skeletal endothelium to ameliorate bone loss. ***Nature Medicine.*** 2018;24(6):823-833.

2. Fukuda T[#], Takeda S*****[#], **Xu R**[#], Ochi H, Sunamura S, Sato T, Shibata S, Yoshida Y, Gu Z, Kimura A, Ma C, Xu C, Bando W, Fujita K, Shinomiya K, Hirai T, Asou Y, Enomoto M, Okano H, Okawa A, Itoh H. Sema3A regulates bone-mass accrual through sensory innervations. ***Nature.*** 2013;497(7450):490-493. (**[#]: Co-first**)

3. **Xu R**, Zhang C, Shin DY, Kim JM, Lalani S, Li N, Yang YS, Liu Y, Eiseman M, Davis RJ, Shim JH*****, Greenblatt MB*****. c-Jun N-terminal kinases (JNKs) are critical mediators of osteoblast activity in vivo. ***Journal of Bone and Mineral Research***. 2017;32(9):1811-1815.

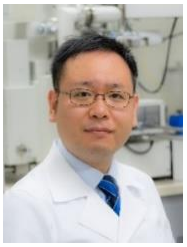
4. Li N, InoueK, Sun J, Niu Y, Lalani S, Yallowitz A, Yang X, Zhang C, Shen R, Zhao B, **Xu R***, Greenblatt MB. Osteoclasts are not a source of SLIT3. ***Bone Research.*** 2020;8:11. (*: **Corresponding**)

5. Zhou T, Chen Y, Liao Z, Zhang L, Su D, Li Z, Yang X, Ke X, Liu H, Chen Y, Weng R, Shen H, Xu C, Wan Y, **Xu R***, Su P*. Spatiotemporal Characterization of Human Early Intervertebral Disc Formation at Single-Cell Resolution. ***Advanced Science.*** 2023;25:e2206296. (*: **Corresponding**)

6. Sun J, Shin DY, Eiseman M, Yallowitz AR, Li N, Lalani S, Li Z, Cung M, Bok S, Debnath, S, Marquez SJ, White TE, Khan A, Lorenz I, Shim JH, Lee FS, **Xu R***, Greenblatt MB*****. SLITRK5 is a novel negative regulator of hedgehog signaling in osteoblasts. ***Nature Communications.*** 2021;12:4611. (*: **Corresponding**)

[Lecture III]

Improved enamel acid resistance by acidulated phosphate sodium monofluorophosphate solution



Ryouichi Satou, DDS, PhD

Senior Assistant Professor
Department of Epidemiology and Public Health, Tokyo Dental College

Abstract:
Sodium monofluorophosphate (MFP) is a component of fluoride-containing dentifrices and is more biosafe than the conventional sodium fluoride (NaF). MFP can respond not only on the tooth surface layer but also deep into the enamel. We aim to confirm that high concentrations of acid phosphate MFP (AP-MFP, 9000 ppmF), used in professional care, could lead to a highly biosafe fluoride application method that acts through the deep enamel layers. Sample groups were respectively treated in vitro with NaF, acidulated phosphate fluoride (APF), MFP, and AP-MFP, and the samples were compared against an untreated group. Characterizations after fluoride application confirmed that MFP and AP-MFP treatments improved the acid resistance of enamel compared to that of conventional methods. Furthermore, the acid resistance of highly concentrated MFPs improved by using phosphoric acid. Although the acid resistance from the AP-MFP method is not as good as that using APF, AP-MFP can act both on the surface layer and deep into the enamel. Moreover, AP-MFP retains fluoride ions as much as APF does on the tooth surface. The proposed fluoride application method using AP-MFP introduces a dental treatment for acid resistance that is highly biosafe and penetrates deep layers of the enamel.

Curriculum Vitae

2012 DDS, Tokyo Dental College, Japan

2013-2014 Visiting researcher of Biomedical Research Division, National Institute of Advanced Industrial Science and Technology (AIST), Japan

2014-2016 Research assistant, Oral Health Science Center of Tokyo Dental College, Japan

2017 PhD, Epidemiology and Public Health, Tokyo Dental College, Japan

2017-2020 Assistant Professor, Department of Epidemiology and Public Health, Tokyo Dental College, Japan

2020-Present Senior Assistant Professor, Department of Epidemiology and Public Health, Tokyo Dental College, Japan

