Kyudai Oral Bioscience

&

OBT Research Center

Joint International Symposium 2020

PROGRAM & ABSTRACTS

February 8 – 9, 2020
Lecture Room A/B, Faculty of Dental Science,
Kyushu University

KOB 2020

KYUSHU OBT

■ Date:

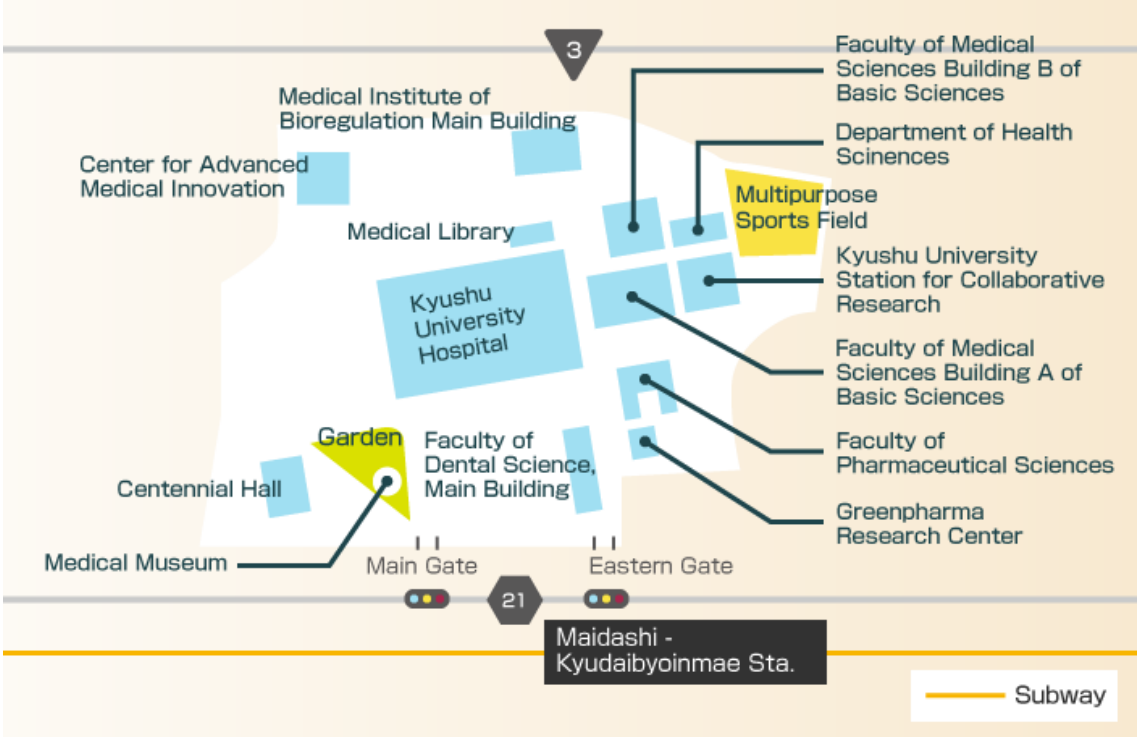
February 8-9, 2020

■ Venue:

Lecture Room A/B, Faculty of Dental Science,
Kyushu University, Fukuoka, Japan

■ Organization

Kyudai Oral Bioscience
Oral Health・Brain Health・Total Health Research Center



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KOB & OBT Joint International Symposium 2020

PROGRAM

February 8 (Saturday)

Time	Title	Presenter
12:50-13:00	Opening Remark	Prof. Seiji Nakamura
Session 1	**Oral/Total Health Session**	**Chair:** Dr. Masafumi Moriyama
13:00-13:30	Establishing periodontal ligament stem cell-like cells derived from iPS cells	Dr. Sayuri Hamano
13:30-14:00	Roles of TRPM7 in tooth development and bone formation	Dr. Masashi Shin
14:00-14:10	Coffee Break	
	Special Lecture on Total Health	**Chair:** Dr. Zhou Wu
14:10-15:10	Fatty acid sensors and their functional distribution in mouse taste tissue	Dr. Keiko Yasumatsu
15:10-15:30	Coffee Break	
	Special Lecture on Brain Health (1)	**Chair:** Prof. Eijiro Jimi
15:30-16:30	Assessment of the olfactory function in the brain using ultra-high field functional magnetic resonance imaging	Dr. Ikuhiro Kida
16:30-16:40	Coffee Break	
	Special Lecture on Brain Health (2)	**Chair:** Dr. Akiko Mizokami
16:40-17:40	Deconstructing the molecular and cellular mechanisms of tolerance to benzodiazepines: a key role for PLCdelta	Dr. Jasmina Jovanovic

