The 69th Annual Meeting of
Japanese Association for Dental Research

Re-defining the Mission of Dental Research towards Post-corona World

October 24 (Sun.) — October 25 (Mon.), 2021
Hybrid Meeting (Onsite at Kyushu University and Online)
JAPANESE ASSOCIATION FOR
DENTAL RESEARCH

The 69th ANNUAL MEETING
October 24-25, 2021
Hybrid Meeting (Onsite at Kyushu University and Online)
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Welcome Message

69th Japanese Association for Dental Research General Session & Exhibition

I would like to welcome all of you to attend 69th JADR General Session & Exhibition, which will be held on October 24th and 25th. Due to the pandemic of Covid-19, it will be held both at onsite (Kyushu University Hospital Campus) and online (hybrid holding).

I assume all the attendants have been struggling and asking themselves as to what we could have done and what we can do in future for our society in this difficult situation caused by Covid-19 pandemic. In this meeting, I would like you to discuss about this issue each other. Therefore, the main theme of this meeting was decided as “Re-defining the Mission of Dental Research towards Post-corona World”. To begin to discuss about this issue, we will welcome Dr. Hiroshi Kiyono, former president of Japanese Society for Immunology, as special lecturer. I am so sure that his lecture not only suggest us thoughtful consideration as a top leading immunologist but also provide us encouraging message as a dentist. Besides this special lecture, we will hold 1st Japan-Korea co-operative symposium which was originally planned last year, and other special symposiums entitled “Japan-Originated Next Generation Biomedical Materials”, “Current Progress of Stem Cell Biology and Regenerative Medicine in Dental Science”. I am confident that the symposiums provide us most up-dated topics on regenerative dentistry and dental biomaterials. We also hold “Rising Scientist Symposium” which was just started last year.

We really wished to host the meeting on site here in Fukuoka. However, unfortunately, this pandemic is still threatening us all over the country, and therefore, we chose hybrid holding. Although we may not discuss each other face to face, we would like to provide opportunity to re-define our important mission imposed to the researchers in dental field toward post-corona world.

Sincerely,

FUSANORI NISHIMURA
President, 69th JADR General Session & Exhibition
Section of Periodontology, Division of Oral Rehabilitation, Kyushu University Faculty of Dental Science
OFFICERS
OF
JAPANESE ASSOCIATION
FOR DENTAL RESEARCH

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Secretary-general ......................................... T. Sanui
## JADR Timetable October 24th (Sun.), 25th (Mon.)
**Video Distribution/ Live Streaming**

### October 24th (Sun.), 2021

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<td>Greeting from IADR President</td>
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<td>9:30 ~ 9:45</td>
<td>Greeting from KADR President</td>
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<td>9:45 ~ 10:30</td>
<td>KADR President Lecture</td>
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<td>10:30 ~ 11:15</td>
<td>Special Lecture</td>
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<tr>
<td>11:15 ~ 12:15</td>
<td>Council Meeting / General Assembly</td>
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<td>12:15 ~ 13:00</td>
<td>Break</td>
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<td>13:00 ~ 13:50</td>
<td>JADR/KADR Joint Symposium</td>
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<td>13:50 ~ 14:45</td>
<td>Break</td>
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<td>14:45 ~ 15:40</td>
<td>Symposium II</td>
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<td>9:00 ~ 10:00</td>
<td>Symposium I</td>
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<td>10:00 ~ 11:00</td>
<td>Japan-Originated Next Generation Biomedical Materials</td>
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<td>11:00 ~ 12:00</td>
<td>Rising Scientist Session</td>
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<td>12:00 ~ 13:00</td>
<td>Break</td>
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<td>13:00 ~ 14:00</td>
<td>Break</td>
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<tr>
<td>14:00 ~ 15:00</td>
<td>Symposium II</td>
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<td>15:00 ~ 16:00</td>
<td>Closing Ceremony</td>
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### Details
- **Opening Ceremony**
- **Greeting from IADR President**
- **Greeting from KADR President**
- **KADR President Lecture**
- **Special Lecture**
- **Council Meeting / General Assembly**
- **JADR/KADR Joint Symposium**
- **Symposium I**
- **Japan-Originated Next Generation Biomedical Materials**
- **Rising Scientist Session**
- **Symposium II**
- **Current progress of Stem Cell Biology and Regenerative Medicine in Dental Science**
- **Closing Ceremony**
JADR Timetable
October 24th(Sun.) - 25th.(Mon.)
Video and Poster File distribution

Greeting from IADR President (Video distribution)
Prof. Eric Reynolds
(President of IADR)

Greeting from KADR President
KADR President Lecture (Video distribution)
Prof. Kung-Rock Kwon
(President of KADR)
“Esthetic & Functional oral rehabilitation : 4 control factors”

Special Lecture (Video distribution)
Prof. Hiroshi Kiyono
(Division of Mucosal Immunology, Department of Microbiology and Immunology, The Institute of Medical Science, The University of Tokyo)
“Past, Present and Future of Mucosal Vaccine: Vital Contributions Made by Dentistry”

Poster Presentation (Poster File distribution of presentation file (PDF))
October 24th, Sunday, ~ October 25th, Monday

Greeting from IADR President  
(Video distribution)  
October 24th, Sunday, 9:00-9:15  
G-1

Dr. Eric Reynolds  
President of IADR

Greeting from KADR President  
KADR President Lecture  
(Video distribution)  
October 24th, Sunday, 9:15-10:15

Dr. Kazunori Ikebe  
(Department of Prosthodontics, Gerodontology and Oral Rehabilitation, Osaka University Graduate School of Dentistry)

KL “Esthetic & Functional oral rehabilitation : 4 control factors”

Dr. Kung-Rock Kwon,  
President of KADR  
(Department of Prosthodontics School of Dentistry, Kyung Hee University, Seoul, South Korea)

Special Lecture  
(Video distribution)  
October 24th, Sunday, 10:30-11:30

Moderator: Dr. Seiji Nakamura

(Section of Oral and Maxillofacial Oncology, Division of Maxillofacial Diagnostic and Surgical Sciences, Faculty of Dental Science, Kyushu University)

SL “Past, Present and Future of Mucosal Vaccine: Vital Contributions Made by Dentistry”

Dr. Hiroshi Kiyono  
(Division of Mucosal Immunology, IMSUT Distinguished Professor Unit  
The Institute of Medical Science, The University of Tokyo)

The 1st Joint Symposium of KADR and JADR  
(Video distribution and Live Session)  
October 24th, Sunday, 13:30-15:30

The 1st Joint Symposium of KADR and JADR  
“Regenerative medicine/Dentistry “

Organizer/ Moderator: Dr. Hiroshi Egusa  
(Division of Molecular and Regenerative Prosthodontics, Tohoku University Graduate School of Dentistry)
JS-1 Comprehensive analysis for the genes associated with epithelial-mesenchymal interactions in tooth
Dr. Keigo Yoshizaki
(Department of Orthodonitics and Dentofacial Orthopedics, Faculty of Dental Science, Kyushu University)

JS-2 Periodontal regeneration by BMP7-overexpressing bone marrow mesenchymal stem cells in a ligature-induced periodontitis rat model
Dr. Jeong-Ho Yun
(Department of Periodontology, Jeonbuk National University College of Dentistry)

JS-3 Exacerbation mechanism of alveolar bone destruction in apical periodontitis caused by inflammatory bowel disease.
Dr. Masahiro Saito
(Department of Ecological Dentistry, Division of Operative Dentistry, Tohoku University Graduate School of Dentistry)

JS-4 Implant Supported Overdentures for the Elderly Edentulous Patients
Professor, Kung-Rock Kwon
(Department of Prosthodontics, School of Dentistry, Kyung Hee University, Seoul, Korea)

Symposium I
(Video distribution and Live Session)
October 25th, Monday 9:00-10:40
Symposium I
“Japan-Originated Next Generation Biomedical Materials “
Organizer/ Moderator: Dr. Yasunori Ayukawa
(Division of Oral Rehabilitation, Department of Dental Science, Kyushu University Faculty of Dental Science)

SI-1 Honeycomb scaffolds: vertical bone augmentation and antibacterial effects
Dr. Koichiro Hayashi
(Department of Biomaterials, Faculty of Dental Science, Kyushu University)

SI-2 Bone quality management effects of newly developed dental implant design
Dr. Takashi Sawase
(Department of Applied Prosthodontics, Institute of Biomedical Sciences, Nagasaki University)

SI-3 Bioactive performance of octacalcium phosphate and its composite materials
Dr. Osamu Suzuki
(Division of Craniofacial Function Engineering, Tohoku University Graduate School of Dentistry)

SI-4 Periodontal regeneration by cytokine therapy- its present status and future perspective-
Dr. Shinya Murakami
(Department of Periodontology Osaka University Graduate School of Dentistry)

Rising Scientist Session
(Video distribution and Live Session)
October 25th, Monday 11:00-12:30
Rising Scientist Session
"Periodontal Medicine "
Organizer/ Moderator: Dr. Kazuhisa Yamazaki
(Niigata University Graduate School of Medical and Dental Sciences)
RS-1 PPARγ-induced global H3K27 acetylation is required to maintain the abilities of extracellular matrix organization and osteo/cementogenesis in periodontal ligament fibroblasts: the possible link between dietary unsaturated fatty acids and periodontal tissue homeostasis
Dr. Shigeki Suzuki
(Department of Periodontology, Tohoku University Hospital)
RS-2 Microbiome-targeted Probiotic Therapy Prevents Hepatic Lipid-metabolism Abnormality following Polymicrobial-Periodontal Infection via Improving Oral and Gut Dysbiosis
Dr. Ryutaro Kuraji
(Department of Life Science Dentistry, The Nippon Dental University, Tokyo, Japan)
RS-3 Infertility and Periodontitis
Dr. Kazuhiro Omori
(Department of Periodontics and Endodontics, Division of Dentistry, Okayama University Hospital, Japan)
RS-4 The role of chronic low-grade inflammation on energy expenditure: association with CCL19/CCR7 axis
Dr. Misaki Iwashita
(Section of Periodontology, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University)

Symposium II
(Video distribution and Live session)
October 25th, Monday 14:00-15:40
Symposium II
“Current progress of Stem Cell Biology and Regenerative Medicine in Dental Science “
Organizer/ Moderator: Dr. Takayoshi Yamaza
(Oral Biological Sciences, Department of Dental Science, Kyushu University Faculty of Dental Science)
SII-1 Single-cell RNA sequence from mouse incisor and molar reveals dental epithelial cell-type specific genes
Dr. Satoshi Fukumoto
(Section of Pediatric Dentistry, Kyushu University Faculty of Dental Science)
SII-2 Recent Progress of Pulp Regenerative Therapy with Dental Pulp Stem Cells for the Application to the Periapical Disease in the Aged.
Dr. Koichiro Iohara
(National Center for Geriatrics and Gerontology, Research Institute, Geroscience Research Center, Regenerative Dental Medicine)
SII-3 Induced tissue-specific stem cell, a non-tumorigenic intermediate cell induced from somatic or pluripotent cell: their generation and possible use in the regenerative medicine of dental science
Dr. Issei Saitoh
(Department of Pediatric Dentistry, Asahi University School of Dentistry)
SII-4 Exosomes secreted from TNF-α-preconditioned gingival tissue-derived stem cells enhance M2 mac-
rophage polarization and inhibit periodontal bone loss

Dr. Takao Fukuda

(Section of Periodontology, Division of Oral Rehabilitation, Kyushu University Hospital)
Poster Presentation

Cariology Research-Microbiological Studies/Biofilm

001: Collagen-binding properties of Streptococcus mutans killed by amoxicillin
   Y. SUEHIRO, S. MATAYOSHI, M. OTSUGU, R. NOMURA, K. NAKANO
   Department of Pediatric Dentistry, Osaka University Graduate School of Dentistry, Osaka, Japan

002: S-PRG eluate inhibits acid and glucan synthesis by Streptococcus mutans
   T. KITAMURA, S. MATAYOSHI, J. OHATA, Y. SUEHIRO, R. NOMURA, K. NAKANO
   Department of Pediatric Dentistry, Osaka University Graduate School of Dentistry, Osaka, Japan

003: Microbiological effects of silver diamine fluoride: an in situ study
   K. KLANLIANG¹, Y. ASAHI¹, H. MAEZONO¹, T. SHIMAOKA¹, N. KURIKI¹, H. MACHI²,
   S. EBISU¹, M. HAYASHI¹
   ¹Department of Restorative Dentistry and Endodontology, Graduate School of Dentistry, Faculty of Dentistry, Osaka University, ²Dental Technology Institute, Osaka University, Osaka, Japan

004: Investigation of Streptococcus mutans collagen-binding protein pathogenicity
   D. MATSUOKA, S. NAKA, K. GOTO, M. MATSUMOTO-NAKANO
   Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

005: Analysis of specific Streptococcus mutans strains associated with non-alcoholic steatohepatitis
   K. TABATA, S. NAKA, M. MATSUMOTO-NAKANO
   Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

006: Inhibitory effect of cyclodextran on caries in animal model
   H. ASAUMI, M. MATSUMOTO-NAKANO
   Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

007: Role of ABC transporter in biofilm formation by Streptococcus mutans
   K. GOTO, M. MATSUMOTO-NAKANO
   Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Craniofacial Biology Research

008: BCOR mediated regulation of ZFPM2 via BCL6 involved in hyperactive root formation of OFCD syndrome
   K.M. SOE, T. OGAWA, K. MORIYAMA
   Department of Maxillofacial Orthognathics, Tokyo Medical and Dental University (TMDU), Tokyo, Japan
Dental Materials 3: Metal-based Materials and Other Materials

009: In vitro degradation test of resorbable GBR membrane, Cytrans ElaShield
Y. SAKAGUCHI, K. YAMANAKA, F. FUSEJIMA
GC Corporation, Tokyo, Japan

Dental Materials 5: Biocompatibility, Bioengineering and Biologic Effects of Materials

010: The effects of MTA exposed to NaOCl on odontoblastic differentiation of a human periodontal ligament stem cell line
K. YAMASHITA1, A. TOMOKIYO2, T. ONO2, K. IPPOSHI1, A. ALHASAN1, A. TSUCHIYA1, A. HAMANO2, H. SUGII1, S. YOSHIDA2, T. TAKAYAMA2, H. MAEDA1,2
1Department of Endodontology and Operative Dentistry, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2Department of Endodontology, Kyushu University Hospital, Fukuoka, Japan

011: Bone reconstruction using three-dimensional interconnected porous CO3Ap block fabricated based on hydrate expansion of CaO granules.
K. TANAKA1,2, A. TSUCHIYA2, Y. OGINO1, Y. AYUKAWA1, K. ISHIKAWA2
1Section of Fixed Prosthodontics, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2Department of Biomaterials, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

Dental Materials 2: Polymer-based Materials

012: Development of Novel Filler-Dispersed Resin Composite for 3D-Printed Permanent Crown
P. KARNTIANG1,2, H. IKEDA1, Y. NAGAMATSU1, H. SHIMIZU1
1Division of Biomaterials, Department of Oral Functions, Kyushu Dental University, Fukuoka, Japan, 2Division of Operative Dentistry, College of Dental Medicine, Rangsit University, Pathum-Thani, Thailand

Dental Materials 5: Biocompatibility, Bioengineering and Biologic Effects of Materials

013: Morphological observation of microvascular changes and bone formation after Alveolar bone regeneration.
M. MATSUO, M. TO
Department of Clinical Oral Anatomy, Kanagawa Dental University, Yokosuka, Japan

014: Tuning macrophage polarization by titanium nanosurfaces through nanotopographic cues to prevent peri-implantitis
N. KARTIKASARI, M. YAMADA, H. EGUSA
Division of Molecular and Regenerative Prosthodontics, Tohoku University graduate school of Dentistry, Sendai, Japan

Dental Materials 6: Instruments and Equipment

015: Effect of repeated use of end mill on the internal fitness of complete crown.
K. NOZAKI, K. KOMINE, W. YANAKA, M. MATSUMURA, S. OMNIA, C. SHIN, M. MATSUMURA, H. MIURA
Department of Fixed Prosthodontics, Graduate School of Medical and Dental Sciences, Tokyo
Dental Materials 5: Biocompatibility, Bioengineering and Biologic Effects of Materials

016: A novel bioabsorbable polysaccharide derivative for minimally invasive bone graft harvesting
K. NAKANISHI1, T. HASEGAWA2, H. HAYASHI1, K. NAGAMOTO4, H. OGUMA1, T. AKASAKA1, Y. YOSHIDA1
1Department of Biomaterials and Bioengineering, Hokkaido University, Sapporo, Japan, 2Department of Developmental Biology of Hard Tissue, Hokkaido University, Sapporo, Japan, 3Clinical Research and Medical Innovation Center Research and Development Division, Hokkaido University Hospital, Sapporo, Japan, 4Department of Oral Diagnosis and Medicine, Hokkaido University, Sapporo, Japan

Dental Materials 4: Adhesion

017: Bond Strengths of 4-META/MMA-TBB Resin Cement to Root Canal Dentin
T. OZAKI, S. OTAKE, W. KOMADA, K. NOZAKI, Y. YOKOSUKA, H. MIURA
Fixed Prosthodontics, Tokyo Medical and Dental University, Tokyo, Japan

Implantology Research

018: Ceria-stabilized zirconia substrate directly bonds to bone-like hydroxyapatite crystals at nano-scale
M.M. SAITO, Y. YAMAKOSHI
Department of Biochemistry and Molecular Biology, School of Dental Medicine, Tsurumi University, Yokohama, Japan

Microbiology/Immunology

019: The Relationship Among Child Dental Caries, Microbiome and Parental Awareness.
Y. KURIYAMA1, E. MIYAMOTO2, M. OHARA2, N. YASUDA1, Y. SHIMIZU1, S. OKAMURA1
1R&D, Sunstar Inc., Hyogo, Japan, 2Sunstar Foundation, Osaka, Japan

020: Involvement of Human Salivary Protein-derived Peptides-specific SIgA In Oral P. gingivalis Colonization.
K. KOYANAGI1, K. KATAOKA1,2, S. YANAGISAWA2, T. MIYAKE1
1Department of Preventive and Community Dentistry, Osaka Dental University, Osaka, Japan, 2Department of Oral Health Science and Social Welfare, Graduate School of Biomedical Sciences, Tokushima University, Tokushima, Japan

021: The Composition and Structure of Oral Microbiome: 16S rRNA Gene Analysis on Saliva, Plaque, Infected Root Canals obtained from a Patient
K. YAMAKI1, T. TAMAHARA2, J. WASHIO3, T. SATO4
1Division of Periodontology and Endodontology, Tohoku University Graduate School of Dentistry, Sendai, Japan, 2Department of Community Medical Supports, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan, 3Division of Oral Ecology and Biochemistry, Tohoku University Graduate School of Dentistry, Sendai, Japan, 4Division of Clinical Chemistry, Niigata University Graduate School of Health Sciences, Niigata, Japan
Mineralized Tissue

022: Bone apatite-clusters in intramembranous and endochondral ossification show distinct morphologies
E. HARA, M. OKADA, T. MATSUMOTO
Department of Biomaterials, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

023: A Materials Science-based Re-evaluation of Initial Tooth Mineralization
R. ANADA, E. HARA, N. NAGAOKA, M. OKADA, H. KAMIOKA, T. MATSUMOTO
1Department of Biomaterials, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 2Department of Orthodontics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 3Advanced Research Center for Oral and Craniofacial Sciences, Okayama University, Dental School, Okayama, Japan

024: Effects of TGF-β isoforms on ameloblasts
Y. MIYAKAWA, Y. YAMAKOSHI, Y. ASADA
1Department of Pediatric Dentistry, Tsurumi University School of Dental Medicine, Yokohama, Japan, 2Department of Biochemistry and Molecular Biology, Tsurumi University School of Dental Medicine, Yokohama, Japan

Neuroscience

025: Decreased expression of Neprilysin induced by P. gingivalis-LPS in mouse hippocampus
T. MORIKAWA, O. UEHARA, D. PAUDEL, K. YOSHIDA, J. SATO, Y. ABIKO
1Division of Oral Medicine and Pathology, Department of Human Biology and Pathophysiology, School of Dentistry, Health Sciences University of Hokkaido, Hokkaido, Japan, 2Division of Disease Control and Molecular Epidemiology, Department of Oral Growth and Development, School of Dentistry, Health Sciences University of Hokkaido, Hokkaido, Japan

026: Tetrahydrobiopterin pathway: A therapeutic target for neuropathic pain model
S. RAMAN, A. WASKITHO, R. RAJU, M. OSHIMA, Y. MATSUKA
Department of stomatognathic function and occlusal reconstruction, Tokushima University, Tokushima, Japan

Nutrition Research

027: Fermented dairy food intake reduces risk of tooth loss in a Japanese community
J. MA, M. FURUTA, T. TAKESHITA, S. KAGEYAMA, M. ASAKAWA, S. SUMA, Y. YAMASHITA
1Section of Preventive and Public Health Dentistry, Division of Oral Health, Growth and Development, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2OBT Research Center, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

Oral & Maxillofacial Surgery Research

028: Two opposite effects of desmoglein 3 expression on the growth of oral squamous cell carcinoma between anchorage-dependent and -independent conditions
J. INADA, M. MINABE, Y. AKIYAMA, K. HIGA, T. TACHIKAWA, S. TAKAHASHI, M. KOUNO, T. NOMURA
Oral Health Research

029: Associations between dental caries and Helicobacter pylori infection: A cross-sectional pilot study
K. IWAI, T. AZUMA, T. YONENAGA, T. TOMOFUJI
Department of Community Oral Health, School of Dentistry, Asahi University, Gifu, Japan

030: Application and Investigation of Total Adenylate(ATP, ADP, AMP) Hygiene Tests for Oral Health Monitoring
B. ALTANKHISHIG, M. YASUHIRO, M. KHATUN, T. SAITO
Division of Clinical Cariology and Endodontology, Department of Oral Rehabilitation, School of Dentistry, Health Science University of Hokkaido, Hokkaido, Japan

Oral Medicine & Pathology Research

031: Chemical direct conversion of human fibroblasts into functional osteoblastic cells
K. YAMAMOTO1,2, T. YAMAMOTO1, T. KISHIDA2, O. MAZDA2, N. KANAMURA1
1Department of Dental medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan,
2Department of Immunology, Kyoto Prefectural University of Medicine, Kyoto, Japan

Orthodontics Research

032: Applicability of neutral hypochlorous acid water for cleaning fixed orthodontic appliances
Y. NAGAMATSU, H. IKEDA, H. SHIMIZU
Division of Biomaterials, Department of Oral Functions, Kyushu Dental University, Kitakyushu, Japan

033: Long Term Effects on Root Resorption: Conventional vs Mini-Screw Assisted Rapid Palatal Expansion
S. Mehta1, S. A. Arqugb, M. Lagravere3, C. Kuo2, A. Tadinada2, M. Upadhyay2, S. Yadav2
1Developmental Sciences/Orthodontics, Marquette University School of Dentistry, Milwaukee, Wisconsin, UNITED STATES, 2University of Connecticut, Farmington, Connecticut, UNITED STATES, 3University of Alberta, Edmonton, Alberta, CANADA

Pediatric Oral Health Research

034: Identification and characterization of von Willebrand factor D and EGF domain as a novel extracellular matrix protein in teeth
K. IWATA1, K. KAWARABAYASHI2, K. YOSHIZAKI1, A. SUGIMOTO1, S. FUKUMOTO4,5, T. IWAMOTO1
1The Department of Pediatric dentistry and special needs dentistry, Tokyo medical and dental University, Tokyo, Japan, 2Department of Pediatric Dentistry, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan, 3Section of Orthodontics, Division of Oral Health, Growth and Development.Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 4Department of Pediatric Dentistry, Graduate School of Dental Science, Kyushu University, Fukuoka, Japan, 5Division of Pediatric Dentistry, Department of Oral Health and Development Sciences,
Periodontal Research-Therapy

035: High-fat diet-induced XAF1 exacerbates diabetes by promoting pancreatic β-cell apoptosis
Y. NISHIMURA1, M. IWASHITA1, M. HAYASHI1, T. SHINJO1, T. ZEZE1, A. YAMASHITA1, T. FUKUDA1, T. SANUI1, T. SANO2, F. NISHIMURA1
1Department of Periodontology, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2Department of Cell Biology and Pharmacology, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