Honors

2017 IADR/AADR/CADR "Salivary Research Group Award"

2018 Tokyo Dental College Research Branding Project travel award

2021 The 70th Annual Meeting of the Japanese Society for Oral Health, Excellent Presentation Award

2022 Tokyo Dental College President's Encouragement Research Award

Research Fields of Interest

Preventive dentistry, Fluoride, De/Remineralization, Erosion, Toothpaste, Circadian rhythm, Clock gene

Selected Publications

1. **Satou R**, Sato M, Kimura M, Ishizuka Y, Tazaki M, Sugihara N, Shibukawa Y. Temporal Expression Patterns of Clock Genes and Aquaporin 5/Anoctamin 1 in Rat Submandibular Gland Cells. ***Frontiers in Physiology***, 8. 320, 2017
2. **Satou R**, Yamagishi A, Takayanagi A, Higuchi T, Oyama T, Suzuki S, Sugihara N. Relationship between Toothpaste Dilution Ratio and Droplets Generated during Tooth-Brushing. ***Int. J. Environ. Res. Public Health***, 19(7), 4157, 2022
3. **Satou R**, Yamagishi A, Takayanagi A, Suzuki S, Dowen B, Sugihara NComparison of interproximal delivery and flow characteristics by dentifrice dilution and application of prepared toothpaste delivery technique. ***PLoS One***,17(10):e0276227, 2022
4. **Satou R**, Iwasaki M, Kamijo H, Sugihara N. Improved Enamel Acid Resistance using Biocompatible Nano-hydroxyapatite Coating Method. ***Materials***, 15(20), 7171, 2022
5. **Satou R**, Yamagishi A, Takayanagi A, Iwasaki M, Kamijo H, Sugihara N. Improved enamel acid resistance by highly concentrated acidulated phosphate sodium monofluorophosphate solution. ***Materials***, 15(20), 7298, 2022
6. Iwasaki M, **Satou R***, Sugihara N. Development of root caries prevention by nano-hydroxyapatite coating and improvement of dentin acid resistance. ***Materials***, 15(22), 8263, 2022

[Lecture IV]

Cell-laden microspheres and oxygenation materials applied in endodontic regeneration

Xie Li, PhD

Associated research fellow
State Key Laboratory of Oral Disease,
West China College of Stomatology, Sichuan University

Abstract:

Stem cell-based dental pulp tissue regeneration has emerged as a promising alternative therapeutic strategy for endodontic treatments. Cell-laden hydrogel microsphere system was demonstrated to be a suitable and effective vehicle for endodontic regeneration applications. Hydrogel microspheres possess many advantages, such as large surface areas, ability to quickly transfer substances, 3D extracellular matrix (ECM)-like structures, capable of acting as efficient carriers for both cell expansion in vitro and cell transplantation in vivo. When inflammated or infected dental pulp tissues are retrieved, a 6- to 9-mm-long root canal space is left empty and severe hypoxia within the root canal space, characterized by a low oxygen content that may hinder the survival of the transplanted cells, which may undergo instant death when the oxygen level drops to 1%. In situ generation of oxygen in the anoxic regions by biomaterials that produce and deliver oxygen to the adjacent cells locally and directly is a distinctive approach to enhance cell survivability. Therefore, closely combined with the frontier of regenerative medicine, we have constructed a series of new materials such as cell-laden hydrogel microspheres, local-sustained oxygen generating materials, etc., and explored the application in dental pulp regeneration. For example, core-shell GelMA/Alginate hydrogel microspheres were developed based on coaxial electrostatic droplet technology to facilitate the high-throughput construction of pre-vascularization microtissues and facilitate the clinical transformation of stem cell-based dental pulp regeneration research. Sustained oxygen-generating biomaterials based on CaO_2/TiO_{2-x}/PDMS were constructed for the regeneration of dental pulp, providing a new strategy to improve the severe anoxic condition in the early stage after stem cell transplantation. Our work demonstrated that core-shell GelMA/Alginate microspheres and CaO_2/PDMS oxygen-generating biomaterials have great application potential in endodontic regeneration field.