February 9 (Sunday)

Time	Title	Presenter
Session 2	**Report from Undergraduate Students**	**Chair:** Prof. Fusanori Nishimura
9:00-9:10	6th UGM Dental Summer Course	4th grade of Undergraduate Student
9:10-9:20	My Life in Vancouver for 3weeks	Akiha Nishinami
Session 3	**Graduate Student's Session**	**Chair:** Taiga Ono and Akira Chinju
9:20-9:35	IL-1 inducing inflammation by CD163+ M2 macrophages contributes to the fibrosis of IgG4-related disease via TLR7/IRAK4/NFκB signaling.	Akira Chinju
9:35-9:50	Oral dysbiosis of patients with hematological disorders on the day of transplantation	Saori Oku
9:50-10:05	A novel inhibitor of NF-κB-inducing kinase improve bone loss by inhibiting osteoclast formation in ovariectomized mice	Nana Takakura
10:05-10:15	Coffee Break	
	Award Lecture (IF Award)	**Chair:** Prof. Tamotsu Kiyoshima
10:15-10:35	Effects of TNF-α on Senescent human dental pulp cells	Dr. Aoi Nozu
10:35-10:55	Janus-faced cathepsin B in microglia and neuron in aging and neurodegenerative diseases	Dr. Junjun Ni
10:55-11:15	Autocrine regulation of mesenchymal progenitor cell fates orchestrates tooth eruption.	Dr. Akira Takahashi
11:15-11:30	Award Presentation (IF Award & FWCI Award)	
11:30-11:40	Coffee Break	
	Special Lectures	**Chair:** Prof. Seiji Nakamura
11:40-12:20	Development of Bone Substitute from Porcine	Prof. Wei-Jen Chang
12:20-13:00	The inter-professional dental education system in TMU	Prof. Hsin-Chung Cheng
13:00	Closing Remarks	Prof. Eijiro Jimi

ABSTRACTS

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Oral Health and Total Health

Chaired by Dr. Masafumi Moriyama

Establishing periodontal ligament stem cell-like cells derived from iPS cells

Sayuri Hamano[1,2], Atsushi Tomokiyo[3], Daigaku Hasegawa[3], Shinichiro Yoshida[3], Hideki Sugii[3], Shoko Fujino[1], and Hidefumi Maeda[1,3]

[1] Department of Endodontology and Operative Dentistry, Faculty of Dental Science,
[2] OBT Research Center, Faculty of Dental Science, Kyushu University,
[3] Department of Endodontology, Kyushu University Hospital

The periodontal ligament (PDL) plays an important role in the maintenance of teeth. Damage to the PDL, such as after severe inflammation, could be treated with a therapeutic strategy that uses stem cells derived from PDL tissue (PDLSCs), which has received intense scrutiny over the past decade. However, the PDLSCs are difficult to obtain, due to their limited cell number in PDL tissue. Therefore, we sought to induce the differentiation of induced pluripotent stem (iPS) cells into PDLSCs as an initial step toward PDL therapy. To this end, we first induced iPS cells into neural crest (NC)-like cells. We then captured the p75 neurotrophic receptor-positive cells (iPS-NC cells) using magnetic cell separation and cultured them on an extracellular matrix (ECM) produced by human primary PDL cells (iPS-NC-PDL cells). These iPS-NC-PDL cells showed reduced expression of embryonic stem cell and NC cell markers as compared with iPS and iPS-NC cells, and enrichment of mesenchymal stem cell markers. The cells also had a higher proliferative capacity, multipotency, and elevated expression of PDL related markers than iPS-NC cells cultured on fibronectin and laminin (iPS-NC-FL cells) or ECM produced by human skin fibroblast cells (iPS-NC-SF cells). iPS-NC-PDL cells were transplanted subcutaneously into the dorsal surfaces of immunocompromised mice. In 8 weeks after transplantation, iPS-NC-PDL cells formed periodontal ligament-like structure. In this study, the culture method to produce high number of PDLSC-like cells from iPS cells was showed. It was suggested that PDLSC-like cells from iPS cells were useful for PDL tissue regeneration.