036: Inhibitory effects of β-Glycyrrhetinic acid on bacterial growth and biofilm formation by supragingival plaque commensals
N. DEWAKE1, X. MA1, K. SATO2, S. NAKATSU2, K. YOSHIMURA2, Y. ESHITA2, H. FUJINAKA2, Y. YANO2, A. YOSHIDA3, N. YOSHINARI1
1Department of Periodontology, Faculty of Dentistry, Matsumoto Dental University, Shiojiri, Japan, 2Personal Health Care Product Research, Kao Corporation, Tokyo, Japan, 3Department of Oral Microbiology, Faculty of Dentistry, Matsumoto Dental University, Shiojiri, Japan

Periodontal Research-Pathogenesis

037: Insulin resistance in vascular endothelial cells contributes to the exacerbation of periodontitis via dysregulation of inflammation-induced VCAM-1 expression
T. ZEZE, T. SHINJO, Y. NISHIMURA, K. SATO, M. IMAGAWA, M. IWASHITA, A. YAMASHITA, F. NISHIMURA
Department of Periodontology, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

038: Dipotassium Glycyrrhizate inhibits LPS-induced alteration of cytoskeleton in gingival fibroblasts
T. YANAGISAWA, A. YOSHIDA, M. INAGAKI, S. SATO
NIPPON ZETTOC CO., LTD, Sagamihara, Japan

Periodontal Research-Diagnosis/Epidemiology

039: The loss of IkBζ accelerates dentin formation and matrix gene expression
H. YUAN1, S. SUZUKI1, H. TERUI2, S. HIRATA-TSUCHIYA2, E. NEMOTO1, K. YAMASAKI2, M. SAITO3, H. SHIBA3, S. AIBA2, S. YAMADA1
1The Department of Periodontology and Endodontology, Tohoku University school of Dentistry, Sendai, Japan, 2Department of Dermatology, Tohoku University Graduate School of Medicine, Sendai, Japan, 3Department of Biological Endodontics, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

Periodontal Research-Pathogenesis

040: Analysis of periodontopathic bacteria related to early primary tooth loss
Y. MIYAI, S. NAKA, M. MATSUMOTO-NAKANO
Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
Periodontal Research-Therapy

041: Hepatocyte growth factor shows antifibrotic effect on nifedipine-induced gingival overgrowth in vitro model
K. YAMAZAKI¹, H. IGARASHI-TAKEUCHI¹², Y. NUMABE¹
¹Department of Periodontology, School of Life Dentistry at Tokyo, The Nippon Dental University, Tokyo, Japan, ²Core Research Facilities for Basic Science, Research Center for Medical Science, The Jikei University School of Medicine, Tokyo, Japan

042: Personalized medicine of oral implant therapy for otorhinolaryngological high-risk patients.
K. TAKAHASHI¹, K. YAMAZAKI¹, M. YAMAZAKI², Y. BABA³
¹Division of Periodontics, Department of Conservative Dentistry, Ohu University School of Dentistry, Koriyama, Japan, ²Ohu University Dental Hospital, Koriyama, Japan, ³Ohu University Hospital Otorhinolaryngology, Koriyama, Japan

Periodontal Research-Pathogenesis

043: Abnormal expression of SGLT2 in the kidney of a P. gingivalis LPS-induced diabetic nephropathy mouse model
K. KAJIWARA¹, S. TAMAOKI¹, Y. SAWA²
¹Division of orthodontics, department of oral growth & development, Fukuoka Dental College, Fukuoka, Japan, ²Department of Oral Function & Anatomy, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Pharmacology/Therapeutics/Toxicology

044: Anti-inflammatory and Anti-oxidative Effects of Febuxostat on Periodontitis Rats Model
N. NESSA¹², M. KOBARA³, T. ADACHI¹, T. YAMAMOTO¹, T. NAKATA², N. KANAMURA¹
¹Dental Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan, ²Pathological Science, Department of Clinical Pharmacology, Kyoto Pharmaceutical University, Kyoto, Japan

045: Effects of smoking and smoking cessation on human gingival and lung fibroblasts
H. TAKEUCHI-IGARASHI¹², T. TACHIBANA², Y. MANOME², Y. NUMABE¹
¹Department of Periodontology, School of Life Dentistry at Tokyo, The Nippon Dental University, Tokyo, Japan, ²Core Research Facilities for Basic Science, Research Center for Medical Science, The Jikei University School of Medicine, Tokyo, Japan

Prosthodontics Research

046: Profiles of Mastication Predominance and Masticatory Performance in Kennedy Class I Patients
K. KINOSHITA¹, K. OKI², Y. OGINO², Y. TSUKIYAMA³, Y. AYUKAWA¹, K. KOYANO⁴
¹Section of Implant and Rehabilitative Dentistry, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, ²Section of Fixed Prosthodontics, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, ³Section of Dental Education, Division of Oral Biological Sciences, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, ⁴Division of Advanced Dental Devices and Therapeutics, Faculty of Dental Science, Kyushu University, Fukuoka, Japan
047: Bacterial flora evaluation using DNA array chip and real-time PCR
Y. KADOTA, E. ARIMA, S. HOU7, F. FUSEJIMA
GC CORPORATION, Tokyo, Japan

048: Effect of Glass Fiber Sleeve for Reinforcement of Flared Root
S. YOSHIMATSU, W. KOMADA, R. NEMOTO, S. OISHI, R. TSUKAHARA, S. OMORI,
K. NOZAKI, H. MIURA
Fixed Prosthodontics, Tokyo Medical and Dental University, Tokyo, Japan

049: The Influence of Zirconia Tube for Stress in Endodontically-Treated Molar
S. OISHI, W. KOMADA, D. KONDO, R. TSUKAHARA, S. YOSHIMATSU, Y. YOKOSUKA,
S. OMORI, K. NOZAKI, H. MIURA
Fixed Prosthodontics, Tokyo Medical and Dental University, Tokyo, Japan

Pulp Biology & Regeneration Research

050: New mechanism of odontoblast differentiation
H. NAKAZATO1, S. ONODERA2, N. AIDA2, T. AZUMA2, M. FURUSAWA1
1Department of Endodontics, Tokyo Dental College, Tokyo, Japan, 2Department of Biochemistry, Tokyo Dental College, Tokyo, Japan

051: Evaluation of Inflammatory Changes During Wound Healing Process in Caries-Stimulated Dental Pulp
H. HUANG, M. OKAMOTO, M. WATANABE, S. MATSUMOTO, K. MORIYAMA, S. KOMICHI,
Y. TAKAHASHI, M. HAYASHI
Department of Restorative Dentistry and Endodontology, Osaka University Graduate School of Dentistry, Osaka, Japan

052: Induction of dental pulp cells into periodontal ligament-like cells using epigenetics
S. TAKAHASHI1, K. YOSHIDA1, D. PAUDEL1, D. ARIWANSA1, A. KHURELCHULUUN2,
A. ONISHI1, T. MORIKAWA1, D. HIRAKI1, F. HARADA2, O. UEHARA4, J. SATOU1,
H. NAGAYASU2, Y. ABIKO1
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053: Dentin-pulp complex tissue regeneration by three-dimensional cell sheet engineering
H. YAN1, M. OSHIMA1, R. RAJU2, S. RAMAN3, A. WASKITHO1, K. OKURA1, Y. MATSUKA1
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Salivary Research

054: Effect of psychological stress on oral microbiome: A metagenomic and bioinformatic analyses
D. PAUDEL1, Y. KURAMITSU2, O. UEHARA3, T. MORIKAWA1, T. KITAGAWA1, K. YOSHIDA1,
Y. ABIKO1
Stem Cell Biology Research

055: Exosomal miR-1260b derived from TNF-α-treated hGMSCs inhibits periodontal bone loss by targeting ATF6β-mediated regulation of RANKL
Department of Periodontology, Division of Oral Rehabilitation, Faculty of Dental science, Kyushu University, Fukuoka, Japan

056: Exosomes derived from GMSCs stimulated with TNF-α and IFN-α promote M2 macrophage polarization via enhanced CD73 and CD5L expression
Department of Periodontology, Division of Oral Rehabilitation, Faculty of Dental science, Kyushu University, Fukuoka, Japan

057: Characterization of neural crest-derived cells for application in bone regenerative medicine
K. SHINOMIYA, A. YAMADA, R. KAMIJO
Department of Biochemistry, School of Dentistry, Showa University, Tokyo, Japan

058: The effect of JNK inhibition on the osteoblastic differentiation of periodontal ligament stem cells and the regeneration of periodontal tissue in vivo
H. KANEKO1, D. HASEGAWA2, T. ITOYAMA2, S. YOSHIDA2, A. TOMOKIYO2, S. HAMANO1,3, H. SUGII, H. MAEDA1,2
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059: Relationship between age-related changes in MSC functions and periodontal tissues destruction in ligature induced periodontitis mouse model
K. AUNG, K. AKIYAMA, T. KUBOKI
Department of Oral Rehabilitation and Regenerative Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

060: MSC conditioned medium from older mice affects its osteogenic differentiation capacity
J. ZHANG, K. AKIYAMA, K. MAEKAWA, T. KUBOKI
Department of Oral Rehabilitation and Regenerative Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

061: Extracellular vesicles-mediated novel therapeutic mechanism of deciduous tooth pulp stem cell-based therapy for systemic lupus erythematosus
S. SONODA, T. YAMAZA
Department of Molecular Cell Biology and Oral Anatomy, Division of Oral Biological Sciences, Kyushu University Graduate School of Dental Science, Fukuoka, Japan
SPECIAL LECTURES
Past, Present and Future of Mucosal Vaccine: Vital Contributions Made by Dentistry

Hiroshi Kiyono, D.D.S., Ph.D.
IMSUT Distinguished Professor
Division of Mucosal Immunology, IMSUT Distinguished Professor Unit
The Institute of Medical Science, The University of Tokyo

Professor
Mucosal Immunology and Allergy Therapeutics
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Professor of Medicine
CU-UCSD Center for Mucosal Immunology, Allergy and Vaccines
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Director, CU-UCSD Center for Mucosal Immunology, Allergy and Vaccines (cMAV)
University of California, San Diego

Considering the global health, vaccine is certainly one of the key strategies for achieving our common goal of healthy society. Through the current and unfortunate SARS-CoV-2 pandemic situation, all of us learned again the value of vaccines. Admireable heroic efforts have been made to develop the first-generation of injection-type vaccines for SARS-CoV-2, and thus for example mRNA-based injectable vaccines are being administered in the different continents. It should be noted that injected vaccines effectively induce systemic immunity (e.g., serum IgG) to prevent severe disease, but not mucosal IgA that prevents pathogen invasion of the airway mucosa. The aerodigestive tract, beginning from oral and nasal cavities are covered by mucosal epithelium. These mucosal surfaces are continuously exposed to environmental antigens including pathogens and allergens, and thus equipped with the mucosal immune system for the initial recognition of their pathogenicity and subsequent induction of pathogen-specific immunity. At the dawn of our scientific effort for the demonstration of the mucosal immune system, dental science demonstrated foreseeability and contributed to building the scientific foundation for the importance of the mucosal immune system and its application for the control of infectious diseases. Thus, the development of mucosal vaccines for the prevention of dental caries was a part of novel approaches which contributed for initiating the scientific area of mucosal immunology. Since then, mucosal immunology and vaccines have gained scientific journey to become one of the major entities of Immunology. Through this presentation, I wish to introduce the past and current efforts and future directions for the development of mucosal vaccines, focusing on our nanogel-based nasal vaccine and rice-based oral vaccine (MucoRice), for the prevention of aero-digestive tract associated infectious diseases by the interdisciplinary blending of mucosal immunology with biomaterial engineering and agriculture science, respectively.
Brief CV

Hiroshi Kiyono, D.D.S., Ph.D.
IMSUT Distinguished Professor
Division of Mucosal Immunology, IMSUT Distinguished Professor Unit
The Institute of Medical Science, The University of Tokyo (IMSUT)

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University of California, San Diego

Dr. Kiyono’s background as a dentist combined with extensive research experience in the field of Mucosal Immunology makes him exceptionally well qualified to discuss the current and future directions of mucosal immunology and mucosal vaccine development. To reflect his scientific contribution, he was listed in ISI Highly Cited Researchers’ List and received several prestigious awards such as NIH New Investigator Research Award, NIH Research Career Development Award, The Japanese Society for Vaccinology Takahashi Award and Hideyo Noguchi Memorial Medical Science Award.

In the late 1970s, Dr. Kiyono has started his significant research career in the launch of the “Mucosal Immunology.” He consistently played an important role as a pioneer in this research area with his excellent mentor, colleagues and collaborators. In particular, his research team explored in 1) Peyer’s patches (PPs), one of core members of Gut-Associated Lymphoid Tissues (GALT) possess antigen-presenting cells and IgA isotype specific helper T cells (now classified in Th2 cells) for the induction of antigen-specific mucosal immunity; 2) intestinal mucosa, epithelial, mesenchymal, and immune cells form a multi-ecological system in concert with the gut microbiota to create and maintain homeostasis; and 3) the respiratory mucosal immune system with its unique immunobiological characteristics. His research team has also actively facilitated the development of the next-generation vaccines, the oral and nasal vaccines, which now are in critical pre-clinical and clinical trial stages.

He is currently the President of the Japanese Society for Immunology and was the former President of Japanese Society for Mucosal Immunology and the editorial board member of scientific Journals such as Vaccine, Mucosal Immunology, Human Vaccines and Frontiers. He himself has a total of 567 publications in peer review journals and edited a total of 22 books.

[Education]
1983 Ph.D., University of Alabama at Birmingham Medical Center (UAB), USA
1977 D.D.S., Nihon University School of Dentistry at Matsudo, Japan

[Career]
2018-Present IMSUT Distinguished Professor, Department of Mucosal Immunology
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2018-Present Professor of Medicine, Division of Gastroenterology
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2015-Present Director, CU-UCSD Center for Mucosal Immunology, Allergy and Vaccines
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2011-2019 Professor and Director
International Research & Development Center for Mucosal Vaccines, IMSUT

2011-2015 Associate Dean, IMSUT
2007-2010 Dean, IMSUT

2002-2018 Professor and Director, Division of Mucosal Immunology, IMSUT
1994-2003 Professor and Chairman, Department of Mucosal Immunology,
Research Institute for Microbial Diseases, Osaka University

1991-2003 Professor, Departments of Oral Biology and Microbiology, UAB
1989-1990 Associate Professor, Departments of Oral Biology and Microbiology, UAB
1986-1987 Visiting Senior Scientist, Max-Planck Institute for Biology
1984-1987 Research and Clinical Assistant Professor, Department of Oral Biology, UAB
Greeting from IADR President  
Sunday, October 24th, 9:00-9:15  
Video distribution  

Laureate Professor Eric C. Reynolds AO FICD FTSE FRACDS  
Centre for Oral Health Research, Melbourne Dental School  
The University of Melbourne  

Laureate Professor Eric Reynolds AO is Chief Executive Officer and Research Director of the Oral Health CRC at the Melbourne Dental School, the University of Melbourne. For 16 years until 2015 Eric was Head of the Melbourne Dental School. He has lectured and published extensively and has chaired and participated in a wide range of professional committees and panels. Eric was appointed an Officer of the Order of Australia for his service to community dental health in 2005. He received the Clunies Ross National Science and Technology award in 2002 and the Victoria Prize for Science in 2005. In 2011 he received the Distinguished Scientist Award from the International Association for Dental Research, and in 2015 the Leach Medal for research excellence and the Global Health Impact Award from the University of Melbourne. In 2016 he received the Award of Merit from the Australian Dental Association and in 2017 the Prime Minister’s Prize for Science Innovation. In 2019 he was elected Vice-President of the International Association for Dental Research and became President in July this year. In 2020 he received the European Organisation for Caries Research Prize for outstanding scientific contribution and the American Academy of Periodontology Clinical Research Award.
Esthetic & functional oral rehabilitation: 4 control factors

Professor, Kung-Rock KWON, DMD, MSD, PhD
Dept. of Prosthodontics, School of Dentistry, Kyung Hee University, Seoul, Korea

Our purpose is to restore the vital function and characteristic beauty of the masticatory apparatus by an intelligent application of the basic requirements such as anatomic, physiologic, mechanical, hygienic, and esthetic which show that no superstructure can be more enduring than its foundation.

How is this achieved? Before going into treatment, precise diagnosis is very important. A tentative treatment plan is made based on the list of problems and diagnosis. Reversible treatment is chosen first to give final treatment through trial-and-error process.

What factors do we think can be controlled?
1. Optimum functional joint position is a physiologic position where condyle head is braced with disk and positioned antero-superiorly in the articular eminence.
2. CR and physiological position of condyle with maximum intercuspation should be considered.
3. Vertical dimension of occlusion is the most important factor to consider.
4. Anterior guide angle must be adjusted to maintain the determined VD, and occlusal stability.

This lecture will focus on vertical dimension in general, method to test and decide the vertical dimension of the patient and the treatment and follow-up check of the vertical height loss with prosthetic perspective.
Brief CV

Kwon, Kung-Rock (DMD, MSD, PhD, MBA, FICD)

Certified Specialty: Prosthodontics
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Education
2007-2010 MBA Kyung Hee Univ. Graduate School of Business, Seoul, Korea
1993-1995 PhD Kyung Hee Univ. School of Dentistry, Seoul, Korea
1988-1990 MS Kyung Hee Univ. School of Dentistry
1981-1987 DMD Kyung Hee Univ. School of Dentistry

Major Careers
2018-2020 Dean Kyung Hee Univ. School of Dentistry, Seoul, Korea
2016-2017 Vice Dean Kyung Hee Univ. School of Dentistry
2002-2003 Visiting Professor Harvard Univ. School of Dentistry, USA
1996-1998 Visiting Professor Geneva Univ. School of Dentistry, Switzerland
1993-1996 Fellow Kyung Hee Univ. Dental Hospital
1988-1990 Resident Kyung Hee Univ. Dental Hospital
1999-present Professor Kyung Hee Univ. School of Dentistry

Academic Societies
2021-present President The Korean Academy of Implant Dentistry
2020-present President The Korean Academy of Prosthodontics
2020-present President elected The Korean Academy of Dental Research
2014-2020 Secretary The Korean Academy of Dental Sciences
2018-2020 Vice President The Korean Dental Hospital Association
2017-2019 President The Korean Academy of Sports Dentistry
2015-Present Vice President The Korean Officials Dental Association

Research papers(SCI(E) : Recent 2yrs)
The 1st Joint Symposium of KADR and JADR:
Regenerative medicine/Dentistry

Symposium I:
Japan-Originated Next Generation Biomedical Materials

Symposium II:
Current progress of Stem Cell Biology
and Regenerative Medicine in Dental Science

Rising Scientist Session:
Periodontal Medicine
Epithelial–mesenchymal interaction plays critical roles for the development of organs such as tooth, lung, salivary gland, kidney and hair. During this process, epithelial thickening and budding into mesenchyme are common phenomenon, while the decision of cell fate is made by the specific transcriptional controls of individual organs. In this study, specific transcriptional start sites (TSS) of each organ were explored by CAGE (Cap Analysis of Gene Expression) analysis. We found that commonly expressed TSS were mainly detected in the epithelia, whereas specific TSS were expressed in mesenchyme in each organ. Furthermore, we identified a tooth specific TSS detected in the chromosome 15qD1 region, which codes microRNA-875 (miR875). MiR875 is specifically expressed in dental mesenchymal cells during the tooth germ formation. Furthermore, PRRX1 binds to the miR875 promoter region and enhances the expression of miR875. To assess the role of miR875 in dental mesenchyme during tooth development, we transfected mimic miR875 into mouse dental pulp (mDP) cells, which showed that cell migration toward dental epithelial cells was significantly induced by miR875 via the PDGF signaling pathway. Further, we also demonstrate that miR875 induced cell migration by inhibiting PTEN and STAT1, which are regulated by miR875 in post-transcriptional regulation. In summary, our findings indicate that tooth specific miR875 has important roles in early tooth development, especially cell condensation of mesenchymal cells around invaginated dental epithelium and induction of epithelial-mesenchymal interaction.
Brief CV

Keigo Yoshizaki
Section of orthodontics and Dentofacial Orthopedics, Division of Oral Health, Growth and Development, Department of Dental Science, Kyushu University

Education
Undergraduate 1998-2004 Kyushu University School of Dentistry, Fukuoka, Japan, D.D.S. Graduate 2004-2008 Kyushu University, Dental Science, Fukuoka, Japan, Ph.D.

Research & Professional Experience:
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2009-2011 Research Fellow, the Japan Society for the Promotion of Science (JSPS)
2010-2013 Postdoctoral Fellow, LCDB, NIDCR, NIH, Bethesda, MD, USA
2013- Assistant professor, Kyushu University, Japan

Award:
2019 Travel Award, 15th The Kyushu Orthodontic Society
Periodontal disease remains a challenge in clinical regenerative dentistry. The complexity of the periodontium, consisting of cementum, periodontal ligament, alveolar bone, and gingiva, adds to the difficulties for regeneration. Although various regenerative techniques have been evaluated, conventional regenerative treatment for periodontal wound is not yet reliable to regenerate the impaired tooth supporting structures. To achieve an advanced reconstruction of lost periodontal tissue, a new technique using additional signaling molecules and cells was introduced, namely tissue engineering.

In the present study, we aimed to evaluate the effect of bone morphogenetic protein 7 (BMP7) with bone marrow mesenchymal stem cell (BM-MSC) transplantation in the regenerative therapy for periodontitis. BMP7 is one of the BMP growth factor family members showing excellent bone forming ability, however its short half-life needs to overcome for clinical application. Therefore, BMP7-expressing immortalized BM-MSCs (BMP7-eBMSCs) were established and they showed superior osteogenic differentiation potential when subcutaneously transplanted with biphasic calcium phosphate scaffold on immunocompromised mice. Furthermore, efficacy of BMP7-eBMSCs transplantation was evaluated for periodontal tissue regeneration in rats with ligature-induced periodontitis. As expected, the damaged alveolar bone in periodontitis was regenerated in BMP7-eBMSC transplantation group both in 2-dimensional and 3-dimensional analyses of micro-CT scan and histology. Interestingly, the amount of regenerated alveolar bone in BMP7-eBMSCs transplantation group was comparable to that in the transplantation of human periodontal ligament stem cells.

Taken together, our results suggest that BMP7-eBMSCs could be one of the feasible treatment options for the regeneration of periodontal tissue damaged by periodontitis.
**Brief CV**

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**Education**

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Graduate 2002-2004 Graduate School of Dentistry, Yonsei University, Seoul, Korea, M.S.D.  
2004-2007 Graduate School of Dentistry, Yonsei University, Seoul, Korea, Ph.D.

**Research & Professional Experience:**

<table>
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<th>Position and Location</th>
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<tr>
<td>2001-2004</td>
<td>Internship and Residency, Department of Periodontics, Yonsei University Dental Hospital</td>
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<tr>
<td>2004-2005</td>
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Apical periodontitis (AP) is an acute or chronic inflammatory disease caused by complex interactions between infected root canal and host immune system. Although reducing the pathogen load from the root canal typically prevents reinfection and leads to healing of the AP, the complex root canal system and host immune system sometimes interfere with these processes resulting in therapy-resistant AP lesions that induce continuous apical bone tissue destruction. Inflammatory bowel disease (IBD) is caused by breakdown by intestinal immunity and affect not only in colon function but also in exacerbate systemic immune system such as causing iritis, uveitis, ankylosing spondylitis and arthritis. Similar to these events, IBD enhanced inflammation of the periapical area, and bone destruction. Thus, a fuller understanding of the relationship of AP and IBD may identify potential new therapeutic targets for therapy-resistance case.

We have previously established mice AP model and shown that macrophage-derived CXCL9, which acts through CXCR3, is recruited by progressed AP. The inhibition of CXCL9 by a CXCR3 antagonist reduced the lesion size in a mouse AP model with decreasing IL-1β, IL-6 and TNFα expression. The treatment of peritoneal macrophages with CXCL9 and LPS induced the transmigration and upregulation of osteoclastogenic cytokines such as IL-1β, IL-6 and matrix metalloprotease 2, a marker of activated macrophages. Thus, CXCL9-CXCR3 axis plays a crucial role in the development of AP, mediated by the migration and activation of macrophages for periapical tissue destruction. From these data we showed that knowledge of the principal factors involved in the progression of AP, and the identification of related inflammatory markers, may help to establish new therapeutic strategies.

