東京医科歯科大学

第8回
グローバルCOE国際シンポジウム
Molecular Science in Oral-Systemic Medicine
~Winter Seminar~

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Tokyo Medical and Dental University
The 8th Global COE International Symposium

グローバルCOEプログラム
歯と骨の分子疾患科学の国際教育研究拠点
デント・メドミクスのインテリジェンスハブ

Molecular Science in Oral-Systemic Medicine ~Winter Seminar~

東京医科歯科大学

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February 3rd~4th, 2013
Tokyo Medical and
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Sixth Retreat Meeting

Molecular Science in Oral-Systemic Medicine
- Winter Seminar -

February 3rd~4th, 2013

2013.2.3 (Sun) Periodontal Medicine

9 : 00 − 9 : 10 President Address
Takashi Ohyama

Session 1 Chairpersons : Denis F. Kinane, Yuichi Izumi

9 : 10 − 10 : 40 **Steven Offenbacher**
An Update in Periodontal Medicine : Managing Oral Infections to Improve Overall Health

10 : 40 − 12 : 10 **Panos N. Papapanou**
Periodontal Infections and Cardiovascular Disease: Biological Plausibility and Epidemiologic Evidence

Session 2 Chairpersons : Steven Offenbacher, Yasushi Furuichi

13 : 00 − 14 : 30 **Denis F. Kinane**
The Role of Host Response Variations in Oral and Systemic Disease Interactions

14 : 30 − 15 : 10 **Fusanori Nishimura**
The Periodontal Host Response with Type 2 Diabetes

15 : 10 − 15 : 50 **Shogo Takashiba**
Periodontal Medicine
− Prediction of Systemic Diseases on Periodontal Infection −

15 : 50 − 16 : 20 Poster Session 3 (Sixth Retreat Meeting) Coffee Break

Session 3 **Chairpersons : Mark Bartold, Shinya Murakami**

16：20 － 17：00 **Yasushi Furuichi**
Association between Periodontal Disease and Adverse Pregnancy Outcome

17：00 － 17：40 **Koji Inagaki**
Interrelationships between Systemic Osteoporosis and Periodontal Disease : Association and Mechanisms

18：30 － Reception

2013.2.4（Mon） Advanced Therapy in Periodontic

Session 4 **Chairpersons : Panos N. Papapanou, Koji Inagaki**

10：00 － 11：30 **Mark Bartold**
Is There a Role for Stem Cells in Periodontal Regeneration?

11：30 － 12：10 **Shinya Murakami**
Periodontal Tissue Engineering
－ The Future Perspective of Cytokine Therapy and Cell Therapy －

12：10 － 12：50 **Yuichi Izumi**
Clinical Application of Er:YAG Laser in Periodontal and Peri-implant Therapy

12：50 － Closing Remark　Yuichi Izumi

Adjourn

C O N T E N T S

An Update in Periodontal Medicine: Managing Oral Infections to Improve Overall Health

Steven Offenbacher D.D.S., Ph.D., M. MSc.

Professor and Chair,
Department of Periodontology,
University of North Carolina at Chapel Hill

Periodontal Medicine was defined in 1996 as the effect of periodontal infections on systemic health. This discipline was initially established to study the observations that linked periodontal disease with an increased risk for heart attack, stroke and preterm delivery among pregnant women. Although this is an emerging field, current findings suggest that periodontitis is associated with mores severe and prevalent cardiovascular disease, kidney disease, chronic obstructive airway disease, diabetes and pregnancy complications. These associations appear to confer additional risk even after adjustments for relevant confounders like smoking, obesity, and other traditional risk factors. Current evidence suggest that the periodontal organisms gain access to the systemic circulation and that periodontal infections create an oral wound that serves as a portal for the systemic dissemination of oral pathogens. Once into the bloodstream these organisms elicit hepatic inflammation, vascular damage, and many appear capable of crossing the placental barrier in pregnant women. Thus, clinical periodontal disease represents an infected wound that can serve as a chronic portal for the systemic dissemination of oral pathogens that has the potential to mediate inflammatory damage to multiple organs systems. The evidence from humans and animal studies would suggest that once periodontal organisms enter into the circulatory system, they induce upstream and downstream mediators of the hepatic acute phase response resulting in increases in serum biomarkers such as sICAM (soluble intracellular adhesion molecule-1), IL-6 (interleukin 6), fibrinogen and CRP (C-Reactive Protein). Many of these inflammatory markers are predictive of cardiovascular, pregnancy and diabetes risk. It appears that, periodontal disease may, in part, explain the association between the observed increases in inflammatory biomarkers of the acute phase response, coagulation and vascular stress as associated with increased risk for certain systemic conditions.