Roles of TRPM7 in tooth development and bone formation

Masashi Shin[1,2], Shihomi Mori[1,3], Fujio Okamoto[1], Hiroshi Kajiya[1,2] & Koji Okabe[1]

[1]Section of Cellular Physiology, Department of Physiological Science and Molecular Biology, [2]OM Research Center, [3]Section of Oral Surgery, Department of Oral and Maxillofacial Surgery, Fukuoka Dental College, Japan

Transient receptor potential M7 (TRPM7) is a protein which has two functions, an ion channel and a kinase. TRPM7 is highly expressed in ameloblasts, although it is expressed ubiquitously among tissues. TRPM7 KR (kinase dead) mice, which channel function is intact, and TRPM7 epithelium specific or mesenchymal specific conditional knock out (cKO) mice were analyzed to elucidate the functions in enamel development and bone formation. TRPM7 KR and cKO were characterized by patch clamp, histological analyses, micro-CT, Scanning Electron Microscope (SEM) and immunoprecipitation assay. There were no significant difference between the amplitudes of the Mg^{2+}-inhibited cation (MIC) current in ameloblasts from wild-type (WT) and TRPM7 KR, while the amplitudes of the TRPM7 cKO MIC current were smaller than that of WT. TRPM7 KR mice displayed minor abnormalities of the enamel, whereas TRPM7 cKO mice showed much severe enamel defects. Phosphorylation of intracellular molecules Smad 1/5/9, p38 and cAMP response element binding protein (CREB) was inhibited in ameloblasts from TRPM7 KR. It is indicated that CREB bound to TRPM7 by immunoprecipitation assay. In bone formation, long bone of TRPM7 cKO was shorter than that of WT, but not in TRPM7 KR. Chondrocyte differentiation was downregulated in TRPM7 cKO, and bone resorption increased in TRPM7 cKO. Our data suggest that TRPM7 kinase regulates enamel development via phosphorylate CREB, Smad1/5/9 and p38, and that TRPM7 channel function is also important in enamel development. On the other hand, in mesenchymal cell TRPM7 ion channel function is critical for bone formation via chondrogenesis.

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Special Lecture on Total Health

Chaired by Dr. Zhou Wu

Fatty acid sensors and their functional distributions in mouse taste tissue

Keiko Yasumatsu[1,2]

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[2]*R&D Center for Five-Sense Devices, Kyushu University, Fukuoka, Japan*

In the last decade, GPR40, GPR120 and CD36 have been reported as fatty acid sensors in rodents' taste systems. To elucidate whether fatty acid taste has a quality that does not overlap with other primary qualities, we investigated potential neuron types coding fatty acid information and how these fatty acid sensors are involved. We found fibers showing a maximal response to oleic acids (F-type) in ~18 % of mouse chorda tympani (CT) nerve. Additionally, a half or more of fibers showing a maximal response to sucrose (S-type) or monopotassium glutamate (M-type) showed responses to fatty acids. GPR120 was revealed to be involved in the responses in these fiber types. Furthermore, to examine potential function of GPR40 and CD36, we performed single fiber recordings from the CT and the glossopharyngeal (GL) nerves in GPR120-KO and wild type (WT) mice. Among recorded GL fibers, percentage of F-type fiber was ~7 % and ~2.4 % in WT and GPR120-KO mice respectively. More than 60% of S-type or M-type fibers showed responses to fatty acids in both mice strain. The proportion of F-type and the other showing response to fatty acid is 2: 3 for the CT and 2: 13 for the GL of WT mouse. In GPR120-KO mice, inhibitors of GPR40 and CD36 were significantly suppressed responses to fatty acids in S- and M-type fibers of the GL. These results suggest that the proportion of neurons for palatable information of fatty acid in the GL is much more than those in the CT. GPR40 and CD36 may be involved in the palatable information. The roles or significances of these fatty acid sensors will be discussed in terms of homeostasis.