In the present study, we report mice AP-IBD model to investigate effect of IBD on alveolar bone destruction induced by AP and provide new evidences how IBD accelerate alveolar bone destruction in this model.
**Brief CV**

Masahiro Saito  
Tohoku University Graduate School of Dentistry Division of Operative Dentistry, Department of Ecological Dentistry

**Education**
Undergraduate 1982-1988 Kanagawa Dental College, Yokosuka, Japan, D.D.S.  
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**Research & Professional Experience:**

<table>
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<tr>
<td>1988-1994</td>
<td>Assistant professor, Department of Operative dentistry, Kanagawa Dental College</td>
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<tr>
<td>1994-1996</td>
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<tr>
<td>1996-2002</td>
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<tr>
<td>2002-2006</td>
<td>Lecturer, Department of Operative Dentistry and Endodontics, Kanagawa Dental College</td>
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<td>2006-2009</td>
<td>Lecturer, Department of Molecular and Cellular Biochemistry, Osaka University Graduate School of Dentistry</td>
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<tr>
<td>2009-2013</td>
<td>Associate professor, Faculty of Biological Science, Tokyo University of Science</td>
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<tr>
<td>2013-present</td>
<td>Professor, Division of Operative Dentistry, Department of Ecological Dentistry, Tohoku University, Graduate School of Dentistry</td>
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Implant Supported Overdentures for the Elderly Edentulous Patients

Professor, Kung-Rock KWON, DMD, MSD, PhD
Dept. of Prosthodontics, School of Dentistry, Kyung Hee University, Seoul, Korea

Edentulous patients with a severely resorbed mandible represent a significant health care problem in the growing elderly population. Despite adequate denture fabrication, it is not possible in many instances to achieve optimal retention and stability in the conventional mandibular denture. This may be caused by poor jaw and ridge relationship, psychologic conditions, reduced neuromuscular coordination, inadequate quality and quantity of available bone and alveolar mucosa. To achieve increased retention, pre-prosthetic surgery to augment the alveolar ridge or increase the vestibular depth may be needed. But the outcome of these pre-prosthetic surgery are less favorable than that of the implant retained overdenture. Zarb et al. described that the quality of life of elderly edentulous patients can be improved using inter-foraminal implants to resolve the edentulism. There also was a consensus statement at McGill University of mandibular two-implant overdenture as the first choice standard of care for edentulous patients. Overdenture retained by two or four implants has shown to be a highly successful prosthetic treatment similar to the fixed implant denture.

A variety of attachment systems have been used to retain overdentures, generally, these can be classified as clips-and–bars, balls, and magnets. The selection of an attachment system is mainly related to the personal choice of the practitioner and/or laboratory responsible, based on experience and training. The clinical trial has compared clinical outcomes.

According to the conventional Branemark protocol, periods of 3 months and 6 months have been recommended as healing times for osseointegrated implants placed in the mandible and maxilla, respectively, during which functional loading should be avoided. However these long healing periods before functional loading are not based on histologic and experimental results, but are from empirical clinical experience. These periods can impose not only functional challenges, but also inconvenience of the edentulous state to the patient.

The evaluation of different early loading protocols for un-splinted implants for mandibular overdentures opposing conventional complete maxillary dentures is best achieved by comparing groups with different reductions in healing times.

In the case of elderly edentulous patient, treatment should be carried out in consideration of the patient’s age and general health as well as oral health related quality of life.
Brief CV

Kwon, Kung-Rock (DMD, MSD, PhD, MBA, FICD)

Certified Specialty: Prosthodontics

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E-mail address: krkwon@khu.ac.kr

Position: Professor

Education

2007-2010  MBA  Kyung Hee Univ. Graduate School of Business, Seoul, Korea
1993-1995  PhD  Kyung Hee Univ. School of Dentistry, Seoul, Korea
1988-1990  MS  Kyung Hee Univ. School of Dentistry
1981-1987  DMD  Kyung Hee Univ. School of Dentistry

Major Careers

2018-2020  Dean  Kyung Hee Univ. School of Dentistry, Seoul, Korea
2016-2017  Vice Dean  Kyung Hee Univ. School of Dentistry
2002-2003  Visiting Professor  Harvard Univ. School of Dentistry, USA
1996-1998  Visiting Professor  Geneva Univ. School of Dentistry, Switzerland
1993-1996  Fellow  Kyung Hee Univ. Dental Hospital
1988-1990  Resident  Kyung Hee Univ. Dental Hospital
1999-present  Professor  Kyung Hee Univ. School of Dentistry

Academic Societies

2021-present  President  The Korean Academy of Implant Dentistry
2020-present  President  The Korean Academy of Prosthodontics
2020-present  President elected  The Korean Academy of Dental Research
2014-2020  Secretary  The Korean Academy of Dental Sciences
2018-2020  Vice President  The Korean Dental Hospital Association
2017-2019  President  The Korean Academy of Sports Dentistry
2015-Present  Vice President  The Korean Officials Dental Association

Research papers (SCI(E): Recent 2yrs


Alveolar ridge deficiencies prevent the long-term success of dental implants. Therefore, bone augmentation is imperative when alveolar bone undergoes advanced resorption. Among various bone defects, vertical bone defects are the most difficult to augment. Autogenous bone graft is still the gold standard for vertical bone augmentation as it exhibits osteoconductive and osteoinductive properties. However, the harvestable quantity of autogenous bone is limited and invasive surgery is ineluctable. Furthermore, autologous bone is commonly associated with rapid resorption owing to mechanical pressure from soft tissues in the recipient sites. Guided bone regeneration (GBR) is another common technique for bone augmentation. GBR provides a relatively predictable outcome for bony defects. Nevertheless, complications attributed to the use of barrier membranes occasionally occur. A synthetic scaffold with high osteoconductive and angiogenic abilities may achieve barrier membrane-free GBR and resolve the current challenges in vertical bone augmentation.

Scaffolds with uniaxial channels from the bottom face contacting the host bone to the top face, such as honeycomb (HC) scaffolds, are deemed to be favorable for vertical bone augmentation, compared to three-dimensional porous scaffolds. Furthermore, uniaxial channels in HC scaffolds may restrict the entry of fibrous tissues. Herein, we developed HC scaffolds constructed by interconnecting carbonate apatite microspheres. When the HC scaffolds with 230-, 460-, and 630-μm-opening size channels were implanted on the rabbit calvarium, the amount of new bone and soft tissues in the HC scaffolds significantly increased and decreased, respectively, with the decrease in the channel opening size. Thus, the HC scaffolds with 230-μm-opening size channels prevented soft tissue invasion and enhanced bone ingrowth. The HC scaffolds with 300-μm struts bore the compression for 12 weeks post-implantation and led to bone augmentation while being replaced with new bone. These results provide significant insights into the scaffold characteristics of the HC structure; it is inherently proper for vertical bone augmentation, and the multiscale-architectural control of HC scaffolds may pioneer barrier membrane-free GBR while resisting compression from soft tissues.

The prevention of surgical site infection (SSI) is required for favorable prognosis. To decrease the risk of SSI, we developed HC scaffolds with both osteoconductivity and antibacterial activity by replacing a minute amount of carbonate apatite on the scaffold surface with silver phosphate. The HC scaffolds exerted in vitro antibacterial effects for various bacteria without cytotoxicity. Furthermore, when the HC scaffolds were implanted with methicillin-resistant staphylococcus aureus (MRSA) into the defect of rabbit femur condyle. At 2 weeks post-implantation, no viable MRSA was detected and new bone formed within the HC scaffolds. In contrast, in the groups implanted with carbonate apatite HC scaffolds containing no silver phosphate, bacteriogenic osteolysis and inflammation occurred. At 4 weeks post-implantation of the HC scaffolds composed of carbonate apatite and silver phosphate, new bone formation further progressed from 2 weeks post-implantation and a portion of the HC scaffold was replaced by new bone.
Brief CV
Koichiro Hayashi
Department of Biomaterials, Faculty of Dental Science, Kyushu University

Education:
Undergraduate 2001-2005 Nagoya University, Nagoya, Japan
Graduate (master’s course) 2005-2007 Nagoya University, Nagoya, Japan
Graduate (doctoral course) 2007-2010 Nagoya University, Nagoya, Japan, Ph.D.

Research & Professional Experience:
2009-2010 Research Fellowship for Young Scientists (DC2)
2010-2014 Assistant Professor, Institute of Health Biosciences, The University of Tokushima
2014-2017 Assistant Professor, Institute of Materials and Systems for Sustainability, Nagoya University
2017-2018 Assistant Professor, Faculty of Dental Science, Kyushu University
2018- Associate Professor, Faculty of Dental Science, Kyushu University

Award:
2007 Outstanding Graduate Student Award, Nagoya University
2008 Wakashachi Excellence Award, Aichi Prefecture
2012 Best Teacher of The Year, The University of Tokushima
2012 Best Presentation Award, The 25th Fall Meeting of the Ceramic Society of Japan
2013 Young Investigator Award, The University of Tokushima
2013 Oka Award, The University of Tokushima
2013 Young Best Presentation Award, The 11st Annual Meeting of the Society of Nano Science and Technology
2015 CerSJ Awards for Advancements in Ceramic Science and Technology, The Ceramics Society of Japan
2015 Best Presentation Award, The 28th Fall Meeting of the Ceramic Society of Japan
2016 Academic Award, Tokai Chemical Industry Association
2016 Best Presentation Award, The 32nd Annual Meeting of the Japan Society of Drug Delivery System
2020 Best-Research Award, Faculty of Dental Science, Kyushu University
2020 Best Presentation Award, The 75th General Session of the Japanese Society for Dental Materials and Devices
Bone quality and quantity are the crucial factors to achieve and maintain Osseointegration. The early days during the end of 20 century, the bone quality in implant dentistry was classified with the thickness of the cortical layer and the amount of the bone marrow. Whereas in 2000, the National Institutes of Health (NIH) has since proposed a new clinical parameter of the “bone quality” from the series of studies on osteoporosis. According to their definition, bone quality is “the sum total of characteristics of the bone that influence on the fracture resistance.” The term of “bone quality” comprises bone architecture, bone turnover, bone mineralization and micro-damage accumulation. Moreover, bone cells such as osteoblasts and osteocytes, characteristics of collagen fibers, including type and alignment, and biological apatite (BAp) c-axis alignment are thought to be the determinant factors of bone quality. Intriguingly, the c-axis of BAp is parallel to the extended collagen fibers associated with mechanical function, indicating that anisotropic changes in BAp c-axis/collagen fibers regulate bone quality in response to mechanical loading.

The question arose what is the bone quality around the dental implant? Since, the dental implants are intrinsically subjected to dynamic loadings such as functional and/or parafunctional forces via implant supported prostheses, we tried to clarify the bone quality around the implant by paying attention on the response to mechanical loading. From the several animal experiments, the dynamic loading on the implant dramatically changes bone quality with increased osteocyte numbers/network, adapted preferential alignment of BAp c-axis/collagen fibers and related cellular kinetics. Furthermore, the studies also demonstrated that dynamic loading upregulates osseointegration, bone quantity (bone volume), and BMD around implants. Surprisingly, these anabolic effects strongly depend on the implant thread design. The upward buttress thread design which oriented in the same direction as the principal stress of the loading force could enhance bone quality comparing to the downward buttress thread and triangle thread designs.

In this presentation, I will introduce the newly developed implant design based on our series of research work.
Brief CV

Takashi Sawase, D.D.S., Ph.D.
Department of Applied Prosthodontics, Institute of Biomedical Sciences, Nagasaki University

Education

Undergraduate: 1983-1989 Nagasaki University School of Dentistry, Nagasaki, Japan, D.D.S
Graduate: 1989-1993 Nagasaki University Graduate School of Dentistry, Nagasaki, Japan, Ph.D.

Research & Professional Experience

1993-2000  Assistant Professor, Dept. of Fixed prosthodontics, Nagasaki Univ.
1996-1998  Visiting researcher at Dept of Biomaterials, Gothenburg University, Sweden
2000-2003  Assistant Professor, Nagasaki University Hospital
2003-2008  Associate Professor, Dept. of Fixed prosthodontics, Nagasaki Univ.
2009-      Professor, Dept. of Applied prosthodontics, Nagasaki Univ.
Octacalcium phosphate (OCP, Ca₈H₂(PO₄)₆·5H₂O) has been advocated to be one of precursors in bone apatite crystal deposition during bone formation. Recently, one of OCP composites with collagen was approved as a bone filling material for the use with dental implant in oral surgery field through a company-initiative clinical trial. We have found first that OCP has a superior osteoconductivity in comparison with hydroxyapatite (HA, Ca₁₀(PO₄)₆(OH)₂) materials through an onlay graft experiment of OCP granules onto mouse calvaria (Tohoku J Exp Med 164:37, 1991). Since then we have been developing OCP composite materials with polymers, such as reconstituted collagen or other natural and synthetic polymers, to increase not only the handling properties but also bone regenerative properties. Concurrently, bone-related cellular responses to OCP have also been analyzed to understand whether OCP itself can stimulate bone-related cellular activities in relation to its structural and chemical properties.

Findings obtained were: 1) OCP-HA conversion accompanied by physicochemical environmental changes around OCP is involved in enhancing bone regeneration (Biomaterials 27:2671, 2006); 2) OCP enhances osteoblastic differentiation of mouse bone marrow stromal ST-2 cells dose-dependently (Tissue Eng Part A 14:965, 2008); 3) OCP accumulates macrophages in the early stage of bone formation and enhances the cellular migration by the effect of ionic dissolution of OCP (Ca²⁺) (RSC Adv 6:57475, 2016); 4) OCP induces osteoclast formation in co-culture of osteoblasts and bone marrow cells with expression of receptor activator of NF-kappaB ligand (RANKL) in osteoblasts in the absence of external RANKL agent (Tissue Eng Part A 15:3991, 2009); 5) OCP enhances osteocyte differentiation from mouse bone marrow IDG-SW3 cells in vitro and within newly formed bone matrices under contactless conditions (Acta Biomater 69:362, 2018; 129:309, 2021); 6) OCP enhances bone regeneration more if combined with polymers such as collagen (J Biomed Mater Res B Appl Biomater 79:210, 2006); 7) On of OCP composites with polymers OCP/Collagen is confirmed to effectively be used in human oral bone defects with dental implant (J Tissue Eng 11:2041731419896449, 2020).

In this presentation, bioactive performance including bone regenerative capacity of OCP composite materials brought about through the activation of bone-related cells, which is induced by the materials function of OCP, will be explained and discussed.
**Brief CV**

Osamu Suzuki  
Division of Craniofacial Function Engineering, Tohoku University Graduate School of Dentistry

**Education**

Graduate Student, 1984-1986 Yamagata University Graduate School of Engineering, Yonezawa, Japan, M.Eng.  
Ph.D., 1991 Tohoku University Graduate School of Medicine, Department of Orthopedic Surgery, Sendai, Japan

**Research & Professional Experience:**

<table>
<thead>
<tr>
<th>Year</th>
<th>Position/Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992-1994</td>
<td>Visiting Scientist, Forsyth Dental Center, Physical Chemistry Department, Boston, MA, USA.</td>
</tr>
<tr>
<td>1994-1998</td>
<td>Associate Researcher, JGC Co., Research Center, Yokohama, Japan.</td>
</tr>
<tr>
<td>1999-2004</td>
<td>Senior Researcher, JGC Co., Research Center, Oarai, Japan.</td>
</tr>
<tr>
<td>2004-Present</td>
<td>Professor, Division of Craniofacial Function Engineering, Tohoku University Graduate School of Dentistry, Sendai, Japan.</td>
</tr>
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**Award:**

<table>
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<tr>
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<tbody>
<tr>
<td>2003</td>
<td>JGC Corp Award: The establishment in design basis of anti-fouling furnace tube</td>
</tr>
<tr>
<td>2003</td>
<td>Award in the 23rd Engineering Advancement Association (ENAA) of Japan: Engineering team for designing pharmaceutical facility with quantitative evaluation containing potent compound. No.238.</td>
</tr>
<tr>
<td>2013</td>
<td>Award in Reviewer for Grants-in-Aid for Scientific Research of Japanese Society for Promotion of Science (JSPS)</td>
</tr>
<tr>
<td>2015</td>
<td>Award of Japanese Society for Biomaterials: Elucidation of osteoconductivity and establishment of biomaterial science of OCP bone substitute materials</td>
</tr>
<tr>
<td>2020</td>
<td>Fellow, Biomaterials Sciences and Engineering (FBSE)</td>
</tr>
</tbody>
</table>
Periodontitis is evoked by dental biofilms. Some success has been achieved in suppressing the progress of periodontitis by mechanically removing the cause of the disease. However, no conventional periodontal and/or surgical treatments can regenerate periodontal tissue or its functionality lost by periodontitis. On the other hand, several lines of evidence clearly demonstrate that periodontal ligament (PDL) contributes to tooth nutrition, homeostasis, and the repair/wound healing of damaged periodontal tissue. Importantly, mesenchymal stem cells and progenitor cells of hard-tissue forming cells, such as osteoblasts and cementoblasts, have been identified within the PDL. Thus, improving the biological potential of these cells and stimulating the regeneration of periodontal tissue are now recognized as clinically possible.

One of the most physiologically efficient methods to stimulate these cells is the use of cytokines or growth/differentiation factors. Topical application of human recombinant cytokines to stimulate proliferation, migration and/or differentiation of those multipotent cells may be an efficient way to accelerate the regeneration of periodontal tissue.

Basis Fibroblast Growth Factor (FGF-2) is known to stimulate the proliferation, migration and differentiation of a variety of cell types and to strongly induce angiogenesis. Animal studies using beagle dogs and non-human primates demonstrated that topical application of recombinant FGF-2 induced statistically significant periodontal tissue regeneration with newly formed cementum and alveolar bone. Further, in a series of human clinical trials, a significant difference in % increase in alveolar bone height at 2- or 3-walled intrabony defects of the patients was demonstrated by standardized radiographs between Placebo Group and 0.3% FGF-2 Group at 9 months after the treatment. Additionally, the efficacy of FGF-2 was not affected by differences in age, sex, type of tooth, and vitality of dentin-pulp. Safety problems were not identified in the studies. This reveals that topical application of 0.3%FGF-2 can stimulate regeneration of periodontal tissue of periodontitis patients.

In order to improve the therapeutic effect of the FGF-2 in a severe intraosseous defects of periodontal tissue or horizontal bone destruction, it is essential to fully introduce the concept of “tissue engineering”. Interestingly, some clinical studies suggest that combination therapy of FGF-2 and bone graft material improves the efficacy of FGF-2. Further, it is demonstrated that stimulation with FGF-2 promotes new bone formation around the dental implants and subsequent osseointegration in a beagle dog model.

In this symposium, the present status of FGF-2 medicine in periodontal treatment will be presented and the future perspective of the medicine in dental field will be discussed with the audience.
**Brief CV**

Shinya Murakami  
Department of Periodontology Osaka University Graduate School of Dentistry

**Education**

Undergraduate 1978-1984 Osaka University Faculty of Dentistry, Japan, D.D.S.  
Graduate 1984-1988 Osaka University Graduate School of Dentistry, Japan, Ph.D.

**Research & Professional Experience:**

1988-1990  Visiting Fellow, National Cancer Institute, National Institutes of Health, USA  
1990-1992  Instructor, Department of Periodontology and Endodontology, Osaka University Faculty of Dentistry  
1992-2000  Assistant Professor, Department of Periodontology and Endodontology, Osaka University Dental Hospital  
2000-2002  Associate Professor, Department of Periodontology, Osaka University Graduate School of Dentistry  
2002-   Professor and Chair, Department of Periodontology, Osaka University Graduate School of Dentistry  
2011-2012  President, Japanese Division of the IADR (JADR)  
2012-2013  President, Periodontal Research Group of the IADR  
2016-2019  Director of Osaka University Dental Hospital  
2019-2020  President, Japanese Society of Periodontology  
2020-  Member of Science Council of Japan

**Award:**

1998  IADR/PRG: Anthony Rizzo Periodontal Research Award  
2009  American Academy of Periodontology(AAP): R. Earl Robinson Periodontal Regeneration Award  
2012  IADR/AADR: William J. Gies Award  
2013  IADR: Distinguished Scientist Award for Basic Research in Periodontal Disease.  
2018  IADR/PRG: Award in Regenerative Periodontal Medicine  
2019  AAP honorary membership Award  
2021  President Award of Japanese Association for Dental Science
Identification of tooth-specific genes plays an important role in tooth development and tooth regeneration researches. We have identified and functionally analyzed ameloblast-specific genes by comprehensive gene screening such as cDNA microarrays. Through these screenings, we succeeded in elucidating the important molecular mechanism in the differentiation process of ameloblasts. However, new molecular mechanisms in other epithelial cells that form teeth germ except ameloblasts have not yet been elucidated. In this study, we analyzed using the single-cell RNA sequence (scRNA seq) method for the clarifying gene expression in all cell populations that form tooth germs. In this screening, it became clear that ameloblasts, which were previously thought to be a single cell population, can be classified into two types: Dspp- and Ambn-positive cells. The former was a cell having a function of secreting growth factors and the like, and the latter was a cell secreting an extracellular matrix such as an enamel matrix. We were also able to identify genes that are specifically expressed in inner and outer enamel epithelium, stratum intermedium, and stellate reticulum. Subsequently, we identified novel dental epithelial cell marker genes, namely Pttg1, Atf3, Cldn10, and Krt15. The results not only provided a resource of transcriptome data in dental cells but also contributed to the molecular analyses of enamel formation.

We have identified genes expressed in tooth germs and conducted research to clarify the molecular function of mature ameloblasts, which had been a black box until now. Gpr115, expressed in newly identified mature ameloblasts, was one of a family of molecules containing G-protein coupled receptors. To investigate the in vivo function of Gpr115, knockout (Gpr115-KO) mice were created and found to develop hypomineralized enamel, with a larger acidic area because of the dysregulation of ion composition. Transcriptomic analysis also revealed that deletion of Gpr115 disrupted pH homeostasis and ion transport processes in enamel formation. In addition, in vitro analyses using the dental epithelial cell line cervical loop-derived dental epithelial (CLDE) cell demonstrated that Gpr115 is indispensable for the expression of carbonic anhydrase 6 (Car6), which has a critical role in enamel mineralization. Furthermore, an acidic condition induced Car6 expression under the regulation of Gpr115 in CLDE cells. Thus, we concluded that Gpr115 plays an important role in enamel mineralization via regulation of Car6 expression in ameloblasts. The present findings indicate a novel function of Gpr115 in ectodermal organ development and clarify the molecular mechanism of enamel formation.

We have been advancing the functional analysis of the molecule by identifying genes that are specifically expressed in tooth germs and mainly creating and analyzing gene-deficient mice. From the results of our research, the whole picture of tooth development has been gradually clarified, and it has greatly contributed to the understanding of the onset of human diseases showing abnormalities in teeth including enamel hypoplasia.
Brief CV

Satoshi Fukumoto
Section of Pediatric Dentistry, Kyushu University Faculty of Dental Science.
Division of Pediatric Dentistry, Tohoku University Graduate School of Dentistry

Education
Undergraduate 1988-1994 Nagasaki University, Nagasaki, Japan, D.D.S.
Graduate 1997-2000 Nagasaki University Graduate School of Dentistry, Nagasaki, Japan, Ph.D.

Research & Professional experience
1994-1997 Instructor, Nagasaki University School of Dentistry
1998-2000 Research fellow of the Japanese Society for the Promotion of Science
2000-2003 Instructor, Nagasaki University School of Dentistry
2000-2002 Visiting Fellow, National Institute of Dental and Craniofacial Research (NIDCR),
National Institute of Health (NIH)
2003-2004 Assistant professor, Nagasaki University School of Dentistry
2004-2007 Associate professor, Kyushu University, Faculty of Dental Science
2007- Professor, Tohoku University Graduate School of Dentistry
2019- Professor, Kyushu University Faculty of Dental Science
Recent Progress of Pulp Regenerative Therapy with Dental Pulp Stem Cells for the Application to the Periapical Disease in the Aged.

Koichiro Iohara
National Center for Geriatrics and Gerontology, Research Institute, Geroscience Research Center, Regenerative Dental Medicine

With the continued increase in the longevity in our society the pulp regenerative therapy may contribute to the functional survival and endurance of the tooth, leading to the improvement of the health and welfare in the aged people by optimal mastication with their functional teeth. Our previous clinical study and recent clinical treatments demonstrated the safety and efficacy of pulp regenerative therapy by the autologous transplantation of dental pulp stem cells (DPSCs) with granulocyte-colony stimulating factor (G-CSF) in pulpectomized teeth with irreversible pulpitis of the young and middle-aged. On the other hand, the incidence of periapical disease is much higher in people over 45 years old compared to patients with pulpitis in the aged. Thus, the main requirement for root canal treatment is shifting to periapical disease in the aged due to pulpitis in the middle-aged.