Curriculum Vitae

2012/07-2012/12 R&D engineer, Chengdu Puchuan Biomaterials Corporation

2013/01-2015/01 Postdoctoral fellow, Sichuan University, West China College of Stomatology, State Key Laboratory of Oral Disease

2015/04-2016/08 Assistant Research Fellow, Sichuan University, West China College of Stomatology, State Key Laboratory of Oral Disease

2016/09-Present Associate Research Fellow, Sichuan University, West China College of Stomatology, State Key Laboratory of Oral Disease

Research Fields of Interest

1. Stem cell-laden hydrogel microspheres applied in dental pulp regeneration
2. Deep decontamination strategy for peri-implantitis management
3. Local-sustained oxygen-generating materials

Selected Publications

1. Xi Liang, **Li Xie***, Qingyuan Zhang, Ge Wang, Siyuan Zhang, Mingyan Jiang, Ruitao Zhang, Ting Yang, Xingyu Hu, Ziyang Yang, Weidong Tian**. GelMA-alginate core-shell microcapsules as efficient delivery platform for prevascularized microtissues in endodontic regeneration, **Acta Biomaterialia**, 144 (2022) 242–257.

2. Ting Yang, **Li Xie***, Ruitao Zhang, Weidong Tian*, Microspheres and their potential in endodontic regeneration application, **Chin J Dent Res** 2022;25(1):29-36.

3. Qingyuan Zhang; Ting Yang; Ruitao Zhang; Xi Liang; Ge Wang; Yuan Tian; **Li Xie*;** Weidong Tian*, Platelet lysate functionalized GelMA microspheres for improving angiogenesis in endodontic regeneration. **Acta Biomaterialia** (2021)136, 441-455.

4. Ting Yang, Qingyuan Zhang, **Li Xie***, Ruitao Zhang, Ruojing Qian, Yuan Tian, Guoqing Chen, Weidong Tian*, hDPSC-laden GelMA microspheres fabricated using electrostatic microdroplet method for endodontic regeneration, **Materials Science and Engineering: C** (2021) 121:111850.

5. Ruitao Zhang, **Li Xie***, Hao Wu, Ting Yang, Qingyuan Zhang, Yuan Tian, Yuangang Liu, Xue Han, Weihua Guo, Min He, Suru Liu, Weidong Tian**, Alginate/laponite hydrogel microspheres co-encapsulating dental pulp stem cells and VEGF for endodontic regeneration, **Acta Biomaterialia** (2020) 113:305–316.

[Keynote Lecture]

Pathophysiology of sleep bruxism in humans and challenges for animal studies

Takafumi Kato, DDS, PhD

Professor
Department of Oral Physiology
Osaka University Graduate School of Dentistry

Sleep bruxism (SB) is characterized by frequent tooth grinding during sleep. Approximately 20% of children and up to 10% of adults are affected by SB. SB is clinically significant since it is associated with damages to orodental tissues, prostheses, implants, and orofacial pain. However, the underlying pathophysiological mechanisms of SB remain unknown. Sleep studies in humans have shown that SB patients exhibit rhythmic masticatory muscle activity (RMMA) more frequently during sleep than normal individuals. The occurrence of RMMA is under the influences of sleep homeostasis: RMMA occurs in clusters particularly in light non-REM sleep during the ascending phase of sleep cycles. These episodes are also associated with transient arousals and a sequence from transient autonomic and cortical activation to RMMA was found. However, SB patients otherwise healthy exhibit a normal sleep architecture and similar level of masticatory muscle tone compared to normal individuals. Therefore, motor system involved in generating RMMA, rather than sleep regulatory system, would be more affected in SB patients. In animals, masticatory muscle contractions occur during sleep, and the characteristics of the contractions differ between sleep states. Repetitive or rhythmic contractions were found to occur during NREM sleep, in association with cortical and cardiac activations. Rhythmic masticatory muscle contractions can be induced by cortico-bulbar stimulation during sleep less but responsiveness to stimulation is fluctuated by sleep and arousal states. Thus, animal studies would provide additional insights into the pathophysiological mechanisms underlying SB. To further understand the pathophysiological mechanisms of SB, further efforts are needed to integrate the findings from human and animal studies to clarify the factors contributing to increased masticatory muscle activity during sleep.

Curriculum Vitae

1994: Osaka University Faculty of Dentistry (DDS)

1998: Osaka University Graduate School of Dentistry (PhD)

1998-2001: Postdoctoral fellow/Research Assistant, Hôpital du Sacré-Cœur de Montréal, Université de Montréal Faculté de médecine dentaire and Centre recherche en science de neurologique, Québec, Canada

2003: Associate Professor, Matsumoto Dental University, Shiojiri, Japan

2008: Chief, Matsumoto Dental University Hospital Dental Sleep Medicine Clinic
Associate Professor, Osaka University Graduate School of Dentistry, Department of Oral Anatomy and Neurobiology, Suita, Japan

2009: President, IADR Neuroscience group

2016-current: Professor, Osaka University, Graduate School of Dentistry, Department of Oral Physiology, Suita, Japan.