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Special Lecture on Brain Health 1

Chaired by Dr. Eijiro Jimi

Assessment of the olfactory function in the brain using ultra-high field functional magnetic resonance imaging

Ikuhiro Kida[1,2]

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[2] *Graduate School of Frontier Biosciences, Osaka University, Japan.*

The mechanism of olfactory information processing in the brain remains unknown because of the difficulty in noninvasively obtaining in vivo data. However, the molecular and physiological knowledge regarding olfactory function in the peripheral receptor level has been well investigated by in vitro and invasively obtained data. Functional magnetic resonance imaging (fMRI) is a robust tool for visualizing brain activation in vivo. FMRI at ultra-high field (UHF) strength has a high signal-to-noise and higher contrast, resulting in high spatial and temporal resolutions; therefore, it has a great potential to be used for investigating the brain function. However, several disadvantages such as image distortion, signal loss, and high specific absorbed rate should be overcome while using fMRI. In the first half part of this lecture, we would like to introduce the advantages and disadvantages of UHF fMRI. We have been developing UHF fMRI for analyzing the brain function, especially the olfactory function, and have successfully mapped the brain activation for odorants. In the last half part of this lecture, a functional representation of the olfactory function in the rodent's olfactory bulb and human brain will be presented. In brief, the functional topographic map was found to conserve odorants in the rodent's olfactory bulb, independent of the odorant concentration and stimulus duration. Odor information, quality and hedonic tone, was also found to be encoded in the piriform cortex and orbitofrontal cortex of the human brain. Therefore, UHF fMRI could improve our understanding on the olfactory information processing by combining functional representations with molecular and physiological knowledge regarding olfactory function in the peripheral receptor level.

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Special Lecture on Brain Health 2

Chaired by Dr. Akiko Mizokami

Deconstructing the molecular and cellular mechanisms of tolerance to benzodiazepines: a key role for PLCdelta

Jasmina N Jovanovic

Department of Pharmacology, School of Pharmacy, University College London, United Kingdom

$GABA_A$ receptors represent a large and diverse family of GABA-gated chloride/bicarbonate channels, which mediate the majority of the fast inhibitory neurotransmission in the brain. To date, cellular and molecular changes in GABAergic system caused by sustained exposure to benzodiazepines remain poorly characterised. Here we report that prolonged $GABA_A$ receptor activation by diazepam, the most widely used benzodiazepine in clinic, leads to a gradual disruption of functional inhibitory GABAergic synapses, which correlates with a pronaunced decrease in the number and size of synaptic clusters of $GABA_A$ receptors as well as their colocalisation with the presynaptic GABA-releasing terminals. Moreover, a concomitant time- and dose-dependent decrease in the overall cell surface expression of $GABA_A$ receptors in response to diazepam was detected, mediated by dynamin-dependent internalisation of these receptors. In the presence of Ro 15-4513, a benzodiazepine site antagonist, bicuculine, a GABA site antagonist, as well as picrotoxin, a $GABA_A$ channel blocker, both the loss of synapses and endocytosis of $GABA_A$ receptors were abolished, indicating that the receptor activation is integral to the mechanisms triggering these processes. Further characterisation has revealed a critical role of $GABA_A$ receptor-associated PLCdelta leading to mobilisation of intracellular calcium and activation of calcium/calmodulin-dependent phosphatase calcineurin, which facilitates internalisation of $GABA_A$ receptors and disruption of GABAergic synapses. Together, these results indicate that changes in intracellular calcium concentration mediated by PLCdelta and subsequent activation of calcineurin are important molecular events leading to development of pharmacological tolerance to benzodiazepines.