Therefore, the first challenge is the complete disinfection prior to stem cell transplantation by irrigants and intracanal medication for the regenerative therapy for periapical disease. We recently developed nanobubbles, which have the ability to remove the smear layer and enhance the delivery of medications to dentinal tubules, thus demonstrating the potential utility of nanobubbles with antibiotics or antimicrobial nanopolymers for the successful treatment of infected root canal and the resultant pulp regeneration. The second challenge is to enhance pulp regeneration in aged teeth. We have demonstrated that the age-dependent decline in regeneration was due to the reduced migration, proliferation, and cell survival of resident stem cells. The potential utility of trypsin pretreatment to enhance pulp regeneration and its underlying mechanisms, the direct effects on resident stem cells and indirect effects on dentin and cementum have been demonstrated in aged dog teeth. The third critical challenge is limited availability of autologous stem cells. Therefore, development of off-the-shelf allogeneic DPSCs will be an advance. We initiated experiments in dogs and observed optimal regeneration of pulp by the allogeneic transplantation of DPSCs both with the matched and mismatched dog leucocyte antigens (DLA).

In conclusion, it is possible to regenerate pulp tissue in the aged teeth in periapical disease by autologous and allogeneic transplantation of DPSCs after complete disinfection and pretreatment of the root canal with trypsin.
**Brief CV**

Koichiro Iohara  
National Center for Geriatrics and Gerontology, Research Institute, Geroscience Research Center, Regenerative Dental Medicine

**Education**

Undergraduate 1995-2001 Kyushu University, Faculty of Dentistry, Fukuoka, Japan, D.D.S.  
Graduate 2001-2005 Kyushu University Graduate School of Dental Science, Fukuoka, Japan, Ph.D.

**Research & Professional Experience:**

2005-2011  Researcher, Department of Oral Disease Research, National Institute for Longevity Sciences, National Center for Geriatrics and Gerontology  
2011-2021  Chief, Department of Stem Cell Research Therapy, National Institute for Longevity Sciences, National Center for Geriatrics and Gerontology  
2021-  
Chief, Geroscience Research Center, Regenerative Dental Medicine, National Institute for Longevity Sciences, National Center for Geriatrics and Gerontology

**Award:**

2002  Japanese Society of Conservative Dentistry Merit Award  
2003  International Symposium on Ultrasound Contrast Imaging Superb Poster Award  
2004  IADR Pulp Biology Travel Award  
2008  Japanese Society of Conservative Dentistry Encouragement Award  
2013  International Federation of Endodontic Association, The 9th World Endodontic Congress, Best Presentation Award  
2017  The 2017 Journal of Endodontics Best paper Awards  
2021  The 2020 Japanese Society of Conservative Dentistry Best paper award
Induced tissue-specific stem cell, a non-tumorigenic intermediate cell induced from somatic or pluripotent cell: their generation and possible use in the regenerative medicine of dental science

Issei Saitoh¹, D.D.S., Ph. D, Masahiro Sato², Ph. D, Emi Inada³, D.D.S., Ph. D, Hirofumi Noguchi⁴, MD, Ph. D
1 Department of Pediatric Dentistry, Asahi University School of Dentistry
2 Department of Genome Medicine, National Center for Child Health and Development
3 Department of Pediatric Dentistry, Kagoshima University Graduate School of Medical and Dental Sciences
4 Department of Regenerative Medicine, Graduate School of Medicine, University of the Ryukyus

Induced tissue-specific stem cells (iTSCs) are partially reprogrammed cells, which are thought to be an intermediate state, like progenitors or stem cells. They originate during transition (de-differentiation) from differentiated somatic cells into pluripotent stem cells [as exemplified by induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs)], or during cellular differentiation of undifferentiated cells. iTSCs have a limited capacity to differentiate and a morphology similar to that of somatic cell stem cells present in tissues, but are distinct from that of iPSCs and ESCs. iTSCs can be generally obtained 7 to 10 days after reprogramming of somatic cells with Yamanaka’s factors. Once established, their fibroblast-like morphology remains unaltered. iTSCs can also be obtained directly from iPSCs when they are maintained under the conditions allowing cellular differentiation. Notably, for more effective induction into iTSCs, it requires additional treatment such as conversion of iPSCs into naïve iPSCs, which are in more undifferentiated state like mouse ESCs. iTSCs can proliferate continuously in vitro, but when transplanted into immunocompromised mice, they fail to generate solid tumors (teratomas), implying loss of tumorigenic potential. The low tendency of iTSCs to elicit tumors is beneficial, especially considering applications for regenerative medicine in humans. To date, several types of iTSCs have been identified. For examples, iTS-L, iTS-P and iTS-D are obtained after partial reprogramming of hepatocytes, pancreatic cells, and human deciduous tooth-derived dental pulp cells, respectively. Our presentation will be focused on recent advances in the establishment of iTSCs and their possible applications in regenerative medicine.
**Brief CV**

Issei Saitoh  
Department of Pediatric Dentistry, Asahi University School of Dentistry

**Education**  
Undergraduate 1993-1999 Kyushu University, Fukuoka, Japan, D.D.S.  
Graduate 1999-2003 Kyushu University Graduate School of Dental Science, Fukuoka, Japan, Ph.D.

**Research & Professional Experience:**  
2005-2007  Assistant Professor, Department of Pediatric Dentistry, Kagoshima University Graduate School of Medical and Dental Sciences  
2007-2010  Lecturer, Department of Pediatric Dentistry, Kagoshima University Medical and Dental Hospital  
2008-2010  Visiting Researcher, Baylor College of Dentistry, USA  
2010-2012  Associate Professor, Department of Pediatric Dentistry, Kagoshima University Graduate School of Medical and Dental Sciences  
2012-2021  Associate Professor, Division of Pediatric Dentistry, Graduate School of Medical and Dental Sciences, Niigata University  
2021-    Professor and Chairman, Department of Pediatric Dentistry, Asahi University School of Dentistry

**Award:**  
2003  Young Investigator Award of Japanese Society of Stomatognathic Function  
2008  Young Investigator Award of Japanese Society of Pediatric Dentistry  
2011  Academic Award “LION Award” of Japanese Society of Pediatric Dentistry  
2015  Machida Memoria Research Award of Japanese Society of Pediatric Dentistry  
2018  Excellent Paper Award of PEDIATRIC DENTAL JOURNAL  
2018  Machida Memoria Excellent Paper Award of J of Japanese Society of Pediatric Dentistry  
2019  Poster Competition Award, The 57th Annual Meeting of Japanese Society of Pediatric Dentistry
Exosomes secreted from TNF-α-preconditioned gingival tissue-derived stem cells enhance M2 macrophage polarization and inhibit periodontal bone loss

Takao Fukuda, D.D.S., Ph. D.
Section of Periodontology, Division of Oral Rehabilitation, Kyushu University Hospital

Periodontitis is one of the most common osteolytic inflammatory diseases in human that adversely affects systemic disorders, such as diabetes. Accumulation of periodontal bacteria-associated biofilm is thought to trigger periodontitis, but is not believed to be sufficient to sustain the disease as the host immune response is critical for inflammatory tissue breakdown and disease progression. Macrophages play an important role in the immune response both during the initiation and resolution of inflammation. Macrophages are broadly classified into two phenotypes, pro-inflammatory M1 and wound-healing M2 cells. Macrophages are involved in bone homeostasis and the increased M1/M2 ratio leads to enhanced osteoclastogenesis. As M2 macrophages contribute to the tissue-remodeling process, effective M2 macrophage induction would provide favorable environment for lower inflammation and better regeneration.

We identified that gingiva-derived MSCs (GMSCs) have unique immunoregulatory capacity and secret large amounts of exosomes. Considering the facts that therapeutic effect of MSC largely depends on the paracrine efficiency of MSC and the advantages of the use of GMSCs include easier isolation from small pieces of gingival tissue (~2×2 mm²) and rapid cell proliferation, we hypothesized that GMSC-derived exosome-based therapy could be suitable for clinical use. Moreover, recent studies indicated that appropriate preconditioning of MSC with disease-related stimuli can optimize contents of exosomes to efficiently support the repair of the tissues in particular diseases. In this context, proteins or miRNA profiles in exosomes may be influenced by the pre-treatment regimens. Therefore, optical molecular-based protocol for MSC-preconditioning needs to be investigated and established.

In this presentation, we report the therapeutic effects of TNF-α preconditioned-GMSC-derived exosomes on periodontal disease and demonstrate underlying molecular mechanisms. Our study revealed that TNF-α-enhanced exosomal CD73 expression leading to anti-inflammatory M2 macrophage polarization and exosomal miR-1260b was important negative regulator of osteoclastogenesis. Accordingly, our findings may provide a novel therapeutic strategy for patients with periodontitis and other inflammatory osteoimmune disorders.
Brief CV

Takao Fukuda
Department of Periodontology, Division of Oral Rehabilitation, Kyushu University Hospital

Education
Undergraduate 1994-2000 School of Dentistry, Kyushu University, Fukuoka, Japan, D.D.S.
Graduate 2000-2004 Graduate School of Dental Science, Kyushu University, Fukuoka, Japan, Ph.D.

Research & Professional Experience:
2000-2004 Department of Medical Biochemistry, Graduate School of Medical Sciences, Kyushu University
2004-2014 Department of Periodontology, Division of Oral Rehabilitation, Kyushu University Hospital
2014-2019 Assistant Professor, Department of Periodontology, Faculty of Dental Science, Kyushu University
2016 Research fellow, Department of Anatomy and Cell Biology, Penn Dental Medicine, University of Pennsylvania
2019- Lecturer, Department of Periodontology, Division of Oral Rehabilitation, Kyushu University Hospital

Award:
2014 Young Investigators Award, The Japanese Society of Conservative Dentistry
RISING SCIENTIST SESSION
PPARγ-induced global H3K27 acetylation is required to maintain the abilities of extracellular matrix organization and osteo/cementogenesis in periodontal ligament fibroblasts: the possible link between dietary unsaturated fatty acids and periodontal tissue homeostasis

Shigeki Suzuki, D.D.S., Ph. D.
Department of Periodontology, Tohoku University Hospital

Dietotherapy is useful for prevention and treatment of lifestyle diseases such as diabetes mellitus, arteriosclerosis, hyperlipidemia, and obesity. For dietary fat control, in addition to quantitative restriction, qualitative selection is important. Generally, unlike saturated fatty acids, ingestion of a proper amount of unsaturated fatty acids, which include ω-3 fatty acid and ω-6 fatty acid, leads to positive systemic effects including thromboprophylaxis, hypotensive action, reducing serum LDL cholesterol, and increasing serum HDL cholesterol. The unsaturated fatty acids bind to cell surface receptors such as G protein-coupled receptors 120 (GPR120), GPR84, GPR41, and GPR43 and also are incorporated into cells and degraded by β-oxidation process. In inflamed periodontal tissue, ingestion of fresh oil, which is high in ω-3 fatty acids (docosahexaenoic acid and eicosapentaenoic acid), altered eicosanoid production in immunoresponses and reduced chronic inflammation. In experimental mouse periodontitis model, alveolar bone loss levels were inversely correlated with ω-3 fatty acid tissue level. Moreover, ingestion of ω-3 fatty acids inhibits osteoclast differentiation and bone resorption. Thus, the unsaturated fatty acids inhibit the progression of periodontitis.

Fibroblasts in periodontal ligament tissue (PDLF: periodontal ligament fibroblasts) retain ability to differentiate into osteo/cementogenic cells and aggressively synthesize and secrete collagen type 1 and the molecules required for collagen fibrillogenesis in order to compensate for the fast turnover of collagen fibers in periodontal tissue, which is essential for maintaining connective attachments. Since advanced periodontitis brings about hematogenous dissemination of activated immunological cells, oral bacteria, and inflammatory cytokines, the maintenance of periodontal tissue homeostasis and the prevention of onset of periodontitis are the ultimate clinical goals in order not to exacerbate systemic diseases. Therefore, the mechanisms by which PDLF utilize unsaturated fatty acids for periodontal tissue homeostasis should be unveiled.

Peroxisome proliferator-activated receptor (PPARγ) is a nuclear receptor that plays a role in lipid metabolism by directly regulating numerous metabolic genes. The dietary unsaturated fatty acids and their metabolites are main endogenous agonists of PPARγ. Therefore, PPARγ is the factor that responds to external unsaturated fatty acids concentration. Indeed, PPARγ exerts anti-inflammatory effects in immunological cells and osteoblastic cells as well as anti-osteoclastogenic effects in periodontal tissue. PPARγ is the master regulator of bone marrow mesenchymal stem cells (BMMSC) for differentiation towards adipogenic cells and inhibits differentiation towards an osteogenic cell lineage. However, the roles of PPARγ in PDLF have not been elucidated yet.

In this presentation, we demonstrate that PPARγ is a key epigenetic modifier in PDLF for the expression of extracellular matrix (ECM)-related and osteo/cementogenic-related genes and also that the agonistic effects of PPARγ enhance osteo/cementogenic abilities. PPARγ maintains an active chromatin status marked with H3K27ac, particularly in the chromatin area in which RUNX2-binding sites were significantly enriched. Consequently, the PPARγ-H3K27ac axis is a main machinery of PDLF to retain periodontal tissue homeostasis and also the dietary unsaturated fatty acids probably keep the machinery in working.
Brief CV

Shigeki Suzuki

Department of Periodontology, Tohoku University Hospital

Education

Undergraduate 1996-2002 Osaka University, Osaka, Japan, D.D.S.
Graduate 2002-2006 Osaka University Graduate School of Dentistry, Osaka, Japan, Ph.D.

Research and Professional Experience

2006  Department of Periodontology, Osaka University Graduate School of Dentistry
2006-2009  National Institutes of Health, National Institutes of Dental and Craniofacial Research, USA
2009  Department of Biological Endodontics, Hiroshima University Graduate School of Dentistry
2018  Department of Periodontology, Tohoku University Hospital

Award

2007  National Institutes of Health Visiting Program Award, USA
2010  Encouragement Award, The Japanese Society of Conservative Dentistry
2010  DENTSPLY Award, The Japanese Society of Conservative Dentistry
Nonalcoholic fatty liver disease (NAFLD), which is currently the most prevalent chronic liver disease worldwide, is defined as cases showing the presence of hepatic steatosis but lacking common causes of secondary hepatic fat accumulation, such as excessive alcohol consumption or chronic viral hepatitis. The majority of NAFLD cases are simple steatosis with good prognosis, but a subgroup of about 20%-30% of these patients can develop into more severe and progressives forms of liver disease, namely nonalcoholic steatohepatitis (NASH). Moreover, a portion of NASH patients progress to cirrhosis and hepatocellular carcinoma, which are end-stage liver diseases.

Recently, there has been a lively debate over the negative effects of periodontal disease on liver abnormalities, especially on NAFLD and NASH. Although the mechanism by which harmful factors are transported from diseased periodontal tissue to the liver is unclear, two routes have been proposed based on the unique anatomical characteristics of the liver, namely a hematogenous diffusion via the systemic circulation and a gut-liver axis via the gastrointestinal tract. Our research team previously reported that *Porphyromonas gingivalis*-derived lipopolysaccharide diffused from periodontal tissues and accumulated markedly in the fatty liver compared to the healthy liver controls.

In addition, gut microbiome dysbiosis induced by enteral translocation of periodontopathic bacteria may be involved in NAFLD. One mechanism assumed to link the gut microbiome with NAFLD is the disruption of the gut epithelial barrier, which may allow leakage of microbial products and metabolites into the portal circulation. Namely, changes in lipopolysaccharide and bacterial metabolites due to gut dysbiosis can induce intestinal inflammation and increase permeability, thereby promoting hepatic exposure to these components, which can directly cause NAFLD and liver fibrosis.

Diverse strategies for manipulating the gut microbiome in the management of NAFLD have been proposed, including the use of antibiotics and probiotics, which are defined as live cultures of beneficial microorganisms for the human body. Antibiotics exert beneficial effects on metabolic disorders by non-specifically suppressing the microbiome, but may be accompanied by harmful side effects and potential emergence of antibiotic-resistant bacterial strains. Therefore, recently, supplementation with probiotics and their products in the treatment of NAFLD has been promoted due to their potential for enhanced safety for humans and the environment.

However, little is known about the significance of probiotics for the management of NAFLD in patients with periodontal disease. In this presentation, we report that oral and gut microbiome-targeted probiotic therapy, especially with the probiotic bacteriocin nisin, which is produced primarily by *Lactococcus* species, may be a useful approach in the management of NAFLD associated with periodontal disease.
**Brief CV**

Ryutaro Kuraji  
Department of Life Science Dentistry, The Nippon Dental University, Tokyo, Japan  
Department of Periodontology, The Nippon Dental University School of Life Dentistry at Tokyo, Tokyo, Japan  
Department of Orofacial Sciences, University of California San Francisco School of Dentistry

**Education and Training**

- **2006-2012**  
  D.D.S., The Nippon Dental University School of Life Dentistry at Tokyo  
- **2012-2013**  
  Resident for clinical training, Department of General Dentistry, Tokyo Medical and Dental University  
- **2013-2016**  
  Ph.D., Department of Periodontology, The Nippon Dental University School of Life Dentistry at Tokyo

**Research and Professional Experience:**

- **2017-Present**  
  Assistant Professor, Department of Life Science Dentistry and Department of Periodontology, The Nippon Dental University School of Life Dentistry at Tokyo  
- **2019-2020**  
  Visiting assistant professor, Division of Periodontology, Department of Orofacial Sciences, University of California San Francisco School of Dentistry

**Award:**

- **2017**  
  JSP/JACP Poster Session General/Basic Research Awards 1st Prize, American Academy of Periodontology 102th Annual meeting in collaboration with the Japanese Society of Periodontology and Japanese Academy of Clinical Periodontology.  
- **2018**  
  Young Researcher’s Award, The Nippon Dental University.  
- **2018**  
- **2021**  
RS-3
Infertility and Periodontitis

Kazuhiro Omori, D.D.S., Ph.D.
Department of Periodontics and Endodontics, Division of Dentistry,
Okayama University Hospital, Japan

In recent years, infertility has become one of social problems. The cause of infertility may be male, female, or both, whereas it is reported that unexplained infertility, in which no obvious cause can be found by conventional infertility tests, accounts for about 30% of all infertility cases. Therefore, there is a strong demand from society to explore new approaches to unexplained infertility. Several risk factors for infertility have been reported, such as age, obesity, stress, and smoking. Recently, periodontitis has been reported to have an adverse effect on pregnancy, thus it may be a new risk factor for infertility.

Periodontitis is an oral infection caused by the continuous infection of periodontal pockets with periodontopathogenic bacteria such as Porphyromonas gingivalis (Pg), resulting vicious circle of inflammation. It has been reported that infected periodontopathogenic bacteria and inflammatory cytokines produced by inflamed-periodontal tissues have a hematogenous effect on systemic diseases such as diabetes, atherosclerosis, premature birth and low birth weight. Recently, it has been reported that women with high salivary IgG antibody titers to Pg take longer to become pregnant than women with low titers. Furthermore, it has been reported that reproductive function (sperm motility, etc.) is decreased in men with severe periodontitis. Thus, it is suggested that periodontitis may have some adverse effects on the ability to conceive in both men and women. However, the mechanism regarding the effects of periodontitis on infertility is still unknown.

We are currently conducting a clinical study to investigate the level of Pg infection in patients undergoing infertility treatment in cooperation with an obstetric clinic with reproductive center. In addition, we have investigated the effects of periodontal infection/inflammation on uterine in mouse periodontitis model using immunological methods. In this presentation, I would like to discuss the possibility of periodontitis as a new risk factor for infertility.
**Brief CV**

Kazuhiro Omori  
Department of Periodontics and Endodontics, Okayama University Hospital, Okayama, Japan

**Education**

<table>
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<th>Undergraduate</th>
<th>1995-2001</th>
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<td>Graduate</td>
<td>2001-2005</td>
<td>Graduate School of Medicine and Dentistry, Okayama University, Okayama, Japan, Ph. D.</td>
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**Research & Professional Experience:**

- 2004-2008: Post-doctoral fellow, Department of Periodontology & Oral Biology, Graduate School of Dental Medicine, Boston University, USA
- 2009-2014: Assistant Professor, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University
- 2014-current: Senior Assistant Professor, Okayama University Hospital

**Awards:**

- 2004: The Japanese Society of Conservative Dentistry Encouragement Award
- 2010: The 17th Kobayashi Magobei Memorial Foundation Award
- 2014: The 36th Ryobi Teien Memory Foundation Award
- 2017: The 20th Wesco Scientific Promotion Foundation Award
- 2020: The Japanese Society of Conservative Dentistry Case Presentation Award
The role of chronic low-grade inflammation on energy expenditure: association with CCL19/CCR7 axis

Misaki Iwashita, D.D.S., Ph.D.
Section of Periodontology, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University

The purpose of our research is to elucidate the molecular mechanisms on the systemic effects of chronic low-grade inflammation like periodontitis originally evoked locally. Previous intervention study in Japanese subjects with type 2 diabetes mellitus accompanied by severe periodontitis demonstrated that patients with body mass index (BMI) around 25 kg/m² showed slightly increased high-sensitivity (hs)-CRP (over 500 ng/mL), and periodontal treatment significantly decreased hs-CRP levels, followed by improved HbA1c. In contrast, subjects with lower hs-CRP (<500 ng/mL) were characterized by significantly lower BMI than those with hs-CRP 500 ng/mL or more. No significant improvement in HbA1c was observed in subjects with lower hs-CRP following periodontal treatment. In an animal study, we demonstrated that administration of low-concentration of lipopolysaccharide (LPS) significantly upregulated serum inflammatory mediators as various cytokines and chemokines in hereditary and diet-induced obese mice compared with lean mice. These human and animal studies suggest that local inflammation like periodontitis tends to be more amplified to the systemic level in subjects with overweight, suggesting that more matured adipose tissue play an important role in systemically amplifying local inflammation. Recent findings suggested that mature adipose tissue is characterized by massive infiltration of immune cells, primarily composed of monocyte/macrophage lineage. In this context, a comprehensive analysis of the gene expression in adipocytes co-cultured with macrophages showed markedly increased gene expression of many CC and CXC chemokines. C-C motif Chemokine ligand 19 (Ccl19) was one of the most highly expressed genes among all chemokine examined in adipocytes. Highly elevated serum CCL19 level in obese individuals has also been reported by others. We therefore hypothesized that CCL19 plays an important role in the pathophysiology of adipose tissue-related metabolic disorder, and, thus, subsequent study focused on the role of CCL19 and its receptor, CC-chemokine receptor 7 (CCR7) (CCL19/CCR7 axis) on inflammation and energy metabolism. Compared with wild-type (WT) mice, Ccr7⁻/⁻ mice showed higher rectal temperature during cold stimulation and significantly increased thermogenesis. Additionally, these mice were resistant to high-fat diet (HFD)-induced obesity, adipose and liver inflammation, fatty liver, and dyslipidemia. Furthermore, the study using adipocyte-specific Ccl19 knock-in (KI) mice demonstrated that activated CCL19/CCR7 pathway induced adipose tissue inflammation, and inhibited adenosine monophosphate-activated protein kinase α (AMPKα) activity in adipocytes via extracellular signal-regulated kinase 1/2 (ERK1/2). The expression of uncoupling protein 1 (UCP1) was significantly reduced in brown adipose tissue of Ccl19 KI mice compared with WT mice. These pathophysiological changes were most obvious in mice fed a 40% HFD than in mice fed a normal diet or a 60% HFD. In summary, activation of CCL19/CCR7 pathway in adipose tissue induced higher inflammation and inhibited AMPKα through activating ERK1/2, resulting in impaired lipid metabolism and energy regulation. In addition, a 40% HFD, which mimics western-style diet, more enhanced these pathological changes. Therefore, we suggest that local inflammation like periodontitis not only influence insulin sensitivity but also affect energy regulation through adipose CCL19/CCR7 system.
Brief CV

Education
2006  D.D.S., School of Dentistry, Okayama University, Okayama, Japan
2011  Ph.D., Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

Professional Experience
2006-2007 Dental resident, Okayama University Hospital
2011-2011 Clinical fellow, Hiroshima University Hospital
2012-2014 Assistant Professor, Graduate School of Biomedical and Health Sciences, Hiroshima University
2014-2018 Assistant Professor, Kyushu University Hospital
2019- Assistant Professor, Faculty of Dental Science, Kyushu University

Award
2010 President’s Poster Award, The American Diabetes Association’s 70th Scientific Sessions
2012 Encouragement Award, The Japanese Society of Periodontology
POSTER PRESENTATION
001: Collagen-binding properties of Streptococcus mutans killed by amoxicillin

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Department of Pediatric Dentistry, Osaka University Graduate School of Dentistry, Osaka, Japan

Objectives: Streptococcus mutans, a major pathogen of dental caries, is regarded as a causative agent of infective endocarditis (IE). For IE prevention, antibiotic therapy with amoxicillin is predominantly administered before an invasive dental procedure. S. mutans cell surface proteins, such as 120-kDa collagen-binding protein (CBP) and 190-kDa protein antigen (PA), have effects on its collagen-binding property and are considered to be involved in IE pathogenicity. Also, bacterial DNA encoding CBP is frequently detected in heart valve specimens extirpated from IE patients, though live S. mutans organisms are rarely isolated. This study evaluated the collagen-binding properties of S. mutans strains after killing by amoxicillin.