During pregnancy, periodontal infection also appears to be a special threat to the placenta and fetus. Case-control and prospective cohort studies have suggested that there is a significant association between maternal periodontal disease and pregnancy complications that result in preterm delivery [gestational age (GA) <37 weeks] and low birth weight [LBW, birth weight <2500g]. Several studies suggest that periodontal disease independently enhances the risk of obstetric complications including preterm birth, growth restriction [birth weight less than 10th percentile of weight for gestational age, adjusting for baby gender and race], preeclampsia and very preterm birth [delivery less than 32 weeks gestation]. Periodontal disease represents a risk for these adverse pregnancy outcomes even after adjusting for a range of potential confounders including previous history of preterm birth, parity, maternal weight gain, smoking, and other infections. Data suggest that maternal periodontal infections may potentially represent a bona fide risk factor for preterm birth and growth restriction by serving as an infectious and inflammatory exposure to the placenta and fetus during pregnancy. This infectious and inflammatory stress which represents the toxicity of the oral biofilm appears to increase neonatal morbidity and may have life-long effects on the health of the offspring.

Estimates of the potential magnitude of the effect of periodontal disease on these conditions are significant, increasing the risk as much as traditional risk factors such as smoking. Furthermore, data from animal models of disease provide a compelling demonstration of biological feasibility. However, data supporting the reversibility of this association in humans is equivocal. Although some early treatment studies show promise, other studies do not show any systemic benefits from treatment. Clearly additional studies exploring the potential benefits of treating periodontal disease to reducing the risk for these systemic conditions are needed. However, since periodontal disease is both a preventable and treatable condition, it represents a potentially modifiable risk factor. Thus, if periodontal disease is proven to be causally related to these conditions, the findings could have a tremendous health care impact.

CURRICULUM VITAE

Education

1972 Boston University B.A. Chemistry
Boston, Massachusetts
1976 Virginia Commonwealth University D.D.S. Dentistry
Medical College of Virginia School of Dentistry
1977 Virginia Commonwealth University Ph.D. Biochemistry
Medical College of Virginia
Graduate School of Basic Sciences
1980 Harvard Medical School M.MSc. Oral Biology
1980 Harvard School of Dental Medicine Certificate Periodontology
Department of Periodontology and Oral Medicine
1980 Harvard Medical School M.MSc. Oral Biology

Position

1981-91	Assistant Professor of Biochemistry Graduate Division of Biological & Biomedical Sciences School of Medicine Dr. Keith Wilkinson, Chairman
1982-91	Guest Researcher, Anaerobic Microbiology Centers for Disease Control
1985-91	Guest Researcher, Yerkes Primate Center Dr. Harold McClure, Chief of Pathobiology & Immunobiology
1987-91	Associate Professor of Periodontology/Oral Biology with tenure School of Postgraduate Dentistry
1988-91	Associate Professor in the Winship Cancer Center
1991-94	Associate Professor of Periodontology Director, Clinical Research Unit
1994-03	Professor of Periodontology Director, Clinical Research Unit
2003-present	OraPharma Distinguished Professor of Periodontal Medicine
2010	Interim Chair, Department of Periodontology
2010-present	Chair, Department of Periodontology

Award and Honors

2006	Norton M. Ross Award for Excellence in Clinical Research
2006	AAP, Clinical Research Award
2007	Distinguished Scientist Honoree, New York University.
2008	AAP, Clinical Research Award
2008	AAP Educator Award for Outstanding Teaching and Mentoring in Periodontics
2008	Alumni Star Award, Virginia Commonwealth University
2009	AAP, Clinical Research Award
2010	Class of 58 Award, Clinical Relevance of Research