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Report from Undergraduate Students

Chaired by Dr. Fusanori Nishimura

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Graduate Student's Session

Chaired by Taiga Ono and Akira Chinju

IL-1 inducing inflammation by CD163$^+$ M2 macrophages contributes to the fibrosis of IgG4-related disease via TLR7/IRAK4/NFκB signaling.

Akira Chinju[1], Masafumi Moriyama[1,2], Noriko Ishiguro[1], Miho Ohta[1], Takashi Maehara[1], Akihiko Tanaka[1], Mizuki Sakamoto[1], Haque A.S.M. Rafiul[1], Keita Mochizuki[1], Yuko Ono[1], Ryusuke Munemura[1], Jun-Nosuke Hayashida[1], and Seiji Nakamura[1]

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Backgrounds: IgG4-related dacryoadenitis and sialoadenitis (IgG4-DS) is characterized by elevated serum IgG4 and marked inflammation with fibrosis in lacrimal and salivary glands (SGs). We previously reported that human *TLR7* transgenic (Tg) mice showed the elevated serum IgG1 (equaled to human IgG4) and the inflammation with fibrosis in SGs. Moreover, we confirmed that TLR7-positive cells were mainly CD163$^+$ M2 macrophages in SGs from IgG4-DS patients. However, the immune-pathogenesis of IgG4-DS via TLR7 pathway remains unclear. In this study, we thus examined the downstream of TLR7 and the mechanism of fibrosis by TLR7-positive cells.

Methods: Gene expression was analyzed by DNA microarray in SGs from Tg mice and IgG4-DS patients. Common upregulated TLR7-related molecules were validated by real-time PCR and immunohistochemical staining in SGs from patient with IgG4-DS (n=15), Sjögren's syndrome (SS) (n=15), CS (n=15), and controls (n=15). Next, CD163$^+$ M2 macrophages isolated by PBMC from healthy controls were stimulated by TLR7 agonist (loxoribine), and then measured the cytokine concentration of culture supernatant by ELISA. Finally, we investigated the interaction between CD163$^+$ M2 macrophages and fibroblast.

Results: In both TG mice and IgG4-DS patients, IRAK4 and IRAK3 were significantly overexpressed by DNA microarray. PCR validated the up-regulation of only IRAK4 in IgG4-DS patients compared with the other groups. Immunohistochemical analysis confirmed strong infiltration of IRAK4-positive cells in/around germinal centers in SGs from only IgG4-DS patients. Double immunofluorescence staining showed that IRAK4-positive cells mainly co-localized with CD163$^+$ M2 macrophages in the SGs. After stimulation of TLR7 agonist, CD163$^+$ M2 macrophages significantly enhanced the mRNA expression of IRAK4 and NFκB, and the supernatant concentrations of fibrotic cytokines (IL-1β and TGF-β). Finally, we confirmed that the supernatant of CD163$^+$ M2 macrophages stimulated by TLR7 agonist were increased the number of fibroblasts.

Conclusion: CD163$^+$ M2 macrophages produce fibrotic cytokines via TLR7/IRAK4/NFκB signaling and then promote the fibrosis in IgG4-DS by production of fibrotic cytokines.

Oral dysbiosis of patients with hematological disorders on the day of transplantation

Saori Oku[1,2], Toru Takeshita[1,3], Toshiko Futatsuki[2], Shinya Kageyama[1], Mikari Asakawa[1], Haruhiko Kashiwazaki[2], Yoshihisa Yamashita[1]

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Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective treatment for hematological malignancies and non-neoplastic blood diseases. Some studies have revealed that disruption of the intestinal microbiota caused by pretransplant chemotherapy and/or irradiation correlated with severe gut graft-versus-host disease and infectious complications, resulting in poorer outcomes among allo-HSCT recipients. However, there are no studies of the bacterial composition of oral microbiota in allo-HSCT recipients. In this study, we collected the tongue microbiota from allo-HSCT recipients and investigated the bacterial composition.