Methods: S. mutans strains were divided into three groups, CBP+/PA- (n=10 strains), CBP+/PA+ (n=10), and CBP-/PA+ (n=10), then cultured under two different conditions; living and killed by amoxicillin at 37°C for 18 hours. Next, each was added to a 96-well plate coated with type I collagen and cultured at 37°C for three hours, then crystal violet staining was performed. The OD595 value of each strain was determined, with the value of TW871 (CBP+/PA+) defined as 100%. Intergroup differences were compared using Student’s t-test.

Results: For the living S. mutans strains, the average collagen-binding rate for the CBP+/PA- group was 119.7±24.9%, significantly higher than that for the CBP+/PA+ group (89.4±22.4%) (P<0.05), whereas the CBP-/PA+ group showed nearly no collagen-binding ability. Among S. mutans strains killed by amoxicillin, the average collagen-binding rate for the CBP+/PA- group was 96.4±26.7%, significantly higher than that for the CBP+/PA+ group (65.3±10.3) (P<0.01), while the CBP-/PA+ group showed nearly no collagen-binding ability.

Conclusions: CBP-positive S. mutans strains killed by amoxicillin demonstrated collagen-binding properties, with that by the CBP+/PA- strains significantly greater as compared to the CBP+/PA+ strains. These results suggest that CBP+/PA- strains killed by amoxicillin have a high level of pathogenicity for IE.

002: S-PRG eluate inhibits acid and glucan synthesis by Streptococcus mutans

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Department of Pediatric Dentistry, Osaka University Graduate School of Dentistry, Osaka, Japan

Objectives: Surface pre-reacted glass-ionomer (S-PRG) filler, a bioactive material used in various dental materials, releases six different ions, including fluoride (F-), sodium (Na+), borate (BO33-), aluminium (Al3+), silicate (SiO32-), and strontium (Sr2+). Streptococcus mutans, a major pathogen of dental caries, produces glucan and acids from sucrose, leading to dental caries development. We investigated the inhibitory effects of S-PRG eluate towards S. mutans cariogenicity in the presence of sucrose.

Methods: S. mutans strain MT8148 was cultured in brain heart infusion broth containing 1% sucrose with or without 25% S-PRG eluate at 37°C for 18 hours. To determine the amounts of ions around S. mutans organisms, bacterial cells were collected by centrifugation, resuspended in sterile distilled water, and subjected to sonication, then the amount of each ion was measured. In addition, pH of the bacterial broths was determined with a pH meter and glucan concentration using a phenol-sulfuric acid method. Statistical analyses were conducted using Student’s t-test, with P<0.05 considered to indicate significance.

Results: Among the six examined ions, amounts of BO33-, F-, Al3+, and Sr2+ around S. mutans were significantly higher in the presence of S-PRG eluate than without S-PRG eluate (P<0.001). In addition, the mean pH value of the bacterial solutions in the presence of S-PRG eluate was 5.5±0.3, significantly higher than without S-PRG eluate (pH 4.2±0.02) (P<0.001). On the other hand, the mean glucan concentration in bacterial broth with S-PRG eluate was 34.2±4.3 μg/ml, significantly lower than that without it (92.8±4.7 μg/ml) (P<0.001). Conclusions: Specific ions contained in S-PRG eluate were found to inhibit cariogenicity of the bacterium in the presence of sucrose, such as acid production and glucan synthesis.
003: **Microbiological effects of silver diamine fluoride: an in situ study**


1Department of Restorative Dentistry and Endodontology, Graduate School of Dentistry, Faculty of Dentistry, Osaka University, 2Dental Technology Institute, Osaka University, Osaka, Japan

Objectives: Supragingival biofilm is a main aetiologic factor of dental caries. Silver diamine fluoride (SDF) was experimentally and clinically proven for the effectiveness in preventing and treating root caries, since it possesses the antimicrobial properties, the efficacy in hardening tooth structure and eventually arresting caries. Our aim was to investigate the effect of SDF on dental biofilm grown on demineralized dentin in in situ condition.

Methods: Root dentin of bovine incisors were prepared into rectangular slabs. The dentin slabs were divided into two groups; control and SDF groups, and were demineralized the surface by 20% citric acid. Unlike in control group, the dentin slabs in SDF group were treated with 38% SDF (Saforide™, Osaka, Japan) 4 min prior to the experiment. Seven healthy volunteers were asked to wear the devices for 96 hours. Biofilms formed on the dentin slabs were harvested from the devices every 24 hours. Viable cell counting, real-time PCR quantification, confocal microscopy and SEM observation were performed to assess the microbiological changes.

Results: CFU and PCR quantification results demonstrated lower number of viable and total bacterial cells respectively in SDF group than in control group. Confocal microscopy showed less thickness and volume of biofilm in SDF group. Dead-to-live ratios in SDF biofilm were also significantly greater than in control group. Fewer biofilm formation and less complex bacterial microcolonies of SDF group were observed from SEM images.

Conclusions: In conclusion, under in situ condition of cultivating biofilm, SDF reduced the viability and biomass of biofilm including increased dead cells were present. The anti-biofilm effect is an important mode in controlling and arresting root carious lesion.

004: **Investigation of Streptococcus mutans collagen-binding protein pathogenicity**

**D. MATSUOKA, S. NAKA, K. GOTO, M. MATSUMOTO-NAKANO**

Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Objectives: IgA nephropathy (IgAN) is the most common form of chronic glomerulonephritis, accounting for half of all child cases. However, the mechanism for IgAN development remains unclear. We previously reported that Streptococcus mutans with collagen binding protein (Cnm), which is associated with the collagen-binding ability of the surface protein of this organism, is frequently detected in the oral cavity of patients with IgAN. For the present study, recombinant Cnm (rCnm) was constructed and the pathogenicity of Cnm was investigated using a silkworm infection model.

Methods: The cnm gene encodes Cnm of S. mutans TW871, was amplified by PCR and ligated to a pGEX 6p-1 glutathione S-transferase fusion protein expression vector. The constructed plasmid was transformed into E. coli BL21 (DE3), and transformed colonies were cultured and cells harvested by centrifugation. Supernatant was obtained by centrifugation and purified using a glutathione Sepharose™ 4B column. Several different rCnm protein concentrations were injected through the dorsal surface into hemolymph of the silkworms (n=10) using a 26-gauge needle. Following injection, larvae were incubated at 37°C and survival was determined every 12 hours for 204 hours.

Results: Purified rCnm was confirmed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and CBB staining. Among the several different concentrations of rCnm administered to the silkworms, a significant difference for survival rate after 204 hours was noted between the group injected with PBS and the 50 μg rCnm injected group (P<0.05). Additionally, survival rates for the other rCnm-injected groups were also lower than that of the PBS-injected group.

Conclusions: These results indicate that the Cnm protein of S. mutans is a pathogenic factor. Additional animal experiments will be necessary to clarify more effective dosage concentrations and the pathogenicity of Cnm.
006: Inhibitory effect of cyclodextran on caries in animal model

H. ASAUMI, M. MATSUMOTO-NAKANO
Department of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Objectives: Cyclodextran, a cycloisomaltooligosaccharide, (CI), is known to function as a dextran analogue and considered to be a possible sucrose substitute. CIs have a structure in which 7 to 12 glucoses are cyclically linked by α-1, 6 bonds. In a previous report, a CI was shown to have inhibitory effects on glucosyltransferase B (GTFB) enzymes, which are produced by the cariogenic bacterium Streptococcus mutans. In the present study evaluated disease progression associated with Cnm- and PA-positive S. mutans using a NASH mouse model. Methods: Specific pathogen-free Sprague Dawley rats (male, 15 days old) were used. Antibiotic treatment was performed at 15 and again at 16 days of age to facilitate establishment of S. mutans. S. mutans MT8148R strains were then directly administered into the oral cavity using a pipette once a day for five days, after which the rats were divided into five groups (n=15). They were fed a caries-inducing diet containing 56% sucrose (Diet 2000), or were given distilled water without CI or with 0.625%, 1.25%, 2.5%, 5% CI. The rats were euthanized under anesthesia at the end of the experiment (73 days of age). Bones were excised, and plaque and dental caries scores determined. Results: Results of both the diet and drinking experiments showed that the amount of plaque adherence to tooth surfaces in all CI added groups was lower as compared to without CI. Conclusions: This study was supported in part by the Fund for Scientific Promotion of Nissin Sugar Co., Ltd., Tokyo, Japan.
008: **BCOR mediated regulation of ZFPM2 via BCL6 involved in hyperactive root formation of OFCD syndrome**

**K.M. SOE, T. OGAWA, K. MORIYAMA**

Department of Maxillofacial Orthognathics, Tokyo Medical and Dental University (TMDU), Tokyo, Japan

Objectives: BCOR interacting corepressor (BCOR) mutations cause oculofaciocardiodental (OFCD) syndrome, which is a rare X-linked dominant condition, with permanent tooth radiculomegaly. Although BCOR-associated downstream molecules might play an important role in hyperactive root formation, its molecular regulation mechanism is far from being fully elucidated. The objectives of this study were to determine these BCOR-associated molecules.

Methods: Comparative expression profiling of periodontal ligament (PDL) cells isolated from a normal and an OFCD patient were analyzed using microarray analysis. In vitro testing included MTT assay, quantitative PCR, chromatin immunoprecipitation (ChIP) assay, and knockdown assay using OFCD (mutant) PDL cells, human periodontal ligament fibroblasts (HPdLF), and COS7 cells.

Results: The gene-specific transcriptional factors group, wherein NFIB, DLX5, and ZFPM2 are the most upregulated genes, was significantly expressed in mutant PDL cells. BCOR overexpression into HPdLF showed ZFPM2 downregulation and DLX5 upregulation, but NFIB expression did not change. Focusing on ZFPM2, whose expression was downregulated after BCOR overexpression into HPdLF, ChIP assay using HPdLF and COS7 cells showed that the wild-type BCOR was recruited in the BCL6 binding of the ZFPM2 promotor region after immunoprecipitation, while the mutant BCOR, which is the same genotype to our patient, failed to recruit these promotor regions. ZFPM2 knockdown expression in the mutant PDL cells also showed significantly reduced cellular proliferation and reduced ALP mRNA expression.

Conclusions: Our findings suggested that BCOR mutation induced ZFPM2 regulation via BCL6, possibly contributing to hyperactive root formation in OFCD syndrome.
010: The effects of MTA exposed to NaOCl on odontoblastic differentiation of a human periodontal ligament stem cell line

K. YAMASHITA1, A. TOMOKIYO2, T. ONO2, K. IPPOSHI1, A. ALHASAN1, A. TSUCHIYA3, A. HAMANO2,4, H. SUGII1, S. YOSHIDA2, T. ITOYAMA2, H. MAEDA1,2

1Department of Endodontology and Operative Dentistry, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2Department of Endodontology, Kyushu University Hospital, Fukuoka, Japan, 3Department of Biomaterials, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 4OBT Research Center Faculty of Dental Science, Kyushu University, Fukuoka, Japan

Objectives: Membranes are a key material to the GBR approach, being able to function as a barrier against fibrous tissue and make the space for bone regeneration. We focused on the chemically synthesized and flexible biodegradable polymer ε-caprolactone and L-lactic acid co-polymer (PLCL) and have developed a resorbable GBR membrane, Cytrans ElaShield. Acid production during degradation become an issue of lactic acid-based polymer. Therefore, we evaluated a degradation behavior of PLCL membrane and pH change during degradation.

Methods: In vitro degradation test was performed in accordance with the ISO15814:1999. φ13 mm specimens were soaked in phosphate buffered saline (PBS, pH 7.4) at 37 °C (n=4). Every 4 or 8 weeks, pH value of PBS solution was measured, and soak solution exchanged to fresh PBS if pH value is under 7. After immersed, each specimen was rinsed and dried to check the mass loss. 50% mass loss period of PLCL was compared to that of poly(lactic-co-glycolic) acid (PLGA) membrane which degrades in 12-16 weeks in vivo.

Results: As a result of in vitro degradation test, membrane weight of each group was decreased in linearly from 8 weeks. Period of 50% mass loss was 28.8 weeks for PLCL and 13.4 weeks for PLGA membrane. pH of PLCL changed from 7.4 to 6.9 for initial 12 weeks immersion. pH of PLGA changed from 7.4 to 6.4 for initial 8 weeks.

Conclusions: Degradation of both PLGA and PLCL membrane were slowly, and no rapid pH change was observed. Furthermore, pH change of PLCL was slower than that of PLGA, and the amount of generated lactic acid can be sufficiently metabolized by the buffer capacity in the body. Therefore, there will be no concern about inflammation caused by a decrease in pH. These results indicated that Cytrans ElaShield is a clinically useful GBR membrane.
011: Bone reconstruction using three-dimensional interconnected porous CO3Ap block fabricated based on hydrate expansion of CaO granules.

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1Section of Fixed Prosthodontics, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, 2Department of Fixed Prosthodontics, Division of Oral Rehabilitation, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

Objectives: Interconnected porous structure may be a key for use of carbonate apatite (CO3Ap) block for massive bone reconstruction. In this research, feasibility to fabricate three-dimensional interconnected porous CO3Ap block was studied based on hydrate expansion of calcium oxide (CaO) granules, followed by carbonation and phosphatization (Figure 1). Also, its potential for bone reconstruction was histologically investigated using rabbits.Methods: CaO granules were hydrated under 100% humidity in a closed vessel, and exposed to CO2 at 25°C. Then, samples were immersed in Na2HPO4 solution at 80°C. XRD and FT–IR were used for compositional analysis, whereas SEM and μ–CT were used for structural analysis. Potential of the porous CO3Ap as artificial bone was evaluated by reconstructing the rabbit femur bone defects. Dense CO3Ap blocks were used as controls. Results: After exposing to the humidity, CaO granules expanded and formed three-dimensional interconnected porous structure. XRD and FT–IR results along with SEM and μ–CT analysis confirmed successful compositional transformation to CO3Ap maintaining its structure (Figure 2). Histological analysis 4 weeks after surgery revealed that new bone was formed interior of the porous CO3Ap block. Additionally, remodeling of the porous CO3Ap was confirmed by the presence of osteoblasts, osteoclasts and osteocytes. 8 weeks after surgery, red blood cells and vascular endothelial cells were confirmed inside the pores, indicating a Haversian system-like structure formation. By contrast, new bone was observed only on the surface of dense CO3Ap blocks even after 8 weeks (Figure 3). Conclusions: Three-dimensional interconnected porous CO3Ap block was successfully fabricated using hydrate expansion of CaO granules, followed by carbonation and phosphatization. The interconnected porous structure was useful to allow penetration of the bone-related cells interior of the block. We concluded, therefore, that the three-dimensional interconnected porous CO3Ap block has a good potential value for treatment of massive bone defects.

012: Development of Novel Filler-Dispersed Resin Composite for 3D-Printed Permanent Crown

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Objectives: This study aimed to develop novel filler-dispersed resin composite for fabrication of a permanent fixed-partial restoration by additive manufacturing. Mechanical properties (MP), physicochemical properties (PP), cell viability (CV), and conversion degree (CD) were evaluated. Methods: Resin-mixture precursors were prepared with variations of filler size and percentage (microfiller: 20%; 40%; 60%; 70% and nanofiller: 10%; 20%; 30%; 40%). Then the specimens were fabricated by SLA 3D-printer. Flexural strength (FS), flexural modulus (FM), Vickers hardness (VH) were evaluated both immediately and after 2 months of water-immersion. Water-sorption (WS) and water-solubility (WL) were evaluated after 2 months of water-immersion. The optimal precursor composition would receive additional CV (by CCK-8 assay at day1, day3, day5, day10) and CD (FTIR) evaluations. Data were analyzed by one- or two-way ANOVA followed by Tukey's test (p=0.05). Results: For both filler types, higher filler-content groups demonstrated better MP and PP. However, higher filler-content groups also had higher viscosity leading to difficult manipulation and defects. Comparing between same filler-content groups, microfiller groups exhibited higher VH, WL, lower FM, WS (p<0.05) than nanofiller groups but FS was not different. Water-immersion decreased FS and VH, but not FM for both filler types. 60% microfiller group (FS = 168.4±10.1MPa, FM = 6.3±0.4GPa and VH = 62.6±0.9, WS = 30.7±1.3μgmm-3, WL = 3.9±0.8μgmm-3) was chosen for CV and CD tests. CV results of experimental material revealed same level of biocompatibility as commercial CAD-CAM block (76.2±18.5% and 89.3±5.2% respectively). CD was 49.9±3.7%. Conclusions: The precursor with moderately high microfiller content, in this experiment 60%, seemed to be the most suitable composition for 3D-printer. Moreover, its mechanical and physicochemical properties complied with ISO 10477:2018 and JDMAS 245:2020. The experimental material is promising and worth further research and development.
013: Morphological observation of microvascular changes and bone formation after Alveolar bone regeneration.
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Objectives: Various kinds of bone regeneration materials have been tried to regenerate the alveolar bone. In this study, synthetic and xenograft materials were used for morphological analysis. This research concerns observation of the relationship of the vascular network and alveolar bone using a stereoscopic and scanning electron microscope (SEM). Methods: All animal experiments were conducted according to the protocol agreed by our Institutional Animal Ethics Committee. Six beagle dogs were used. Both mandibular premolars were extracted. Right side of tooth sockets were filled with Carbonated apatite granule (CO3Ap: Cytrans granule, GC, Japan) with L-lactide-ε caprolactone copolymer membrane (Cytrans elashield, GC, Japan) as a synthetic graft group. Left side was filled with bovine porous bone graft material granule (Bio-Oss, Geistlich, Switzerland) with porcine collagen membrane (Bio-Gide, Geistlich, Switzerland) as xenograft group. The vascular synthetic resin was injected from inferior alveolar arteries after postoperative 14, 30 and 90 days. Microvascular resin specimens were examined by stereoscopic microscope and SEM. Results: Postoperative fourteen days in both groups, granule filled the extraction sockets tightly. Newly formed blood vessels from the pre-existing bone marrow penetrated the spaces between the granules in the socket. Thirty days after surgery, the bone addition had progressed where the blood vessels were buried in the newly formed bone. Bone formation in the central region of sockets is more advanced in the synthetic graft group than xenograft group. Nineteen days after, Extraction socket was regenerated the dense compact bone. Thick blood vessels formed a network around the granules. The height of alveolar margin was maintained in both groups. Conclusions: The results of this research indicate that both materials are beneficial for bone regeneration. In the future we have to decide whether animal-derived materials or chemically synthesized materials are more beneficial to patients.

014: Tuning macrophage polarization by titanium nanosurfaces through nanotopographic cues to prevent peri-implantitis.
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Objectives: Definitive prevention of peri-implantitis remains unestablished. M1 macrophages play a key role in innate immunity against inflammatory osteolysis around biomaterials. Macrophage polarization is controlled by environmental stimuli and hence a titanium nanosurface might tune macrophage polarization and function. The purpose of this study was to determine whether titanium nanosurfaces with dense nanospikes prevent peri-implantitis by tuning macrophage polarization toward inhibiting osteoclast differentiation of osteoclast precursors. Methods: Nanoroughened titanium surfaces created by alkaline-etching treatment were evaluated for the surface properties. Mouse macrophage-like cell line (J774A.1) were cultured on machined, micro-roughened, or nanoroughened titanium surfaces and analyzed for the relationship between macrophage polarization and the surface properties. Mouse osteoclast precursor cell line (RAW264.7) were co-cultured with osteoclast differentiation factors and macrophage culture supernatants from each titanium surface and evaluated for osteoclast differentiation. Micro-roughened or nanoroughened titanium mini-implants osseointegrated with the rat’s maxilla were ligated to induce peri-implantitis, followed by histologic evaluations of inflammatory osteolysis. Results: Nanoroughened surfaces had anisotropically patterned dense nanospikes together with superhydrophilicity, as well as hydroxyl groups. J774A.1 cells on nanoroughened surfaces exhibited M1-like circular shapes and highly expressed M1, but not M2, markers, even under the conditions that eliminated the surface’s superhydrophilicity and hydroxyl groups. The other titanium surfaces hardly evoked any polarization markers in macrophages. Macrophage culture supernatants on nanoroughened surfaces inhibited osteoclast differentiation of RAW264.7 cells in contrast to differentiation into large TRAP-positive cells in the supernatants from the other surfaces. Nanoroughened titanium implants significantly inhibited peri-implant bone resorption and osteoclastogenesis compared to those around the micro-roughened titanium implants. Conclusions: Titanium nanosurfaces with dense nanospikes can prevent peri-implantitis by tuning macrophage polarization through nanotopographic cues toward inhibiting osteoclast differentiation of osteoclast precursors.
016: A novel bioabsorbable polysaccharide derivative for minimally invasive bone graft harvesting

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Objectives: The cancellous bone harvested from the ilium is commonly utilized for bone grafting of the cleft lip and palate; nevertheless, it leads to heavy burdens on children with clefts. The bone regeneration ability of implanted cancellous bone is high, so that the development of alternative materials remains difficult and challenging. Here we developed a novel bioabsorbable polysaccharide derivative termed “phosphopullulan” and investigated its safety and function.

Methods: To survey the biological safety of phosphopullulan, the following tests were conducted: The skin sensitization test in guinea pigs, pyrogen test in rabbits, intracutaneous reactivity test in rabbits, acute systemic toxicity test in mice, implantation test in rabbit bone, subchronic toxicity study by implantation in the rat medullary cavity, bacterial reverse mutation test, in vitro mammalian chromosome aberration test, in vitro cytotoxicity test, and endotoxin test. Furthermore, the granular or powdered artificial bone mixed with or without phosphopullulan was implanted in the rabbit bone to test the inflammatory potential.

Results: A marginal and axial wall area discrepancies increased after around 80 repeated uses of an end mill. Up to 80 times, the discrepancies of a marginal area were under 100 μm, which has been reported as the value for the clinical tolerance. SEM images of the end mill showed that the diamond coatings peeled off after 10 repeated uses, and most of the coatings at the edge of the end mill detached from the base material after 80 repeated uses. Although the chipping of the coated surface was observed after using 10 times, the discrepancies were not affected. Similarly, the surface roughness rapidly increased after 80 repeated uses.

Conclusions: This study indicated that the repeated use of end mill should be within 80 times to get good internal fitness of crown.
017: Bond Strengths of 4-META/MMA-TBB Resin Cement to Root Canal Dentin
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Objectives: The purpose of this study was to evaluate an adhesion promoting effect of 4-META/MMA-TBB by the pretreatment method of root canal dentin in resin build-up restoration.

Methods: Six freshly extracted single root human teeth were used in this experiment. After pulpal tissue were removed by endodontic files, root canals were prepared to be one-third of the diameter of the root section width and two-third of the vertical root length. After root canal preparation, each root was longitudinally hemisected and pulpal dentin walls were polished flat. One of the roots sectioned into halves was used as the immersion group, the other was the control group. Dentin surface treatment of the control group was treated with Green Activator (Sun Medical) in 10 sec and Teeth Primer (Sun Medical) in 30 sec and immersed in a large amount of Super-Bond Activated Liquid (Monomer : Catalyst V = 4:1) (Sun Medical) for 1min. Commercially available resin composite block was bonded to treated dentin with 4-META/MMA-TBB (Super-Bond) after sandblasting (Al2O3, 70 μm, 0.1 MPa) and treating with PZ Primer (Sun Medical). After storage in a 100% humidity incubator at 37°C for 1 hour, all specimens were stored in water at 37°C for 24 hours in darkness and were shaped hourglass configuration with a cross-sectional area of approximately 1mm2 for micro-TBS testing. The specimens were loaded in the testing device (AUTOGRAPH AGS-H, Shimadzu) at a CHS of 1.0 mm/min. Data were analyzed by paired sample t-test (p<0.05).

Results: Micro-TBS values between the immersion group (60±7.94 MPa) and the control group (38±17.6 MPa) was statistically significant difference (t=2.955, p<0.05).

Conclusions: The immersion in the activated liquid was effective method to promote a root canal dentin adhesive.