2022-current: Vice Dean, Osaka University, Graduate School of Dentistry

Adjunct: Osaka University Hospital Sleep Medicine Center, and Osaka University United Graduate School of Child Development

Awards:

1. Prix Jean-Paul Lussier (Ordre des dentists du Quebec, 2001)
2. Postdoctoral Research Award (CADR, 2001)
3. Distinguished Scientist Award/Young Investigator Award (IADR, 2005)
4. Yumikura Research Award (Osaka University School of Dentistry, 2014)
5. LION Award (Japanese Association for Oral Biology, 2022)

Selected Publications

1. Toyota R, Fukui KI, Kamimura M, Katagiri A, Sato H, Toyoda H, Rompré P, Ikebe K, Kato T. Sleep stage-dependent changes in tonic masseter and cortical activities in young subjects with primary sleep bruxism. Sleep. 2022;45(4):zsab207.
2. Shiraishi Y, Tachibana M, Shirota A, Mohri I, Taniike M, Yamashiro T, Kato T. Relationships between cortical, cardiac, and arousal-motor activities in the genesis of rhythmic masticatory muscle activity across sleep cycles in primary sleep bruxism children. Sleep. 2021;44(11):zsab156.
3. Kishi A, Haraki S, Toyota R, Shiraishi Y, Kamimura M, Taniike M, Yatani H, Kato T. Sleep stage dynamics in young patients with sleep bruxism. Sleep. 2020;43(1):zsz202.
4. Yamada KI, Higashiyama M, Toyoda H, Masuda Y, Kogo M, Yoshida A, Kato T. Experimentally induced rhythmic jaw muscle activities during non-rapid eye movement sleep in freely moving guinea pigs. J Sleep Res. 2019;28(5):e12823.
5. Kato T, Toyota R, Haraki S, Yano H, Higashiyama M, Ueno Y, Yano H, Sato F, Yatani H, Yoshida A. Comparison of rhythmic masticatory muscle activity during non-rapid eye movement sleep in guinea pigs and humans. J Sleep Res. 2018;27(4):e12608.

[Lecture V]

The effect of cigarette smoke on interaction of host cells with periodontal pathogen and periodontal healing

Kentaro Imamura, DDS, PhD

Senior assistant professor

Department of Periodontology, Tokyo Dental College

Oral Health Science Center, Tokyo Dental College

Abstract:

Cigarette smoking is a significant environmental risk factor for periodontal disease. Previous studies have mainly focused on the effects of smoking on periodontal tissues, particularly in relation to nicotine. However, there is still limited understanding of the overall impact of cigarette smoke on host cells, especially in the presence of periodontal pathogens. Our previous research revealed that cigarette smoke condensate (CSC) exerts a concentration-dependent biphasic effect on the migration of human gingival epithelial cells by altering the cytoskeleton and integrin expression. Additionally, we reported that a significantly increased *P. gingivalis* invasion into epithelial cells when exposed to low concentrations of CSC.

We further investigated the influence of CSC and *P. gingivalis* on the host cell signaling pathway, specifically mitogen-activated protein kinase (MAPK) pathway. Through the stimulation of the MAPK, ERK1/2, and p38 signaling pathways, CSC influences cell migration. The activation of ERK1/2 and p38 is suppressed by *P. gingivalis* infection, which reduces the CSC-induced migration at least in part. However, other pathways are likely implicated in this modulatory process.

In recent years, there has been an increasing demand for new types of tobacco products. The market share of heat-not-burn cigarettes (HNBCs) is 26% in Japan. HNBCs are characterized by lower levels of nicotine and tar compared to conventional cigarettes. However, the effects of HNBC on periodontal tissue and its healing remain largely unknown. Currently, we are actively investigating the impact of HNBC on these aspects.