Oral microbiota samples were collected from the tongue dorsum on the day of transplantation with a cotton swab. We compared the oral microbiota between 45 allo-HSCT recipients and 164 community-dwelling adults by sequencing V1–V2 regions of the 16S rRNA gene. In addition, we employed full-length 16S rRNA gene sequencing analysis with a high taxonomic resolution by using a third-generation sequencer, PacBio Sequel to identify the nonindigenous taxa colonizing the oral cavity of the allo-HSCT recipients.

The microbiota of allo-HSCT recipients had less diversity and some unique bacterial taxa not present in community-dwelling adults. The full-length 16S rRNA gene sequences obtained by PacBio Sequel identified 114 bacterial taxa in the allo-HSCT recipients, of which 34 bacterial taxa did not correspond to oral bacteria deposited in the expanded Human Oral Microbiome Database. We found that the presence of *Staphylococcus haemolyticus* (n = 8) or *Ralstonia pickettii* (n = 13) was significantly associated with higher mortality rate during the follow-up period. We further analyzed and found that additional antibiotics use for febrile neutropenia infection and/or infection was significantly relevant for the detection of these bacteria.

Dysbiosis was observed also in the oral cavity among allo-HSCT recipients, which might affect their transplant outcome. We should have careful attention to bacterial composition of the disrupted oral microbiota in allo-HSCT recipients.

A novel inhibitor of NF-κB-inducing kinase improve bone loss by inhibiting osteoclast formation in ovariectomized mice

Nana Takakura[1,2], Miho Matsuda[1], Fumitaka Hiura[1], Kayo Mori[1], Chiaki Kitamura[2], Eijiro Jimi[1,3]

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Musculoskeletal diseases and disorders, including osteoporosis and rheumatoid arthritis are known as diseases that threaten our healthy life. In such diseases, increased osteoclastic bone resorption induced by excessive immune responses leads to bone destruction. Transcription factor NF-κB regulates gene expression during immune responses as well as receptor activator of NF-κB ligand (RANKL)-induced osteoclastogenesis. RANKL activates both the canonical and the non-canonical NF-κB signaling pathway. We previously reported that Alymphoplasia (*aly/aly*) mice, which has an inactive form of NF-κB-inducing kinase (NIK) show mild osteopetrosis with a decrease in osteoclast number and without processing of p100 to p52 in the non-canonical NF-κB pathway. Then we suggested that the non-canonical NF-κB pathway is effective drug target to prevent bone destruction. Recently, a novel NIK selective inhibitor, compound 33 (Cpd33) was developed and we examined the effect of Cpd33 on differentiation and function of osteoclasts in vitro and in vivo. Cpd33 inhibited RANKL-induced osteoclastogenesis in a dose-dependent manner without bad effects on cell viability. And Cpd33 suppressed expression of nfatc1, dc-stamp and cathepsin K, markers of osteoclast differentiation. Cdp33 selectively suppressed RANKL-induced the processing of p100 to p52 without inhibition of the canonical NF-κB pathway. Cpd33 also suppressed function of bone resorption in mature osteoclasts. Furthermore, Cdp33 treatment prevented bone loss by suppressing osteoclast number without affecting osteoblastic bone formation in ovariectomized (OVX) mice. Taken together, NIK inhibitor might useful for the treatment of bone diseases for patients who had lower response to conventional pharmacotherapy or who have serious side effects.

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Award Lectures

Chaired by Dr. Tamotsu Kiyoshima

Effects of TNF-α on Senescent human dental pulp cells

Aoi Nozu[1], Sayuri Hamano[1,2], Atsushi Tomokiyo[3], Daigaku Hasegawa[3], Shinichiro Yoshida[3], Hideki Sugii[3], Tomohiro Itoyama[1], Taiga Ono[1], Shoko Fujino[1], Keita Ipposhi[1], Hidefumi Maeda[1,3]

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Objectives: Aging is characterized by chronic, low-grade inflammation, and this phenomenon has been termed as inflammaging. It has been reported that the concentration of tumor necrosis factor-α (TNF-α) is higher in the blood of aged people compared with that of young people. Therefore, the aim of this study was to investigate how TNF-α affected pulp cells during aging.