018: Ceria-stabilized zirconia substrate directly bonds to bone-like hydroxyapatite crystals at nano-scale
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Objectives: The osseointegration ability of ceria-stabilized tetragonal zirconia polycrystals/aluminum oxide (Ce-TZP/Al2O3), a promising dental implant material, has been unclear at microscopic level despite its recent clinical use. Our objective is to characterize the crystal structures of the cell-induced precipitates and investigated the bonding interface between the precipitates and ceria-stabilized zirconia at nanoscale.

Methods: C2C12 cells were cultured on a Ce-TZP/Al2O3 substrate. The differentiation potency was investigated by qPCR analysis for differentiation marker genes in C2C12 cells. The nodule formation and mineralization capacities of the cells were assessed with Alizarin Red S staining. Proteins in cell-induced precipitates were extracted and characterized by SDS-PAGE. Cell-induced precipitates were characterized by X-ray diffraction, scanning electron microscopy, transmission electron microscopy (TEM) and scanning-TEM energy-dispersive X-ray spectroscopy. Results: The inorganic component of precipitates consisted of hydroxyapatite single phase that exhibited a characteristic morphology, i.e., flexible nanofibers less than 10 nm wide with nanometer-thick plates filling the spaces between nanofibers. No metastable phases such as amorphous calcium phosphate and octacalcium phosphate were found in the precipitates. The precipitates had two bone proteins, osteocalcin and osteopontin, as organic substances. High-speed and less-destructive elemental analysis revealed that the hydroxyapatite contained alkaline metal cations (Na, Mg, and K) as minor elements and that its average Ca/P atomic % ratio was ~1.40, similar to that of bone apatite. This hydroxyapatite directly bonded to the zirconia nanocrystals at lattice fringe scale, indicating nanoscale osseointegration. Crystal structure models showed that the hydroxyapatite face could grow epitaxially on the zirconia face. Conclusions: These findings provide crucial information about the osseointegration of ceria-stabilized zirconia, which facilitates the further study using this material both in fundamental science and application fields, and contribute to improving the success rate of dental implant treatment. This study was supported by a JSPS KAKENHI Grant-in-Aid for Early-Career Scientists (15K21457 and 19K19078).
019: The Relationship Among Child Dental Caries, Microbiome and Parental Awareness.

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Objectives: Parental awareness is the key to preventing child dental caries. The purpose of this study was to assess the differences in salivary microbiome between mother and child, the child microbiome differences due to their caries history and the relationship between child salivary microbiome/caries history and parental awareness.

Methods: Saliva, examinations and questionnaire were collected from Children and/or Mothers (64). The V3-V4 region of 16S rRNA gene was amplified and sequenced on Illumina MiSeq platform. Sequencing analysis was performed against the Human Oral Microbiome Database (HOMD). Children were classified by caries history into three groups: Non-caries (42), Former caries experience (12) and Current caries (10) or two groups: Non-caries (42) and Caries (22). There were six questions about child oral care that his/her mother usually took care of in the questionnaire and those were answered by mothers.

Results: The mother and child microbiome was significantly more similar than the non-mother and child microbiome. Streptococcus mutans and Scardovia wiggsiae that have been suggested to be associated with caries, were significantly more abundant in Caries group than Non-caries group. Comparing the three caries groups, only S. wiggsiae was significantly less abundant in Non-caries group than Former caries experience group. The all current caries teeth were mild and followed closely without treatment, while former caries teeth were severe and required treatment. Mothers of children with current caries performed more oral care habits than mothers of children with former caries.

Conclusions: The children with caries had more caries-related bacteria than without caries (Non-caries). Parental oral care may be important as well as child oral care, since the mother and child microbiome was more similar. This study suggests that enhancing parental awareness of oral care and continuing appropriate oral care habits make it possible to reduce the risk of caries occurrence and progression.

020: Involvement of Human Salivary Protein-derived Peptides-specific SfGA In Oral P. gingivalis Colonization.

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Objectives: We have previously showed that fimbriae on Porphyromonas gingivalis (Pg), one of putative periodontopathogenic bacteria, specifically bound to a peptide domain (stat23, prp21) shared by statherin or acidic proline-rich protein 1 (PRP1), human salivary proteins. In this study, we investigated whether double DNA adjuvant (DA) consisting of DNA plasmid expressing Flt3 ligand (pFL) and CpG oligodeoxynucleotide (CpG ODN) would induce stat23- and prp21-specific secretory-IgA (SIgA) antibodies (Abs) in saliva of mice administered nasally stat23 and prp21 plus DA, and the induced SIgA would inhibit Pg-binding to human whole saliva-coated hydroxyapatite beads (wsHAPs).

Methods: Female 8-weeks-old, C57BL/6 (IgA+/+) or IgA-deficient (IgA-/-; background C57BL/6) mice were nasally immunized with respectively 50 mg of stat23 and prp21 as antigens (Ags) plus 50 mg of pFL and 10 mg of CpG ODN as DA four times at weekly intervals. Seven days after the last immunization, saliva samples were collected, and examined stat23- and prp21-specific IgA antibodies (Abs) responses by ELISA and ELISPOT assay. In addition, SfGAA-enriched saliva samples deleted both IgG and IgM by using affinity columns were tested in the Pg-binding inhibition assay to wsHAPs.

Results: Significant induction of salivary SfGA Abs to stat23 and prp21 was seen in IgA+/+ mice. Furthermore, the SfGAA-enriched saliva samples induced in mice administered nasally the mixture of stat23 and prp21 with DA showed significant Pg-binding inhibition to wsHAPs. Of interest, saliva samples in IgA knock-out mice given nasally Ags plus DA displayed no inhibitory effects on Pg-binding to wsHAPs.

Conclusions: These findings showed that human salivary protein-derived peptides-specific SfGA Abs induced by nasal administration with stat23 and prp21 plus DA have a potential inhibitory effect in Pg colonization to wsHAPs in vitro, and suggested that SfGA induced by the nasal vaccination might be an effective tool preventing Pg colonization on tooth surface by cohering fimbriae-binding domains on salivary proteins.
022: Bone apatite-clusters in intramembranous and endochondral ossification show distinct morphologies
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Objectives: The objective of this study was to perform a comparative analysis of the structure and composition of bone apatite clusters formed in intramembranous (IO) and endochondral ossification (EO).

Methods: For analysis of IO, calvaria were isolated from ICR mice at embryonic days (E) 14.5 to 15.5. For analysis of EO, femur epiphysis and diaphysis were isolated from newborn mice at post-natal days (P) 6 to 7 and embryos at E15.5, respectively. Bone apatite crystals were also analyzed during bone repair in a 1-mm femur defect model in 6-week-old ICR female mice.

The morphology of bone apatite clusters was analyzed by scanning electron microscopy (SEM) after selective removal of organic matter in the bones with NaClO. The NaClO-treated bones were washed and dehydrated before SEM observation. The composition of bone apatites were analyzed by inductivity coupled plasma-optical emission spectroscopy (ICP) and energy dispersive X-ray spectroscopy (EDS). Biomimetic mineralization assay was performed to investigate the role of pH in apatite cluster growth. The mineralization products were analyzed by X-ray diffraction. Image analysis was performed with ImageJ.

Results: SEM observation and image analysis revealed that bone apatite clusters in EO (epiphysis) were > 10 times larger than those in IO (calvarium). No significant changes in ion composition were detected by ICP or EDS. Similar findings were observed in femur diaphysis, where cortical (IO) and trabecular (EO) bone can be observed at the same site. During femur repair, the minerals formed in the callus through EO were also similar to those formed in epiphysis and diaphysis, but were gradually resorbed until day 14 of healing. The minerals formed through IO inside the bone defect were similar to those observed in calvaria. In vitro mineralization assay suggested that a slow P supply into a Ca-rich alkaline microenvironment could facilitate the formation of large apatite clusters.

Conclusions: The results revealed the distinct morphologies, without significant difference in ion composition, of bone apatite clusters in IO and EO.
023: A Materials Science-based Re-evaluation of Initial Tooth Mineralization

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Objectives: The objective of this study was to re-evaluate the initial stages of mouse molar formation from a materials science viewpoint.

Methods: For identification of the initial site and time of molar mineralization, pregnant mice were injected with calcein (20 mg per kg) at embryonic day (E) 17.5, and calcein-positive mineralized areas in the first molar were observed under a fluorescence stereoscopic microscope. The molars were isolated at E18.5, postnatal day (P) 0 and P1. Ultrastructural analysis of the initial mineralization process was performed with scanning (SEM) and scanning-transmission electron microscopy (STEM) using resin-embedded P0, P1 and P3 first molars. Elemental mapping and electron diffraction were performed for qualitative analysis of the initial minerals in dentin and enamel.

Results: At E18.5, calcein staining was not observed, and the morphology of the crown was not clear. At P0, the morphology of the crown was well-defined, and the initial calcification indicated by calcein staining was observed at the tip of the distobuccal cusp. At P1, the calcein-stained calcified area was observed along the morphology of the crown surface layer. SEM / STEM observations revealed that calcification begins in the dentin and occurs in the following steps: 1. collagen deposition, 2. formation of amorphous calcium phosphate (ACP), and 3. crystallization into apatite. Subsequently, enamel formation was observed, and similar to dentin, involved the initial formation of ACP and transformation into apatite, as analyzed by electron diffraction.

Conclusions: Based on a systematic and spatio-temporal analysis of initial tooth formation stages, this study identified the very initial minerals in P0 mouse molars at the distobuccal cusp. ACP was found to be a precursor of apatite in both dentin and enamel.

024: Effects of TGF-β isoforms on ameloblasts

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Objectives: Transforming growth factor beta (TGF-β) is one of the physiologically active substances produced by various cells in the body, and three types of isoforms (TGF-β1, β2, β3) are known in mammals. In general, TGF-β isoforms transmit signals into cells via a common receptor, and it has not been clarified whether there are different signal transductions between isoforms.

Our objective: is to compare the cell morphology and the results of gene expression analysis in order to clarify whether there is a difference between isoforms in the signal transduction of TGF-β1, β2 and β3.

Methods: Mouse enamel epithelial cell line (mHAT9d) was seeded on a 6-well plate. Upon confluent, TGF-β1, β2 and β3 was individually added and cultured for 8 days. After culture, cell morphology was observed by Rhodamine-Phalloidin and DAPI staining. In addition, comprehensive gene expression analysis (next-generation sequencing) was performed using mHAT9d cultured under the same conditions for 10 days.

Results: In cell morphology, paving stone-like cells were observed in the control, but cells stimulated with TGF-β1 and β3 lost their morphology and possessed the cell process. Many cells with paving stone-like morphology were observed in TGF-β2 as well as control, and it was found that there were few cells with the cell process compared to TGF-β1 and β3. From the results of next-generation sequencing, there were categories in which the expression level did not increase when TGF-β2 was added compared to the control. In addition, the gene expression levels of kallikrein 4 and carbonic anhydrase 2 were found to be increased in the group to which TGF-β1 and β3 was added as compared with control and TGF-β2.

Conclusions: TGF-β reacts differently between isoforms to ameloblasts.
025: Decreased expression of Neprilysin induced by *P. gingivalis*-LPS in mouse hippocampus

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Objectives: Alzheimer’s disease (AD) is the most frequent neurodegenerative disorder in ageing populations in the world. Although periodontal diseases may be a risk factor of AD, the mechanism is still unknown. The deposition of the amyloid-β peptide (Aβ) in the brain parenchyma is a crucial step in AD. Aβ is usually eliminated from the brains by clearance mechanism. The overproduction of Aβ or a lack of the clearance mechanism induce increased deposition of the Aβ in the brain. Neprilysin (NEP) is an enzyme that in humans is encoded by the metallo-endopeptidase gene. NEP is thought to be involved in the clearance mechanism. In the present study, we examined the effects of systemic administration of Lipopolysaccharide derived from *P. gingivalis* (PG-LPS) on NEP expression in the hippocampus of adult and senescence-accelerated mice.Methods: Eight to ten week-old C57BL/6J mice and SAM-P/8 mice were administrated LPS derived from *P. gingivalis* intraperitoneally once every 3 days for 3 months. The normal serine was administrated as a negative control. We extracted the hippocampus from mice. NEP expression levels are measured by quantitative RT-PCR (qRT-PCR), immunofluorescence staining and western blot analysis. The data were statistically analyzed using Mann-Whitney’s U test.Results: Eight to ten week-old C57BL/6J mice and SAM-P/8 mice were administrated LPS derived from *P. gingivalis* intraperitoneally once every 3 days for 3 months. The normal serine was administrated as a negative control. We used the hippocampus extracted from mice as samples. NEP expression levels are evaluated by quantitative RT-PCR (qRT-PCR), immunofluorescence staining and western blot using anti-NEP antibody (Proteintech Group, Inc.). The data were statistically analyzed using Mann-Whitney’s U test.Conclusions: These results indicate that decreased expression of NEP may be involved in AD associated with *P. gingivalis*.

026: Tetrahydrobiopterin pathway: A therapeutic target for neuropathic pain model

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Objectives: Tetrahydrobiopterin (BH4) is an essential cofactor involved in the production of several neurotransmitters. Previous research reports suggested upregulation of BH4 in chronic pain. This study aimed to evaluate the effect of a novel drug, Tranilast in blocking the BH4 pathway in chronic neuropathic pain model.Methods: Four weeks old male Sprague-Dawley rats were used. Trigeminal neuropathic pain was induced by infraorbital nerve constriction (IONC). Tranilast (50/75/100/200 mg/kg) or Carbamazepine (30 mg/kg) or saline were injected intraperitoneally (1ml) for evaluating the response of pain post-intervention. von Frey’s behavior test was done for measuring the mechanical sensitivity of the whisker pad area. The rotarod performance test was done for evaluation of motor coordination (n = 6 in each group). Trigeminal ganglia were excised and tested for BH4 RT2 Profiler PCR Array (n = 6).Results: von Frey test showed significant changes in the ipsilateral side of the nerve injury model (p < 0.05). Tranilast (75, 100 & 200 mg/kg) and Carbamazepine responded well with significant changes in pain tolerance (p < 0.05). The rotarod performance test showed, no significant changes in the Tranilast group whereas a reduced retention time on the rod for Carbamazepine treated group which signifies reduced motor coordination. The BH4 array analysis showed significant changes in Spr and Akr genes. These genes code for one of the key enzymes, sepiapterin reductase involved in the production of BH4.Conclusions: Current medications for neuropathic pain show relative efficacy and cause disturbing side effects. Tetrahydrobiopterin (BH4) mechanism would be a new avenue for neuropathic pain intervention. Our results are suggestive of the use of Tranilast in the treatment of trigeminal neuropathic pain.
027: Fermented dairy food intake reduces risk of tooth loss in a Japanese community
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Objectives: Consumption of a variety type of dairy foods has been reported to be associated with oral health status. However, the longitudinal association between fermented dairy food intake and oral health has not been well elucidated. This study aims to explore this association in the population-based study.

Methods: In 2012, 1,966 residents in Hisayama town, Japan, aged 40-79 years, received dental examinations. Among them, 1,469 participants were followed up in 2017 for incidence of tooth loss representing ultimate oral health, which was defined as two or more teeth lost over a 5-year period. A semi-quantitative food frequency questionnaire grouped into quartiles was used to evaluate the intake of fermented dairy foods, such as yogurt and lactic acid beverages. The salivary microbiota composition was evaluated.

Results: The cumulative incidence of tooth loss over 5 years was 17.7%. The Poisson regression model showed a negative association between higher fermented dairy foods intake and incidence of tooth loss (p for trend = 0.020) after adjusting for age, sex, toothbrushing frequency, regular dental visit, smoking, body mass index, diabetes, number of teeth at baseline, job, and number of decayed and filled teeth at baseline. The mediation analysis confirmed that periodontal condition partly mediated the effect of fermented dairy foods intake on tooth loss, while dental caries experience did not. Additionally, we revealed the association between high intake of fermented dairy foods with low percentage of the salivary microbiota patterns which was connected to poor oral health.

Conclusions: These findings suggest that a higher intake of fermented dairy foods is associated with a lower risk of tooth loss resulting from periodontal disease via a probable change in oral microbiota composition.

028: Two opposite effects of desmoglein 3 expression on the growth of oral squamous cell carcinoma between anchorage-dependent and -independent conditions
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Objectives: Desmoglein 3 (Dsg3) is one of the desmosomal cadherins that mediate epithelial intercellular adhesion. Dsg3 is overexpressed in oral squamous cell carcinoma (OSCC), and considered as a candidate biomarker for lymph node metastasis. Previously we have demonstrated that OSCC cells from metastatic lymph nodes showed higher Dsg3 expression, compared to those from the primary tumor of the same patients. Here, we investigated the effect of Dsg3 expression on the growth of OSCC cells between anchorage-dependent (AD) and -independent (AID) conditions.

Methods: Cell lines established from the primary tumor (P cells) and metastatic lymph nodes (LY cells) of three OSCC patients (No.7, 17, 58) and two commercial OSCC cell lines (HSC3, SAS) were cultured under AD and AID conditions. Cell proliferation ability was quantified using WST-1 cell proliferation assay. Cell migration ability was evaluated by wound healing assay. Dsg3 expression was examined by real-time qPCR.

Results: Under AD conditions, P cells (Dsg3-low) showed higher proliferation and migration rates than LY cells (Dsg3-high) in the same patients. In contrast, under AID conditions, the ability of cell proliferation and multicellular aggregation of Dsg3-high cells were higher than the Dsg3-low cells of the same patients. After transferred into AID conditions, all the cell lines except for Dsg3-negative 7P showed increased Dsg3 expression by up to 50-fold, compared with AD conditions. Dsg3 knockdown under AD conditions increased the cell proliferation ability of all the cell lines except for 7P cells.

Conclusions: Our findings suggested that Dsg3 may have inverse effect on the growth of OSCC cells under AID conditions. Inverse effect of Dsg3 expression on the AID cell growth could be associated with lymph node metastasis of OSCC.
029: **Associations between dental caries and Helicobacter pylori infection: A cross-sectional pilot study**

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Objectives: Helicobacter pylori (H. pylori) is widely known as a cause of gastric disorders. Presence of H. pylori in dental pulp has been reported. Dental caries may influence the presence or absence of H. pylori infection by serving as a source of H. pylori. In this cross-sectional pilot study, we examined whether H. pylori infection were associated with dental caries.

Methods: A total of 210 patients were recruited. Information about family history, medical history, and lifestyle were collected using a questionnaire. In addition, oral conditions including decayed, missing, and filled (DMF) teeth, and community periodontal index (CPI) score were measured. Urine antibody test was utilized to detect H. pylori infection.

Results: The prevalence of H. pylori infection was 14%. The number of decayed teeth were higher in patients with H. pylori infection than in those without H. pylori infection (p< 0.05). The logistic analysis showed that presence of H. pylori infection was positively associated with number of decayed teeth (OR, 3.717; 95% CI, 2.292 to 6.026) after adjusting for age, gender, family history of gastric cancer, heart disease, stress, CPI score, number of decayed teeth, and number of missing teeth. Furthermore, the prevalence rate of H. pylori infection increased according to number of decayed teeth (p< 0.05). This study was indicated that H. pylori infection rate in subjects with two or more decayed teeth was 55% (23/42).

Conclusions: The results indicate that H. pylori infection were associated with number of decayed teeth. We would like to express our gratitude to the Department of Dental Medicine, Kyoto Prefectural University of Medicine, Graduate School of Medical Science (Director: Professor Narisato Kanamura) and other related parties for their cooperation in this study.

030: **Application and Investigation of Total Adenylate(ATP, ADP, AMP) Hygiene Tests for Oral Health Monitoring**

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Objectives: Prevention of oral inflectional diseases requires good oral hygiene, and a test method that can objectively measure it is needed. Recently, a test method using adenosine triphosphate (ATP) as a marker has been developed. On the other hand, new instruments have been developed that can detect ATP, adenosine diphosphate (ADP), and adenosine monophosphate (AMP). This study compared ATP analysis methods with total adenosine nucleotide (ATP, ADP, and AMP) analyzers.

Methods: CariScreen (CS, Oral Biotechnologies) as an ATP detection instrument and LuciPac A3 Sanitation System (A3, Kikkoman Biochemifa) as a total adenosine nucleotide (ATP, ADP, AMP) analyzer were prepared. 1) Examination of detection sensitivity A standard sample (100 μL) was diluted ten times with the ENLITEN® ATP Assay System (Promega Corporation), and the fluorescence level (RLU) was measured. (2) Measurement of the bacterial suspensions S. mutans (ATCC 25175) was cultured anaerobically in BHI medium for 24 h, and the sample was prepared at a density of 1 × 10⁹ cells/mL. From 1 ml of the prepared sample, a bacteria-removed sample was prepared by 0.2 μm filtering, and a bacteria-killed sample was prepared by heating at 100°C for 10 min. Each instrument measured the fluorescence level (RLU) of 100 μL of each sample. The results were statistically analyzed using t-tests (*p<.05). Results: A3 showed a higher relative light unit (RLU) value than CS, indicating that A3 could detect the presence of bacteria with high sensitivity, whereas CS could not detect the RLU value in the supernatant solution. In addition, in the heat-sterilized sample, the RLU of CS was lower than that of viable bacteria, whereas A3 was higher.

Conclusions: These results indicate that A3 could detect the presence of bacteria, even in the absence of bacteria.
031: Chemical direct conversion of human fibroblasts into functional osteoblastic cells

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Objectives: Large jawbone defects after removal of jawbone cyst or tumor, and tooth loss induced by alveolar bone resorption associated with advanced periodontitis decrease patient’s quality of life (QOL). The osteoblasts play central roles in bone formation and remodeling by producing calcified bone matrix. A procedure to generate functional osteoblasts from human somatic cells will be effective regenerative therapy for bone disorders. Thus, we had established procedures to directly convert human fibroblast into functional osteoblasts by transducing some transcription factor genes. However, genetic manipulations cause safety concerns and are not desirable in most of clinical applications. From this perspective, we tried to establish a procedure that realizes chemical molecules-driven conversion of human fibroblasts into osteoblasts.Methods: Normal human fibroblasts were cultured with various types of small molecules in addition to conventional osteogenic medium. The resultant cells were tested in vitro for expressions of OB-specific genes, the production of calcified bone matrix, and global gene expression pattern. Moreover, to assess in vivo efficacy, the resultant cells were transplanted into immunodeficient mice.Results: Osteoblast-like phenotypes including high alkaline phosphatase (ALP) activity, bone matrix production and osteoblast-specific gene expression were induced in normal human fibroblasts cultured with Repsox. The chemical compound-mediated directly converted osteoblasts (cOBs) were similar to human primary osteoblasts in terms of expression profiles of osteoblast-related genes. The C0Bs abundantly produced bone matrix in vivo and facilitated bone regeneration after they were transplanted into immunodeficient mice at an artificial bone defect lesion of femur.Conclusions: Taken together, the present procedure may realize direct conversion of human fibroblasts into transgene-free osteoblasts that may applicable to a novel strategy of bone regeneration therapy for bone diseases including jawbone cyst or tumor, and severe periodontitis. Furthermore, this technique has advantages not only in cell therapy but also disease modeling, and drug discovery.