Curriculum Vitae

2010 DDS, Tokyo Dental College, Tokyo, Japan

2015 PhD, Graduate School of Dentistry, Tokyo Dental College, Tokyo, Japan

2015-2019 Assistant professor, Department of Periodontology, Tokyo Dental College, Tokyo, Japan

2016-2018 Visiting Scholar, Department of Prosthodontics, New York University College of Dentistry, New York, NY

2019-Present Senior assistant professor, Department of Periodontology, Tokyo Dental College, Tokyo, Japan

Selected Publications

1. **Imamura K.**, Hamada Y., Yoshida W., Murakami T., Nakane-Koyachi S., Yoshikawa K., Saito A. Investigating the effects of dehydrated human amnion-chorion membrane on periodontal healing. Biomolecules 12: 857, 2022.
2. **Imamura K**, Suzuki E, Takeuchi T, Saito A. Clinical Outcomes of Periodontal Regenera tive Therapy Using Recombinant Human Fibroblast Growth Factor-2 (FGF-2) with Modif ied Minimally Invasive Surgical Technique for Intrabony Defects: A Case Series with 12 -month Follow-up. Int J Periodontics Restorative Dent 42:507-513, 2022.
3. **Imamura K.**, Tachi K., Takayama T., Shohara R., Kasai H., Dai J., and Yamano S. Re leased fibroblast growth factor18 from a collagen membrane induces osteoblastic activity involved with downregulation of miR-133a and miR-135a. J Biomater Appl 32:1382-139 1, 2018.
4. **Imamura K.**, Kokubu E., Kita D., Ota K., Yoshikawa K., Ishihara K., and Saito A. Rol e of mitogen-activated protein kinase pathways in migration of gingival epithelial cells in response to stimulation by cigarette smoke condensate and infection by *Porphyromonas gingivalis.* J Periodontal Res 51:613-21, 2016.
5. **Imamura K.**, Takayama S., Saito A., Inoue E., Nakayama Y., Ogata Y., Shirakawa S., Nagano T., Gomi K., Morozumi T., Akiishi K., Watanabe K., and Yoshie H. Evaluation of a novel immunochromatographic device for rapid and accurate clinical detection of *Po rphyromonas gingivalis* in subgingival plaque. J Microbiol Methods 117:4-10, 2015.
6. **Imamura K.**, Kokubu E., Kita D., Ota K., Ishihara K., and Saito A. Cigarette smoke c ondensate modulates migration of human gingival epithelial cells and their interactions w ith *Porphyromonas gingivalis.* J Periodontal Res 50:411-21, 2015.

[Lecture VI]

POMC neuron targeting peptide regulates energy homeostasis

Ki Woo Kim, PhD

Professor
Division of Physiology, Department of Oral Biology, Yonsei University College of Dentistry
Department of Applied Biological Science, BK21 FOUR, Yonsei University College of Dentistry

The small humanin-like peptide (SHLP) is a mitochondrial-derived peptide (MDP) and known to be implicated in diverse biological processes, including oxidative stress and senescence. However, its functional roles in the regulation of energy homeostasis are not fully understood and its cognate receptor is not identified. Here, we show that systemic or intracerebroventricular (ICV) administrations of SHLP protected mice from high-fat diet (HFD)-induced obesity and improved insulin sensitivity. In addition, SHLP suppressed food intake and promoted thermogenesis through the activation of pro-opiomelanocortin (POMC) neurons of the arcuate nucleus of the hypothalamus (ARC). Furthermore, we, through a high-throughput structural complementation screening, identify that chemokine receptor (CXCR) as a receptor for SHLP and it is required for POMC neuron activation. Taken together, our study illustrates potential therapeutic actions of the SHLP on metabolic disorders and provides mechanistic insights into its effects on energy homeostasis.

Curriculum Vitae

2004-2009	UT-Southwestern Medical Center, Dallas, TX	PhD
2009-2013	UT-Southwestern Medical Center, Dallas, TX	Postdoctoral Fellow
2013-2018	Yonsei University Wonju College of Medicine	Assistant Professor
2018-2022	Yonsei University College of Dentistry	Associate Professor
2023-Present	Yonsei University College of Dentistry	Professor

Research Field of Interest

Neuronal Control of Energy Metabolism and Alzheimer's Disease
Energy Homeostasis and Psychological Disease

Selected Publications

1. Primary cilia regulate adaptive responses to fasting. Yang DJ, Tran LT, Yoon SG, Seong JK, Shin DM, Choi YH, and **Kim KW**. ***Metab. Clin. Exp.*** **2022 Oct**;135:155273. doi: 10.1016/j.metabol.2022.155273. Epub 2022 Aug 1

2. Ventromedial Hypothalamic Primary Cilia Control Energy and Skeletal Homeostasis. Sun JS, Yang DJ, Kinyua AW, Yoon SG, Seong JK, Kim J, Moon SJ, Shin DM, Choi YH, and **Kim KW**. ***J Clin Invest.*** **2021 Jan 4**;131(1):e138107. doi: 10.1172/JCI138107

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