Methods: Human dental pulp cells (HDPCs) were cultured until reaching the plateau of their growth, and the cells were isolated at actively (yHDPCs) or inactively (sHDPCs) proliferating stages, whose gene expression of senescence-related factors, TNF-α, and its receptor, *TNFR1* was examined by quantitative PCR. In addition, on odontoblastic differentiation of yHDPCs and sHDPCs cultured in control culture medium (CM) or CM containing 2mM $CaCl_2$ as differentiation medium (DM) with or without TNF-α was examined by quantitative PCR and alizarin red staining. Furthermore, the contribution of the signaling via *TNFR1* to mineralization of sHDPCs was examined by transfection of TNFR1 siRNA.

Results: sHDPCs expressed senescence-related molecules while yHDPCs did not. The expression level of *TNF-α* in sHDPCs was significantly higher than that in yHDPCs. When these HDPCs were cultured in DM, the mineralization activity of sHDPCs was lower compared with that of yHDPCs. However, the administration of TNF-α to this culture medium altered these responses: yHDPCs showed downregulated mineralization per a cell, while sHDPCs exhibited a significant increase. Furthermore, the expression of *TNFR1* in sHDPCs was significantly upregulated compared with that in yHDPCs. Downregulation of *TNFR1* expression led to decreased mineralization of TNF-α-treated sHDPCs.

Janus-faced cathepsin B in microglia and neuron in aging and neurodegenerative diseases

Junjun Ni

Department of cell biology and pharmacology, Faculty of Dental Science, Kyushu University, Japan.

Cathepsin B (CatB, EC 3.4.22.1), a typical cysteine lysosomal protease, is believed to disintegrate proteins as well as larger structures because they irreversibly cleave peptide bonds; however, there is increasing evidence it also exerts modulator actions, by which substrates are activated after limited cleavage. CatB has been found to express in both microglia and neuron during development, aging and neurodegenerative diseases. However, findings from different groups are controversial and confusing. We herein studied the functions of CatB separately in microglia and neurons.

In hypoxic-ischemia mice, we found CatB could work as a phenotypic switch in microglia along the M1-M2 phenotypic continuum through the dynamics of NF-κB activity (Ni et al., 2015); In aged mice, we found that increase and leakage of CatB in microglia are responsible for the increased generation of mitochondria-derived ROS and proinflammatory mediators, culminating in memory impairment (Ni et al., 2019); In Alzheimer's disease model mice, we have found that the expression of CatB was increased gradually in microglia from 2 to 8-month old AD mice, while decreased significantly in neuron from 6 to 8-month old AD mice. It was noted that, 6-month old APP-KI mice has showed the AD pathology including Aβ accumulation, microgliosis, and memory decline. Combined with *in vitro* studies, we found that CatB in microglia initiates the inflammation and promotes Aβ pathology, while CatB in neurons plays a role in the clearance of Aβ.

Early intervention and late resolution are both important in the AD treatment processes. Therefore, inhibition of CatB in microglia in the early stage and upregulation of CatB in neurons in the late stage of AD will provide preventing and therapeutic strategies for AD.

Autocrine regulation of mesenchymal progenitor cell fates orchestrates tooth eruption.

Akira Takahashi[1,2], Yoichiro Ogino[1], Kiyoshi Koyano[1], Noriaki Ono[2], Wanida Ono[2]

[1]*Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University*
[2]*Department of Orthodontics and Pediatric Dentistry, University of Michigan, School of Dentistry*