032: Applicability of neutral hypochlorous acid water for cleaning fixed orthodontic appliances

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Objectives: For patients taking orthodontic treatment with fixed appliances, especially pediatric patients, it is not easy to clean narrow areas between a bracket and a wire and tooth surface around the bracket. For constructing a simple and safe cleaning method, we focus on neutral hypochlorous acid water (NHW) due to its high microbicidal activity and no negative effect on human enamel. In this study, we examined the bactericidal effect of NHW to a bracket ligated with a wire to evaluate its applicability in dental practice.Methods: A Co-Cr alloy wire (2cm) was ligated with a metal or resin bracket using with a preformed ligature wire. A metal bracket bonded to an apatite pellets (10×10×2 mm) with an adhesive resin cement were also prepared. After contamination by 15-h immersion in bacteria (Streptococcus mutans) suspension, each specimen was cleaned by brushing with an interdental brush, water flow washing or water jet washing with an oral irrigator using NHW (NHW30 or NHW100: 30ppm or 100ppm). The treated specimen was ultrasonically cleaned in sterile phosphate-buffered saline for 5 min to collect bacteria, and each extract solution was added to an agar medium, and incubated for 48 h at 37°C. After incubation, the total number of surviving bacteria on the specimens was calculated from CFU on the agar plate. As comparisons, the specimens treated with tap water or commercial mouthwashes, Listerine or Concool were also tested.Results: The number of surviving bacteria after water jet washing was significantly less than those after other treatments (p<0.05). The combination of NHW30 or NHW100 and water jet washing had a significantly higher bacteria removal effect than other combinations and commercial mouthwashes (p<0.05).Conclusions: The water jet washing with NHW showed an excellent ability to remove Streptococcus mutans. This finding suggests that NHW might be applicable for cleaning fixed orthodontic appliances contaminated with oral bacteria.
Objectives: To evaluate the immediate and long-term effects of conventional and mini-screw assisted rapid palatal expansion appliances on root resorption in comparison to controls using Cone Beam Computed Tomography (CBCT). Methods: A total of 180 CBCTs for 60 patients were assessed at three time-points T1 (initial), T2 (post-expansion), and T3 (deband) for three groups: i) Controls, ii) Rapid Palatal Expansion Appliance (RPE), and iii) Mini-screw Assisted Rapid Palatal Expansion appliance (MARPE). Time-period T1 to T3: Controls: 2 years 7 months (n=19), RPE: 2 years 9 months (n=21), MARPE 2 years, 8 months (n=20). The length of mesiobuccal, distobuccal, and palatal root of maxillary first molar, buccal root of maxillary first premolar, and second premolar were measured. The inclination of maxillary first molar, inter-cuspal width (ICW), inter-root width (IRW), ratio of ICW/IRW, maxillary skeletal width (MSW) were measured in all three groups at the different time-points. Results: Immediately following expansion, both RPE and MARPE showed a significant increase in the molar inclination, ICW, ICW/IRW ratio, and MSW as compared to controls at T2. RPE showed a decreased palatal root length than MARPE when adjusted for age and treatment time at post-expansion by 1.38 mm (95% CI: 0.17 mm, 2.60 mm, p<.05). However, the long-term comparison did not show any significant difference for root resorption and expansion parameters between the three groups, except ICW/IRW ratio which was higher in MARPE compared to controls at T3. A significant negative association was observed between the length of mesiobuccal root of maxillary first molar and molar inclination (beta= -0.025, 95% CI: -0.050 to 0.0008, p<.05). The amount of expansion at cuspal level (ICW) and root level (IRW) did not show a significant association with root resorption. Conclusions: The long-term outcomes showed no difference in the amount of root resorption between the RPE, MARPE, and control groups. Molar inclination showed a significant negative association with the length of mesiobuccal root of maxillary first molar.

Objectives: The process of tooth development is involved in the epithelial-mesenchymal interaction. Problems that arise in this process affect the number, structure, morphology, and hardness of teeth, which in turn leads to developmental abnormalities and diseases such as anodontia, congenital deficiency, morphological abnormalities, and hypoplasia. Therefore, it is important to understand the molecular mechanisms of tooth development and its anomalies. Here, we aimed to analyze the expression and function of von Willebrand factor D and EGF domain (Vwde) in tooth development. Methods: In order to find the tooth specific gene, a bioinformatics method was performed with the expression tag database in NCBI. Then, to clarify the gene expression in mouse tissues by RT-PCR, the cDNAs of organs including molar, brain, lung, heart, liver, kidney, and bone were prepared from newborn ICR mice. Furthermore, the molar tooth germs were collected from embryonic day (E)11, E13, E14, E15, E16, E18, post-natal day (P)1, P3, and P7 mice. Then, gene expression was analyzed by RT-PCR and northern blotting. The frozen sections were prepared for each stage of tooth development, and Vwde expressing cells were analyzed by in situ hybridization. In addition, the Vwde expression vector was transfected into a mouse dental epithelial stem cell line (M3H1) for expression analysis by RT-PCR and for cell proliferation experiments by cell counting methods. Results: Vwde was found to be specifically expressed in teeth of newborn mice compared to other tissues. Northern blotting revealed that the total length of mRNA was about 7.0kbp. Furthermore, in situ hybridization showed that Vwde was expressed in the inner enamel epithelial cells. Overexpression of the Vwde expression vector significantly reduced the cell proliferation in M3H1 cells. Conclusions: We have demonstrated for the first time that Vwde is a new member of extracellular matrices and is preferentially expressed in teeth. Interestingly, Vwde was observed in inner enamel epithelial cells and inhibited the cell proliferation of M3H1 cells. These results suggest that Vwde functions as a regulator for cell proliferation in dental epithelium. In future, elucidation of the molecular mechanism of Vwde may contribute to understanding of tooth development and diseases.
036: **Inhibitory effects of β-Glycyrrhetinic acid on bacterial growth and biofilm formation by supragingival plaque commensals**

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Objectives: β-glycyrrhetinic acid (BGA), a major component of licorice extract, displays anti-inflammatory effects in humans. The purpose of this study was to investigate the inhibitory effects of BGA on bacterial growth and biofilm formation by supragingival plaque commensals. Methods: We first determined the minimum inhibitory concentration (MIC) of BGA against oral bacteria. Then, we determined the MIC against biofilm formation by glucan synthesizing *Streptococcus mutans* and *Streptococcus sobrinus*. Next, the effects of BGA on coaggregation of *Porphyromonas gingivalis* and *Streptococcus gordonii* and human supragingival plaque bacteria were evaluated. The human supragingival plaque samples were obtained from 12 healthy donors. All procedures were conducted in accordance with the guidelines of the ethics committee at the Faculty of Dentistry, Matsumoto Dental University (No. 0295). Results: BGA inhibited the growth of oral bacteria and biofilm formation. The same effect was observed for bacteria in human supragingival plaque commensals. While antimicrobial agents do not penetrate the biofilm, BGA around the MIC of supragingival bacteria significantly inhibited biofilm formation. In addition, inhibition of *P. gingivalis* and *S. gordonii* coaggregation may inhibit supragingival colony formation and subsequent coaggregation and plaque maturation. Therefore, BGA represents a candidate therapy for the prevention of periodontal disease by inhibiting the development and progression of gingivitis.
038: Dipotassium Glycyrrhizate inhibits LPS-induced alteration of cytoskeleton in gingival fibroblasts

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Objectives: Cytoskeleton is a key factor of maintenance in cell morphology and functions. It is known that Lipopolysaccharide (LPS) derived from periodontopathic bacteria disorganizes cytoskeleton in human gingival fibroblasts. In vitro study for cosmetic research, the relation between cytoskeleton and elasticity development of skin is well known. Skin elasticity is maintained by actin cytoskeleton generating cell tension. It is expected that similar mechanisms occur in gingival tissue. In this study, we focused on vascular endothelial cells which play an important role in the infiltration of inflammatory immune cells in response to periodontal infection. This study aims to investigate the regulatory mechanisms of insulin and IR on inflammation-induced cell adhesion molecules (CAMs) expressions in these cells, and to explore the possible mechanism underlying the deterioration of periodontitis by IR.

Methods: The regulatory effect of insulin on E. coli LPS- and TNFα- induced CAMs expression was confirmed by qPCR and Western blot (WB) using TKD2, a cell line derived from murine renal small vascular endothelium. The signaling pathways were investigated by using specific inhibitors for PI3K and MEK1 (wortmannin and PD98059). Cell adhesion assay was performed using THP-1, a human monocyte-derived cell line, and TKD2 cells.

Results: Insulin pretreatment significantly suppressed E. coli LPS- and TNFα-induced up-regulation of VCAM-1, but not other CAMs such as ICAM-1 and E-selectin mRNA and protein expressions. This regulatory effect of insulin was inhibited by wortmannin, but not PD98059. Consistent with the changes in VCAM-1 expression, the cell adhesion between TKD2 and THP-1 cells was regulated by insulin, and the effect was inhibited by wortmannin but not PD98059.

Conclusions: It was suggested that IR in vascular endothelial cells may contribute to the exacerbation of periodontitis by dysregulation of inflammation-induced VCAM-1 expression, thereby enhancing inflammatory cell infiltration.

037: Insulin resistance in vascular endothelial cells contributes to the exacerbation of periodontitis via dysregulation of inflammation-induced VCAM-1 expression

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Objectives: The prevalence and severity of periodontitis are known to be higher and severer in subjects with diabetes. Recent basic studies have shown that insulin resistance (IR) was also induced in the gingiva under diabetes. However, it remains unclear how IR in gingiva contributes to the exacerbation of periodontitis. In this study, we focus on vascular endothelial cells which play an important role in the infiltration of inflammatory immune cells in response to periodontal infection. This study aims to investigate the regulatory mechanisms of insulin and IR on inflammation-induced cell adhesion molecules (CAMs) expressions in these cells, and to explore the possible mechanism underlying the deterioration of periodontitis by IR.

Methods: The regulatory effect of insulin on E. coli LPS- and TNFα- induced CAMs expression was confirmed by qPCR and Western blot (WB) using TKD2, a cell line derived from murine renal small vascular endothelium. The signaling pathways were investigated by using specific inhibitors for PI3K and MEK1 (wortmannin and PD98059). Cell adhesion assay was performed using THP-1, a human monocyte-derived cell line, and TKD2 cells.

Results: Insulin pretreatment significantly suppressed E. coli LPS- and TNFα- induced up-regulation of VCAM-1, but not other CAMs such as ICAM-1 and E-selectin mRNA and protein expressions. This regulatory effect of insulin was inhibited by wortmannin, but not PD98059. Consistent with the changes in VCAM-1 expression, the cell adhesion between TKD2 and THP-1 cells was regulated by insulin, and the effect was inhibited by wortmannin but not PD98059.

Conclusions: It was suggested that IR in vascular endothelial cells may contribute to the exacerbation of periodontitis by dysregulation of inflammation-induced VCAM-1 expression, thereby enhancing inflammatory cell infiltration.
039: The loss of IκBζ accelerates dentin formation and matrix gene expression


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Objectives: Enforced enhancement of H3K4me3 and H3K27ac by inhibiting histone demethylases and deacetylases is positively linked with hard tissue formation by inducing matrix synthesis and osteo/odontogenic differentiation. However, the key endogenous epigenetic modifier of odontoblasts to regulate the expression of the genes coding for dentin extracellular matrix (ECM) proteins has not been identified yet. IκBζ was originally identified as the regulator for NF-kB and recently regarded as the epigenetic modifier by independently on NF-kB. Therefore, the aim of this study was to delineate the roles of IκBζ for dentin formation.

Methods: The roles for IκBζ in dentin formation were explored by analyzing dentin phenotypes in IκBζ knockout mice (IκBζ KO) and the roles of IκBζ for epigenetic status evoked by the knockdown of IκBζ were clarified in odontoblast-like cells. Results: IκBζ KO mice exhibited thicker dentin width and narrower pulp chamber with aged mice having more drastic phenotypes. At 6 months old, fluorescent labeling exhibited that dentin synthesis was significantly accelerated in the incisors of IκBζ KO mice. In molaros of IκBζ KO mice, aggressive reactionary dentin adjacent to pulp horn was exhibited. Mechanistically, Col1a2 and Col1a1 collagen genes were significantly increased in the odontoblasts rich fraction of IκBζ KO mice than that of wild type in vivo. Human odontoblasts-like cells transfected with siRNA for IκBζ expressed higher COL1A2 and COL1A1 than the cells transfected with control siRNA in vitro. Furthermore, FLAG tagged IκBζ overexpression in odontoblast like cells showed direct binding of IκBζ to COL1A2 promoter, suppressed COL1A2 expression, and activated the local chromatin status marked with H3K4me3. Whole-genomic identification of H3K4me3 enrichments revealed that ECM and ECM organization-related gene loci were selectively activated by the knockdown of IκBζ whereby resulted in the up-regulation of these gene expression. Conclusions: IκBζ is the key negative regulator of dentin formation in odontoblasts since the deletion of IκBζ expression enhanced dentin formation by inducing dentin ECM and ECM organization-related gene expression via altering the chromatin status marked by H3K4me3. Therefore, IκBζ is a potential target for improving the clinical outcomes of dentin regeneration therapies.

040: Analysis of periodontopathic bacteria related to early primary tooth loss

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Objectives: Early primary tooth loss is often associated with a genetic disease or chromosomal abnormality, though rarely occurs in individuals without a systemic disorder. Generally, periodontal disease with loss of teeth is considered to be associated with the presence of subgingival periodontopathic bacteria. This study, we examined subgingival periodontopathic bacteria in children with early primary teeth loss as well as those without systemic disease. Methods: Gingival crevicular fluid and subgingival plaque samples were collected from 12 children (5 patients, age 7.5 ± 1.1 years; 7 healthy subjects, 8.3 ± 2.1 years). Those were obtained with paper points from the deepest pocket in each patient and from the backmost molars in the healthy subjects without a systemic disorder. Bacterial DNA was extracted from the specimens, then PCR analyses were performed for detection of 10 major periodontal pathogens using specific primers. Results: The number of periodontopathogenic bacterial species in the patient group was significantly higher as compared to the healthy group (6.2 ± 1.6 vs. 1.8 ± 1.6, P<0.01). Positive rates were significantly higher in the patient group for Porphyromonas gingivalis (60.0% vs. 0.0%, P<0.05), Tannerella forsythia (80.0% vs. 0.0%, P<0.05), Prevotella nigrescence (80.0% vs. 0.0%, P<0.05), and Eikenella corrodens (100.0% vs. 28.5%, P<0.05). Thus, the number of red complex, orange complex, and green complex were significantly higher in the patients (1.4 ± 0.8 vs. 0.0 ± 0.0, P<0.01; 1.8 ± 0.4 vs. 0.5 ± 0.5, P<0.01; 3.0 ± 0.7 vs. 1.4 ± 1.1, P<0.05, respectively). Conclusions: The present results suggest different periodontopathic bacteria that may be associated with early primary tooth loss, which were detected with higher frequency in the oral cavity of patients with early primary tooth loss as compared with healthy subjects.
041: Hepatocyte growth factor shows antifibrotic effect on nifedipine-induced gingival overgrowth in vitro model

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Objectives: Nifedipine-induced gingival overgrowth is a gingival hyperplasia that occurs as a side effect in patients taking nifedipine. The aim of this study is to establish an in vitro model of nifedipine-induced gingival overgrowth and confirm the antifibrotic effect of hepatocyte growth factor (HGF).

Methods: Human gingival fibroblasts were cultured in DMEM/F-12 with 10% FBS and treated with 0.1, 1, 10 μg/ml nifedipine, 10 ng/ml IL-1β + 0.1, 1, 10 μg/ml nifedipine (N0.1, N1, N10, IL + N0.1, IL + N1, IL + N10, IL + N0.1, IL + N1, IL + N1, IL + N10). The number of cells and type I collagen, TGF-β1, CCN2/CTGF and α-SMA proteins were measured. After 10 and 50 ng/ml HGF were added simultaneously with the IL-1β and nifedipine, type I collagen, TGF-β1 and CCN2/CTGF were measured after 48 hours.

Results: For type I collagen, TGF-β1 and CCN2/CTGF, there was a significant increase at 48 hours after treatment in the N1 and IL + N0.1 groups. And, for type I collagen and CCN2/CTGF, there was a significant difference in IL + N0.1 + 50HGF group compared to IL + N0.1 group. Also, the production of type I collagen was significantly increased by the addition of anti-HGF antibody.

Conclusions: A nifedipine-induced gingival overgrowth model was established in vitro, and it was suggested that HGF had an anti-fibrotic effect in this model.

042: Personalized medicine of oral implant therapy for otorhinolaryngological high-risk patients.

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Objectives: Maxillary sinus floor elevation surgery (SES) is a reliable technique. However, this treatment is not riskless of postoperative complications such as maxillary rhinosinusitis and postoperative infection. We present different managements of periodontitis patients with otorhinolaryngological high-risk for SES.

Methods: Three periodontitis patients with otorhinolaryngological high-risk for SES were collected. Results: For a 48-year-old male with anatomical-structural impairments, such as septal deviation, concha bullosa, the presence of Haller cell and nasal mucosal swelling by the nasal allergy, while no sinusitis, preoperative topical steroid and leukotriene receptor antagonist in addition to peri-operative antibiotic prophylaxis has been performed and then his complication after SES was completely prevented. For a 69-year-old female with neutrophilic chronic rhinosinusitis and olfactory disorder, long-term low-dose macrolide therapy was performed with good outcome and then implant treatment was successfully performed after SES. In contrast, for a 46-year-old male with eosinophilic chronic rhinosinusitis, SES were not performed because this patient showed the recurrence of nasal polyps after endoscopic sinus surgery performed by a previous otolaryngologist. The implant overdentures were applied alternatively for his oral rehabilitation.

Conclusions: We need to choose the optimal treatment regimen according to the pathological conditions of paranasal sinus and the collaboration between dentists and otolaryngologists is crucial to get precise diagnosis and personalized medicine for oral implant therapy of otorhinolaryngological high-risk patients.
043: Abnormal expression of SGLT2 in the kidney of a \textit{P. gingivalis} LPS-induced diabetic nephropathy mouse model

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Objectives: The present study aims to examine the renal SGLT2 induction by the TLR2/4 ligand \textit{Porphyromonas (P.) gingivalis} lipopolysaccharide (Pg-LPS) in mouse diabetic nephropathy. Methods: Immunohistochemical study and tissue RT-PCR analyses were performed on mouse kidneys in streptozotocin (STZ)-induced diabetic ICR mice (STZ-ICR), in healthy ICR mice administered Pg-LPS (LPS-ICR), and in diabetic ICR mouse kidneys with Pg-LPS-induced nephropathy (LPS-STZ). Results: In the quantitative analysis of blood sugar levels, the mean time to reach 600 mg/dl was shorter in the LPS-STZ than in the STZ-ICR kidneys. The rise in blood glucose levels was significantly steeper in the LPS-STZ than in the STZ-ICR kidneys. According to these data the LPS-STZ model suggests a marked glucose intolerance. The expression of SGLT2 was significantly stronger in the whole of the renal parenchyma of the LPS-STZ than in the LPS-ICR or in the STZ-ICR. The expression of SGLT2 was observed both in the renal tubules and around the renal tubules, and in the glomeruli of the LPS-STZ kidneys. In the analysis by tissue real-time PCR and cell ELISA, the expression of the SGLT2 gene and protein was significantly stronger in the LPS-STZ than in the LPS-ICR or in the STZ-ICR kidneys. There were no differences in the renal SGLT2 production in the LPS-ICR and the STZ-ICR kidneys. Conclusions: Abnormally high renal expression of SGLT2 occurs in diabetic kidneys with \textit{P. gingivalis} LPS. Periodontitis may be an exacerbating factor in diabetic nephropathy as well as in diabetes.

044: Anti-inflammatory and Anti-oxidative Effects of Febuxostat on Periodontitis Rats Model

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Objectives: Periodontal disease is quite prevalent and affects about 20-50% of global population. Periodontitis is a chronic inflammatory disease of the supporting structures of the teeth. When periodontal pathogens enter into the blood stream, such lifestyle diseases develop. Febuxostat, a xanthine oxidase inhibitor, exerts anti-inflammatory and antioxidant effects. This study aims to evaluate the effects of febuxostat on periodontitis in a rat model. Methods: Wistar rats were used in this study being divided randomly into 3 groups: control, periodontitis, and febuxostat-treated periodontitis groups. Experimental periodontitis was induced by placing the ligature wire around the upper 2nd molar of the rat; the administration of febuxostat (5 mg/kg/day) was then initiated. After 4 weeks, alveolar bone loss was evaluated by micro-computed tomography and methylene blue staining. The expression of bone resorption inhibitor osteoprotegerin (OPG), in gingiva was detected by quantitative RT-PCR and immunological staining. Tartrate-resistant acid phosphatase (TRAP) staining was used to assess the number of osteoclasts in gingival tissue. Quantitative RT-PCR and immunological staining were used to examine the inflammatory cytokines expression. Oxidative stress in gingiva was also evaluated by the expression of 4-hydroxy-2-nonenal (4-HNE), and 8-hydroxy-2-deoxyguanosine (8-OHdG). In addition, blood pressure and glucose tolerance were examined to clarify the systemic effects of periodontitis. Results: In rats with periodontitis, alveolar bone loss was evaluated by micro-computed tomography and methylene blue staining. The expression of bone resorption inhibitor osteoprotegerin (OPG), in gingiva was detected by quantitative RT-PCR, in gingiva was detected by quantitative RT-PCR and immunological staining. Tartrate-resistant acid phosphatase (TRAP) staining was used to assess the number of osteoclasts in gingival tissue. Quantitative RT-PCR and immunological staining were used to examine the inflammatory cytokines expression. Oxidative stress in gingiva was also evaluated by the expression of 4-hydroxy-2-nonenal (4-HNE), and 8-hydroxy-2-deoxyguanosine (8-OHdG). In addition, blood pressure and glucose tolerance were examined to clarify the systemic effects of periodontitis. Results: In rats with periodontitis, alveolar bone resorption increased with reductions in OPG; the number of TRAP positive osteoclasts grew. The expression of TNF-\(\alpha\), IL-1\(\beta\), and 4-HNE, and 8-OHdG in the gingiva was up-regulated in the periodontitis group and treatment with febuxostat significantly reduced alveolar bone loss, proinflammatory cytokine levels, and oxidative stress. It also attenuated periodontitis-induced glucose intolerance and blood pressure elevation. Conclusions: Febuxostat prevented the progression of periodontitis and associated systemic effects by suppressing proinflammatory mediators and oxidative stress. Febuxostat is extremely promising for drug repurposing in dentistry.
045: Effects of smoking and smoking cessation on human gingival and lung fibroblasts
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Objectives: The adverse effects of smoking have been widely reported. However, the effects of smoking cessation have not been fully elucidated. The purpose of this study was to investigate the effects of smoking and the changes in the repair period due to smoking cessation in a time-dependent manner and to compare the results with those of human gingival fibroblasts (HGF) and human lung fibroblasts (HFL1). Methods: HGF cells were obtained from human normal gingiva. Human lung fibroblast cell line was purchased. When cells were cultured until confluence, medium was replaced 1μg/ml nicotine contained medium for 24 hours. Then cells were washed by medium and replaced non-nicotine fresh medium until 48hours. Cell proliferations were measured by MTT assay. The migration of cells in response to eliminated nicotine for 48hours was investigated in an in vitro wound healing model. The cell cultures were analysed by morphorogically examination under phase-contrast microscope and transmission electron microscope (TEM). Results: It was detected that ability of cell migration of smoking cessation group was significantly increased comparing with smoking group in both cells (p<0.001). Smoking group ware significantly decreased with control group and smoking cessation group (p<0.05). Following 24hours nicotine stimulation, there were observed a lot of vacuolization in cytoplasm by phase-contrast microscope and TEM. However it trended to disappear time-dependently from cytoplasm by removing nicotine. Conclusions: Our study demonstrated the cell damaging effects of smoking in HGF and HFL1. On the other hand, damage caused by smoking still remained in cell, we also indicated ability of the cell repairing effect of smoking cessation. This work was supported by Grant-in Aid for Scientific Research (C) Grant number 20K10280 from the Japan Society for the promotion of Science.

046: Profiles of Mastication Predominance and Masticatory Performance in Kennedy Class I Patients
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Objectives: Missing posterior teeth declines masticatory performance and may cause mastication predominance. Previous studies have shown that Kennedy class I (KCI) patients have mastication predominance, but it has not been well defined. The aim of this study was to investigate the effect of remaining posterior teeth and removable partial denture (RPD) treatment on mastication predominance and masticatory performance in KCI patients. Methods: The subjects in this study were the patients who visited the Department of Prosthodontics, Kyushu University Hospital. The following patients were included as the subjects: patients over 20 years old who had missing posterior teeth bilaterally (KCI) in one jaws and complete dental arch with natural teeth or fixed dental prostheses in opposite jaws; patients who were scheduled for bilateral RPD treatments. KCI patients who had difference in the number of posterior teeth between the right and left sides (D+) and KCI patients who had no difference (D-) were registered in this study. Healthy dentate (HD) subjects were also enrolled as control group. Mastication predominance was defined by mastication predominance index (MPI; range 0-100%) using electromyography. MPI and masticatory performance were compared statistically between pre and post RPD treatments. Results: Pre-MPI in KCI D+, but not in KCI D-, was significantly higher than in HD. RPD treatment significantly improved MPI and masticatory performance in KCI D+ and D- patients. However, there was a significant difference in mastication performance between both groups of KCI and HD, regardless of RPD treatment. Conclusions: Mastication predominance in KCI patients was thought to be influenced by the difference of the number of remaining posterior teeth between left and right side. RPD treatment could improve mastication predominance and masticatory performance in KCI patients, although the latter was not greater than HD group.
047: Bacterial flora evaluation using DNA array chip and real-time PCR

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Objectives: Periodontal disease is an inflammatory condition caused by a bacterial infection. Generally, periodontopathic bacteria and residental bacteria are well-balanced. However, some periodontal risks cause the disruption of a balance of periodontopathic bacteria and residental bacteria, which leads to pathogenesis or progress of the periodontal disease. Since more than one bacterial species are associated with periodontal disease, it is important to evaluate the bacterial flora of the patient, in order to manage the periodontal disease. By the bacterial test using a DNA array chip (Mitsubishi Chemical, Japan), periodontopathic bacteria could be detected at once. In this study, we detected periodontal disease bacteria by DNA chip and real-time PCR for the purpose of quantification.Methods: Three patterns, A to C, of the standard bacterial mixture were tested as samples (n = 3). DNA was extracted from the Standard bacterial genome mixture using QuickGene-810 (FUJIFILM, Japan). DNA extracted from the genome mixture was fluorescence-labeled by PCR method. Fluorescence-labeled DNA was hybridized with the DNA array chip, and fluorescence intensity was measured by Genopal Reader (Mitsubishi Chemical, Japan). 5 bacterial species (Pg, Td, Tf, Pi, Aa) were also evaluated by real-time PCR.Results: In all mixtures, differences in fluorescence intensity were observed depending on the presence or absence of the mixture, and the same trend as in the real-time PCR was confirmed. In the standard bacterial genome mixtures A to C, the fluorescence intensities of some bacteria disappeared on the DNA array chip, but this was because they were below the detection limit. In the case of Fusobacterium species, fluorescence was also detected in non-mixed species. It is possible that cross-hybridization occurred when bacteria were present in the sample, and fluorescence was detected even in non-mixed species.Conclusions: The real-time PCR method is a generally known quantitative test method for bacterial tests. It can be thought that quantitative detection is possible even in measurements using the DNA array chip method. The DNA array chip method can measure multiple periodontal disease bacteria at one time, and it is expected to know more detailed periodontal condition than the real-time PCR method for several bacterial species.

048: Effect of Glass Fiber Sleeve for Reinforcement of Flared Root

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Objectives: Endodontically treated tooth with flared root often occurs root fracture because of its weakened root canal wall. It has been reported that composite resin core tends to occur horizontal root fracture due to stress concentration in the cervical area. The aim of this study is to evaluate to reinforce the cervical area in flared root canal with glass fiber post and glass fiber sleeve in the case of composite resin core.Methods: Six extracted bovine mandibular incisors free of cracks and fractures were prepared. They were endodontically treated and uniformly shaped to simulate human maxillary central incisor with flared roots. Cores were made on plaster models by indirect method. One group was used composite resin core (DC core automix, Kuraray Noritake Dental) with glass fiber post (Clearfil Fiber Post II, Kuraray Noritake Dental) inserted glass fiber sleeve (i-TFC sleeve, Sun Medical) inside (PS), while another group was used only composite resin core (RC). Crowns made of lithium disilicate were used. Cores and crowns were cemented with dual-cure resin cement. Four strain gauges were attached to surfaces on each specimen: cervical area of root and crown, both in labial side and palatal side. The surface strain on each cervical area was measured in loading-test, and the data was analyzed statistically by t-test at a statistical significance of 0.05. Results: The surface strain of root in labial side was -561.18 (16.67) με in PS group, and -943.98 (150.53) με in RC group. That of root in palatal side was 450.85 (40.93) με in PS group, and 748.45 (113.09) με in RC group. Both in labial side and palatal side, the strains in PS group were significantly lower than RC group.Conclusions: This result suggests that it is effective to use glass fiber post and glass fiber sleeve with composite resin core for reducing strain concentration in cervical area.
049: The Influence of Zirconia Tube for Stress in Endodontically-Treated Molar


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Objectives: Endodontically-treated molars are usually restored with post and core systems for the final restoration. Some studies reported that tooth restored using composite resin core increased stress concentration at the cervical region of the tooth. This study aims to evaluate the surface strain at the cervical region of molar restored using composite resin core with a prefabricated zirconia tube. Methods: Reproduction models of human mandibular molars with prepared post spaces were used in this study. The roots that were duplicated with composite resin were used as experimental teeth. Three types of core build up systems were used: composite resin core (RC), composite resin core with fiber posts (FC) and composite resin with the zirconia tube (ZC). Each group consisted of 8 specimens. Crowns made of yttria partially stabilized zirconia were cemented with dual-cure resin cement. Four strain gages were attached to surfaces on each specimen: cervical region of root and crown, both in buccal side and lingual side. The surface strain at each cervical region was measured in static loading test, and the data was analyzed statistically. Results: In the case of static loading to the buccal cusp inner slope, ZC showed a significant lower strain than RC in the crown buccal and FC in the root. As a result of the experiment in the central fossa, in the crown ZC showed a significant lower strain than RC. In the root lingual FC showed a significant greater strain than RC and ZC. As a result of the experiment in the distal marginal ridge, ZC showed a significant lower strain than RC in the crown and FC in the root. Conclusions: This study indicated the zirconia tube reduce stress at the cervical region in the molar restored using composite resin core.

050: New mechanism of odontoblast differentiation

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Objectives: Tooth developments is initiated by oral epithelium and adjacent mesenchyme. The phase of development relies on several signals such as BMPs, Hedgehogs and WNTs for cross interaction of epithelium and mesenchyme. In this study, we aimed to uncover the signal of late differentiation stage of mesenchymal cells. Methods: The epithelium and mesenchyme derived from first molar of newborn C57BL/6J were isolated by enzymatic reaction. The isolated mesenchymal were cultured each day and checked Dspp and Dmp1 gene expression by RT-PCR. RNA-seq was performed with day 0 and day 2 cultured isolated mesenchymal cell to identify significantly downregulated gene after isolation. The genes identified by RNAseq were cloned into lentiviral vectors and produce each lentivirus. Dental mesenchymal cells (Dmc) and human dental pulp cells (HDP) were transfected with these lentiviral vectors and were cultured in odontoblastic differentiation medium with or without FGF4, FGF9, and CHIR99021 for 7 days. Odontoblastic gene expressions were analyzed by qRT-PCR. Results: Dspp and Dmp1 expression were decreased after isolation. Pearson analysis of RNA-seq data showed different expression patterns between day0 and day2 samples. Immediate early genes (Egr1, Egr2, Fos, Fosb and Jun), Notch-related genes (Hey1), and Hedgehog-related genes (Gli1) expression were remarkably decreased after isolation. In the isolated Dmc cultured in basic medium with FGF4, FGF9, and CHIR99021, the expressions of Egr1, Fosb, and Gli1 were increased, while Egr2, Gli1, and Hey1 expressions were increased in HDP. We found that forced expression of all genes described above were required to increase odontoblast markers in Dmc and HDP. Conclusions: Mesenchymal cells are regulated by multiple factors including Notch pathway, Immediate early genes, and Hedgehog pathway.
052: Induction of dental pulp cells into periodontal ligament-like cells using epigenetics
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Objectives: Since dental pulp stem cells are present, application to regenerative medicine is expected, but the ratio of dental pulp stem cells in the entire dental pulp (DP) is as low as a few percent. When applying DP to periodontal ligament regeneration, it is desirable to apply the entire DP including stem cells. In this study, we created an epithelial-mesenchymal cell population which express the periodontal ligament-related genes, consist of whole DP, epithelial cell rests of Malassez (ERM), and human umbilical vein endothelial cells (HUVEC).

Methods: ERM was dedifferentiated with 5-Azacytidine, a DNA methyltransferase inhibitor, and valproic acid, a histone deacetylase inhibitor, to produce progenitor stem-like cells (Pro-DSLCs). The DP / Pro-DSLCs / HUVEC cell populations were co-cultured in mesenchymal stem cell medium for 1 week to induce periodontal ligament-like cells. mRNA expression analysis was performed on periodontal ligament-related genes and mesenchymal stem cell positive/negative genes by the qPCR method. DNA methylation analysis was performed by the qMSP method.

Results: Expression of TLR2 and PCNA were observed in the moderate caries group in the pulp. M2 macrophages were predominant in the moderate caries induced inflamed pulp before capping. During wound healing process after capping, M2 macrophages and PCNA cells showed maximum population on day 3, and started to decrease after day 7 in caries group. Significant higher population of M2 macrophages and PCNA-positive cells were observed on day 3 compared with sound group (p<0.05, Student’s t-test), which indicated inflammatory changes in caries group might differ from sound tooth during wound healing process.

Conclusions: We successfully established caries-stimulated reversible pulpitis model for pulp capping. M2 macrophages could play pivotal role in wound healing process of reversible pulpitis.
053: Dentin-pulp complex tissue regeneration by three-dimensional cell sheet engineering

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Objectives: To regenerate dentin-pulp complex by scaffold-free technique, we designed a composite cell sheet which consists of dental pulp cells (DPCs) layered over odontogenic differentiated DPCs (OD cells). Methods: We compared the regenerative capacity of composite cell sheet to two single cell sheets containing either DPCs or OD cells. And we confirmed the composite cell sheet by histological, immunohistochemistry (IHC), and Scanning Electron Microscope (SEM). A carrier tooth was prepared by removing the enamel, dentin and pulp to mimic tooth decay. Following which carrier tooth was covered with one of the three cell sheet types and transplanted into subrenal capsule of ICR mice to check for ectopic regeneration. After 8 weeks, transplants were analyzed using H&E staining, Micro-computed tomography (CT) and IHC. Results: The results in H&E staining and IHC of composite cell sheet indicated that were successful in layering two type of cells combine in one cell sheet. And the findings in Micro-CT images showed hard tissue formation in the composite cell sheet group. Regenerated hard tissue formation was significant in composite cell sheet group compared to the single cell sheet groups as tested by One-way ANOVA, Tukey HSD test (p< 0.05, **p< 0.001). Furthermore, histological and IHC analysis demonstrated disciplined dentin-pulp-like tissue formation in the composite cell sheet group resembling natural tooth. Conclusions: In conclusion, our composite cell sheet enables to regenerate an organized three-dimensional structure comparable to that of natural teeth. The successful capping of the cavity by the regenerated dentin-pulp complex by our composite cell sheet can be a significant contribution to the future dental medicine. Our research aids as a guide for the future prospects in the field of regeneration with multiple complex tissue types.

054: Effect of psychological stress on oral microbiome: A metagenomic and bioinformatic analyses

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Objectives: Various oral diseases are associated with psychological stress. However, limited information about the effect of psychological stress on oral microbiomes using a rat model of chronic restraint stress. Methods: Sprague Dawley rats were divided into the control and stress groups. The stress group rats underwent restraint stress by enclosing them in a plastic tube for 4 hours daily for 1 month. The stress level was confirmed with various stress markers after 1 month. The rats were sacrificed to collect oral swabs. The bacterial DNA was extracted and used to perform metagenomic analyses using 16S rRNA sequencing. The sequencing data was analyzed using QIIME 2 software. A linear discriminant analysis (LDA) effect size (LEfSe) tool was used to analyze bacterial population discrepancy between two groups. Metagenomic analyses showed significantly reduced alpha diversity of oral microbiome in stress group as compared to control (Kruskal-Wallis test, p<0.05). The LEfSe analysis showed 10 significantly altered bacteria such as Facklamia, Corynebacterium, Prevotella, and others between two groups. PICRUSt2 tool and STAMP software were used to predict the alteration in microbial functional pathways. Results: The stress markers such as low body weight, reduced activity in the open arm of the elevated plus-maze, high adrenal gland weight, and high serum corticosterone level confirmed high-stress level in stress group rats as compared to control. Conclusions: The present study showed that psychological stress significantly affected the oral microbiome. These findings might be helpful in understanding the pathogenesis of stress-related oral diseases.
**055: Exosomal miR-1260b derived from TNF-α-treated hGMSCs inhibits periodontal bone loss by targeting ATF6β-mediated regulation of RANKL**


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Objectives: Human MSCs from gingiva (hGMSCs) are easier to isolate, and appear to secrete higher amounts of exosome than other MSCs. We recently demonstrated that exosome from TNF-α treated GMSCs increased the level of miR-1260b and inhibited periodontal bone loss (Nakao Y, et al., Acta Biomater, 2021). We further screened novel miR-1260b targeting genes by database analysis and found that it could be associated with ER stress by targeting ATF6β. It has reported that ER stress-related genes were up-regulated in periodontal tissue (Yamada H, et al. J Periodontal Res., 2002). In this study, we investigated the therapeutic effect of miR-1260b in periodontal disease by targeting ATF6β-mediated regulation of ER stress.

Methods: Human periodontal ligament cells (hPDLCs) were transfected with miR-1260b mimic to validate miR-1260b-mediated inhibition of ATF6β. The effect of miR-1260b on inflammatory bone loss was examined using mouse ligature-induced periodontitis model under an institutionally approved animal research protocol (Kyushu University, #A21-131-0). The expression levels of ATF6β in mice were compared by qRT-PCR and immunohistochemistry, and alveolar bone loss was analyzed by Micro CT. To validate the effect of miR-1260b on osteoclast differentiation, miR-1260b mimic transfected THP-1 cells were stimulated with M-CSF and RANKL for osteoclast differentiation and the number of TRAP-positive cells were counted.

Results: Transfection of miR-1260b mimic inhibited ATF6β expression and knock down of ATF6β decreased expression of RANKL mRNA in hPDLCs. Increased expression of ATF6β was observed in the ligated periodontal tissue and local injection of miR-1260b mimic decreased periodontal bone resorption in mice. The number of TRAP positive cells were decreased in miR-1260b mimic transfected THP-1-differentiated osteoclasts.

Conclusions: miR-1260b inhibited osteoclastogenesis and periodontal bone loss by targeting ATF6β-mediated regulation of RANKL.

**056: Exosomes derived from GMSCs stimulated with TNF-a and IFN-a promote M2 macrophage polarization via enhanced CD73 and CD5L expression**


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Objectives: MSC-derived exosome plays a central role in the cell-free therapeutics and recent studies indicated that exosomal contents can be customized under disease-associated microenvironments. We recently demonstrated that preconditioning of human gingival tissue-derived MSCs (hGMSCs) with TNF-α was ideal for the treatment of periodontitis by enhancing exosomal CD73 expression which induced anti-inflammatory M2 macrophage polarization (Nakao Y, et al., Acta Biomater, 2021). The aim of this study was to investigate the detailed molecular mechanisms.

Methods: hGMSCs were isolated from human gingival tissues under the approved of Institutional Review Board (IRB) protocol at Kyushu University Hospital (#2019-374). After pre-treatment of the cells with 100 ng/mL of TNF-α/INF-α or 50 ng/mL of TNF-α/IFN-α for 48h, exosome from hGMSCs were isolated from the serum-free conditioned media using the MagCapture™ Exosome Isolation Kit PS. Macrophages were obtained by culturing CD14+ monocytes with M-CSF in DMEM. The effect of GMSC-derived exosome on M2 macrophage polarization were examined by FACS.

Results: TNF-α combined with IFN-α stimulated hGMSC-derived exosome more effectively promoted the polarization of M2 macrophage than TNF-α or IFN-α alone. TNF-α/IFN-α stimulation induced nuclear accumulation of HIF-1α and enhanced mRNA expression of CD73 in hGMSCs. Transfection of HIF-1α expression plasmids in hGMSCs dose dependently increased exosomal CD73 expression, while knockdown of HIF-1α decreased exosomal CD73 expression. TNF-α/IFN-α-stimulation also upregulated the expression of CD5L, which was a known M2 driver.

Conclusions: Compared with single cytokine stimulation (TNF-α or IFN-α), hGMSC-derived exosome from combined stimulation (TNF-α/IFN-α) significantly promoted M2 macrophage polarization. TNF-α and IFN-α treatment resulted in enhanced expression of CD73 through induction of HIF-1α in hGMSCs. Increased expression of CD73 and CD5L in hGMSC-derived exosome was essential for M2 macrophage polarization.
057: Characterization of neural crest-derived cells for application in bone regenerative medicine

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Objectives: The neural crest is formed on both sides of the neural plate by invagination in the embryonic period, after which neural crest cells migrate throughout the embryo as neural crest-derived cells. It has been shown that some neural crest-derived cells remain in colonization destination tissue as somatic stem cells and have pluripotency. To obtain tissue stem cells from neural crest-derived cells as a resource for bone regeneration high efficiently, it is important to identify target cell properties and determine suitability for use as tissue stem cells. For this purpose, a new analysis method termed single cell RNA-sequence (scRNA-seq) was developed and found capable of detecting factors involved in transcriptional regulation of individual cells.

Methods: Mouse neural crest-derived cells were obtained from P0-Cre/GFP mice expressing GFP under control of the myelin protein 0 (P0) gene promoter, which is specifically expressed in neural crest cells. scRNA-seq analysis was performed using a chromium single-cell gene solution. Results: Nearly all cells collected from mouse inferior turbinate specimens after culturing for 14 days were GFP-positive neural crest-derived cells. Furthermore, treatment with mineralization medium containing BMP-2 increased the gene expression of ALP and osteocalcin, markers of osteoblast differentiation. Next, based on the gene expression of approximately 1000 cells, two-dimensional mapping using uniform manifold approximation and projection (UMAP) analysis, also cell clustering analysis were performed, with a total of 13 clusters observed. Those results indicated that expression of genes characteristic of tissue stem cells was particularly present in clusters specifically expressing Sox2. Furthermore, they revealed cell membrane surface proteins specifically expressed in clusters with specific Sox2 expression.

Conclusions: We will conduct additional studies to identify cell surface proteins in clusters specifically expressing Sox2, then purify and apply them for bone regenerative medicine.

058: The effect of JNK inhibition on the osteoblastic differentiation of periodontal ligament stem cells and the regeneration of periodontal tissue in vivo

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Objectives: Few clinical treatments to regenerate periodontal tissue lost due to severe endodontic and periodontal disease have yet been developed. Therefore, the development of new treatment methods for the regeneration of periodontal tissue is required. The purpose of this study was to evaluate whether a JNK inhibitor, SP600125 is effective for periodontal tissue regeneration.

Methods: An immortalized human periodontal ligament (PDL) cell line, 2-23 cells showed PDL stem cell-like properties, such as high growth capacity, multipotency, and the expression of stem cell-related surface markers (Hasegawa et al., J Cell Physiol. 2018). Alizarin red S staining, quantitative RT-PCR analysis, and western blotting analysis were performed to determine whether SP600125 affected osteoblastic differentiation of 2-23 cells and intracellular signaling. The effect of SP600125 on the regeneration of alveolar bone was assessed by using a rat periodontal defect model. Two weeks after application of SP600125, the recovery of periodontal defects was evaluated using micro-CT scans and histological analysis. Results: SP600125 promoted Alizarin red S-positive mineralized nodule formation and the expression of osteoblast-related genes such as osteonexin, bone sialoprotein, and osteopontin in 2-23 cells under osteogenic conditions. This inhibitor upregulated BMP2 expression and phosphorylation of Smad1/5/8 in 2-23 cells under the same conditions, while it did not affect phosphorylation of Erk1/2. SP600125 induced regeneration of alveolar bone compared with the control at two weeks after application into periodontal defects, as well as reformation of periodontal ligament tissues.

Conclusions: This study suggests that inhibition of JNK signaling promoted osteoblastic differentiation of HPDLSs, probably through increased expressions of BMP2 and the phosphorylation of Smad1/5/8, leading to the regeneration of periodontal tissues.
059: Relationship between age-related changes in MSC functions and periodontal tissues destruction in ligature induced periodontitis mouse model
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Objectives: Mesenchymal stem cells (MSCs) play important roles in the repair of damaged tissues and immunotolerance. On the other hand, aging is known to impair MSCs function. However, how functionally impaired MSCs affect the local inflammatory condition and tissue deterioration is still not known. The purpose of this study is to clarify the relationship between MSC’s function and local tissue destruction in disease conditions using a ligature-induced mouse periodontitis model.

Methods: Characterization of MSCs in vitro were performed by CFU-f, scratch, cell-surface antigen expression, senescence, cell differentiation, and immunomodulation assays. A periodontitis model was developed in 5- (young) and 50-week-old (aged) C57BL/6J mice, by ligating mandibular first molars with silk threads. Mice were sacrificed at 0, 3, and 10 days after ligation for further experiment. Alveolar bone destruction was evaluated by m-CT, HE, and IHC analysis.

Results: In vitro characterization data showed that MSCs markers (Sca-1, CD90, CD146), colony formation, migration, and osteogenic differentiation of aged MSCs was significantly declined than young MSCs. Moreover, senescence-associated β galactosidase activity was significantly higher in aged MSCs. Importantly, aged MSCs presented a decreased expression of FAS-L, which was associated with a lower immunomodulatory property of aged MSCs to induce T cell apoptosis compared with young MSCs. The m-CT and histological analysis showed a more severe bone loss associated with increased osteoclast activity in aged mice than young mice. In aged mice, the accumulation of inflammatory T and B cells was higher, whereas the percentage of PDGFRα+ MSCs, was significantly lower than in young mice.

Conclusions: This is the first study showing that aging-induced impairment of MSC function, including immunomodulatory response, is potentially correlated with progressive periodontal tissue deterioration. Finding out the mechanism of aging in MSCs improve the effectiveness of MSCs therapy and tissue destruction in the elderly patient.

060: MSC conditioned medium from older mice affects its osteogenic differentiation capacity
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Objectives: Mesenchymal stem cells (MSCs) have self-renewal and multipotent differentiating abilities, therefore many studies have been conducted in the field of tissue regeneration. It is known that MSC functions are affected by various factors such as host aging, but why this functional impairment occurs and the detailed mechanism is still not clear until now. To uncover this, we investigated osteoblastic differentiation capacity of conditioned medium of MSCs from different ages of mice.

Methods: The bone marrow derived MSCs from different aged (5-week-old and 50-week-old), female C57BL/6J mice were cultured as previously described (Aung et al., 2020). The conditioned medium was obtained by centrifuging culture supernatant from different aged mice MSCs (Amicon Ultra filter Unit). Passage 2 cells were used for differentiation assay with osteogenic medium containing with 0, 10, 30% of the conditioned medium for 14 days. The osteogenic gene expression levels were evaluated by real time RT-PCR for alkaline phosphatase (Alp) and osteocalcin (Ocn).

Results: Alp expression level was significantly decreased in 5-week MSCs group with 30% conditioned medium from 50-week-old mice MSCs. Ocn expression was also decreased in 5-week-old MSCs with 30% conditioned medium from 50-week mouse MSCs but not significantly. Meanwhile, expression levels of both Alp and Ocn were not changed in 50-week-old MSCs with any concentration of conditioned medium from 5-week-old mice MSCs.

Conclusions: These results indicated that MSCs from older hosts may produce soluble factors to inhibit osteogenic differentiation of MSCs, while it might be difficult to recover the osteogenic differentiation capacity of aged mice MSCs even if cultured with soluble factors from younger MSCs. Identifying these inhibition factors for osteogenic differentiation might lead to a new strategy to recover the function of aged MSCs by blocking their signals.
Objectives: Therapeutic efficacy of single systemic transplantation of stem cells from human exfoliated deciduous teeth (SHED) for systemic lupus erythematosus (SLE) is reported. However, the mechanisms underlying the SHED-based therapy in SLE remain unclear. In this study, we examined therapeutic function of SHED-releasing extracellular vesicles (SHED-EVs) on SLE-like disorders in MRL/lpr mice.

Methods: Secretion of EVs from SHED were suppressed by RAB27A knockdown via siRNA transfection (RAB27A knocked-down-SHED). Then, RAB27A knocked-down-SHED and non-treated SHED were systemically transplanted into MRL/lpr mice. SHED-EVs were isolated from the culture supernatant of SHED. Then SHED-EVs were systemically administered to MRL/lpr mice with or without RNase pre-treatment. Recipient bone marrow mesenchymal stem cells (BMMSCs) were isolated from SHED-EVs-administrated MRL/lpr mice. Then recipient BMMSCs were systemically transplanted into MRL/lpr mice.

Results: While non-treated SHED ameliorated SLE-like disorders in MRL/lpr mice, RAB27A knocked-down-SHED showed reduced therapeutic efficacy. Systemic administration of SHED-EVs ameliorated SLE-like disorders in MRL/lpr mice via improving activity of hematopoietic niche formation and immunoregulation of recipient BMMSCs by rescuing Tert associated telomerase activity. The secondary transplantation of recipient BMMSCs ameliorated SLE-like symptoms of MRL/lpr mice. RNase treatment depleted RNAs within SHED-EVs attenuated the therapeutic benefit in MRL/lpr mice.

Conclusions: These results indicated that RNAs within SHED-EVs ameliorated SLE-like disorders in MRL/lpr mice by improving telomerase activity-mediated recipient BMMSCs functions. The present study reveals the novel mechanism of SHED-based therapy.
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下記の団体・企業様より多大なご支援を賜りました。ここに厚く御礼申し上げます。

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The 69th Annual Meeting of
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第69回 国際歯科研究学会
日本部会総会・学術大会

Re-defining the Mission of Dental
Research towards Post-corona World

October 24 (Sun.) – October 25 (Mon.), 2021
Hybrid Meeting (Onsite at Kyushu University and Online)