Formation of functional skeletal tissues requires highly organized steps of mesenchymal progenitor cell differentiation. The dental follicle (DF), a sac-like membranous tissue surrounding the developing tooth bud, harbors mesenchymal progenitor cells for various differentiated cells constituting the tooth root-bone interface, and coordinates tooth eruption in a manner dependent on signaling by parathyroid hormone-related peptide (PTHrP) and its receptor, PTH/PTHrP receptor (PPR). In humans, primary failure of tooth eruption (PFE), a rare autosomal dominant disorder that exclusively affects tooth eruption, is characterized by a cessation of tooth eruption before emergence despite an unobstructed eruption path. PFE is caused by loss-of-function mutations in PPR. However, the identity of mesenchymal progenitor cells in the DF and how they are regulated by PTHrP-PPR signaling remain unknown. Here we show that the PTHrP-PPR autocrine signal maintains physiological cell fates of DF mesenchymal progenitor cells to establish the functional periodontal attachment apparatus and orchestrates tooth eruption. Cell lineage analysis using tamoxifen-inducible *PTHrP-creER* mice revealed that PTHrP^{+} DF cells differentiated into cementoblasts on the acellular cementum, periodontal ligament (PDL) cells and alveolar cryptal bone osteoblasts during tooth root formation. PPR-deficiency induced a cell fate shift of PTHrP^{+} DF mesenchymal progenitor cells to non-physiological cementoblast-like cells precociously forming the cellular cementum on the root surface associated with upregulation of *Mef2c* and matrix proteins, resulting in loss of the proper periodontal attachment apparatus and PFE closely resembling human genetic conditions caused by PPR mutations. These findings reveal a unique mechanism whereby proper cell fates of mesenchymal progenitor cells are tightly maintained by an autocrine system mediated by PTHrP-PPR signaling to achieve functional formation of skeletal tissues.

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Special Lectures

Chaired by Dr. Seiji Nakamura

Development of Bone Substitute from Porcine

Wei-Jen Chang[1,2] Eisner Salamanca[1,] Chia-Chen Hsu[1,2], Haw-Ming Huang[1], Nai-Chia Teng[1,3,] Che-Tong Lin[1,3], Yu-Hwa Pan[1,4,5,6]

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4Department of General Dentistry, Chang Gung Memorial Hospital, Taipei, Taiwan.
5Graduate Institute of Dental & Craniofacial Science, Chang Gung University, Taoyuan, Taiwan.
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In the past decades, bone substitute were developed and applied for the periodontal and bone reconstruction. Among the bone substitutes, the biocharacteristics of xenogeneic grafts make them a possible substitute for autogenous bone grafts in dental bone graft procedures. Especially, xenogeneic grafts from bovine were wide applied in the dental clinic and perfomed the excellent clinical outcome. However, Creutzfeldt–Jakob disease (CJD) was reported to be transmitted by the bovine grafts after 2000. Therefore, this study aimed to develop a novel porcine graft with /without collagen capable of generating new bone in bone defects. The porcine grafts were made to undergo a cell viability test (MTT) and alkaline phosphatase assay (ALP). The developed grafts were implanted into the New Zealand rabbits for the radiographic and histological examination. Histological and micro-CT scan results showed that the performance of the porcine collagen graft is superior for regenerating new bone. Porcine collagen graft showed cell viability and osteoblastlike cell diferentiation in vitro. The results indicate that porcine collagen graft is a potential bone substitute for clinical application.

The Inter-Professional Dental Education System in TMU

Hsin-Chung Cheng, DDS, MS, PhD

Dean and professor, College of Oral Medicine, College of Oral Medicine,
Director, Orthodontic Department, Taipei Medical University Hospital,
Taipei, Taiwan

The formal simulation training programs have been developed in school of dentistry (SOD) of Taipei Medical University since 2009. The first program was Objective Structured Clinical Examination (OSCE) and performed in the 6th grade students of SOD. From that time, SOD began to develop and incorporate the OSCE systems into all clinical dental curriculums. Though the OSCEs have become the requirement of medicine licenses examination in Taiwan since 2013, the dentist license examination is not yet. SOD provide the new regulation that all dental students should pass the OSCEs before entering internship and will be implemented in 2017. By the way, SOD has also created GOSCE (Group practice in OSCE) cooperated with students of school of dental technology and school of oral hygienists. At the same time, we also carried out TRM (Team Resource Management) on clinical dental emergency in senior dental students in 2015. The presenter will further introduce and share our experience in "Integrated Clinical Teaching System in Dental Group Practices" for the past years in College of Oral Medicine, College of Oral Medicine in this report.