Publications

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3. Bobetsis YA, Barros SP, Lin DM, Arce RM, Offenbacher S. Altered gene expression in murine placentas in an infection-induced intrauterine growth restriction model; a microarray analysis. J Reprod Immunol. 2010 Jun;85(2):140-148.
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5. Barros SP, Wirojchanasak S, Barrow DA, Panagakos FS, Devizio W, Offenbacher S. Triclosan inhibition of acute and chronic inflammatory gene pathways. J Clin Periodontol. 2010 May:37(5):412-418.
6. Offenbacher S, Barros S, Mendoza L, Mauriello S, Preisser J, Moss K, de Jager M, Aspiras M. Changes in gingival crevicular fluid inflammatory mediator levels during the induction and resolution of experimental gingivitis in humans. J Clin Periodontol. 2010 Apr;37(4):324-333.
7. Fisher EL, Moss K, Offenbacher S, Beck JD, White Jr RP. Third molar and non-third molar caries experience in middle-aged Americans, a prevalence study. J Oral and Maxillofacial Surg. 2010 Mar;68(3):634-640.
8. Horton AL, Boggess KA, Moss KL, Jared HL, Beck J, Offenbacher S. Periodontal disease, oxidative stress, and risk for preeclampsia. J Periodontol. 2010 Feb;81(2):199-204.
9. Friedewald VE, Kornman KS, Offenbacher S, Beck J, Taylor GW, Borgnakke WS Letter to the Editor: Authors' response. J Periodontol. 2010 Feb;81(2):199-204.
10. Blakey GH, Gelesko S, Marciani RD, Haug RH, Offenbacher S, Phillips C, White Jr RP. Third molars and periodontal pathology in American adolescents and young adults: a prevalence study. J Oral Maxillofac Surg. 2010;68:325-329
11. Arce RM, Diaz PI, Barros SP, Galloway P, Bobetsis Y, Threadgill D, Offenbacher S. Characterization of the invasive and inflammatory traits of oral Campylobacter rectus in a murine model of fetoplacental growth restriction and in trophoblastic cultures. J Reproductive Immunology. J of Reproductive Immunology. 2010;84:145-153.
12. Zhang S, Barros SP, Niculescu MD, Moretti AJ, Offenbacher S. Alteration of PTGS2 promoter methylation in chronic periodontitis. J Dent Res. 2010 Feb;89(2):133-137.
13. Hickman MA, Boggess KA, Moss KL, Beck JD, Offenbacher S. Maternal periodontal disease is associated with oxidative stress during pregnancy. Am J Perinatol.

2011 Mar;28(3):247-252.
14. Preisser JS, Sen PK, Offenbacher S. Multiple hypothesis testing for experimental gingivitis based on Wilcoxon Signed Rank Statistics. American Statistical Association Statistics in Biopharmaceutical Research. 2011:3(2).
15. Xiong X, Buekens P, Goldenberg RL, Offenbacher S, Qian X. Optimal timing of periodontal disease treatment for prevention of adverse pregnancy outcomes: before or during pregnancy? Am J Obstet & Gynecol. 2011 Mar 16.
16. Bell KP, Phillips C, Paquette DW, Offenbacher S, Wilder RS. Incorporating oral-systemic evidence into patient care: practice behaviors and barriers of North Carolina dental hygienists. J Dent Hyg. 2011:85(2):88-113.
17. Barros SP, Arce RM, Galloway P, Lawter JR, Offenbacher S. Therapeutic effect of a topical CCR2 antagonist on induced alveolar bone loss in mice. J Periodontal Res. 2011;46:246-251.
18. Garaas R, Moss Kl, Fisher EL, Wilson G, Offenacher S, Beck JD, White RP Jr. Prevalence of visible third molars with caries experience or periodontal pathology in middle-aged and older Americans. J Oral Maxillofac Surg. 2011 Feb;69(2):463-470.
19. White RP Jr., Fisher EL, Phillips C, Tucker M, Moss KL, Offenbacher S. Visible third molars as risk indicator for increased periodontal probing depth. J Oral Maxillofac Surg. 2011 Jan;69(1):92-103
20. Perri R, Nares S, Zhang S, Barros SP, Offenbacher S. MicroRNA modulation in obesity and periodontitis. J Dent Res. 2012;91(1):33-38. PMID:22043006.
21. Fisher EL, Garaas R, Blakey GH, Offenbacher S, Shugars DA, Phillips C, White RP Jr. Changes over time n the prevalence of caries experience or periodontal pathology on third molars in young adults. J Oral Maxillofac Surg. 2012 May;70(5):1016-1022.
22. Broder MB, Schwartz S, Carlson J, Dibble CF, Kohitfarber H, Offenbacher S, Buse JB, Bencharit S. Exploring salivary proteomes in edentulous patients with type 2 diabetes. Mol Biosyst. 2012 Apr;8(4):1304-1310. PMID:22314925.
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25. Bell KP, Phillips C, Paquette DW, Offenbacher S, Wilder RS. Dental hygienists' knowledge and opinions of oral-systemic connections: implications for education. J Dent Educ. 2012 Jun;76(6):682-694. PMID: 22659696.
26. Matula K, Ramamurthy R, Bose C, Goldstein R, Couper D, Peralta-Carcelen M, Stewart D, Gustafson KE, Offenbacher S. Effect of antenatal treatment of maternal periodontitis on early childhood neurodevelopment. Am J Perinatol. 2012 Jul 6;29(10):815-822. PMID: 22773286.
27. Divaris K, Monda KL, North KE, Olshan AF, Lange EM, Moss K, Barros SP, Beck JD, Offenbacher S. Genome-wide association study of periodontal pathogen colonization. J Dent Res. 2012 Jul;91(7 Suppl):21S-28S. PMID: 22699663.
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29. Taxman DJ, Lei Y, Zhang S, Holley-Guthrie E, Offenbacher S, Ting JP. Asc-dependent RIP2 kinase regulates reduced PGE2 production in chronic periodontitis. J Dent Res. 2012 Sep;91(9):877-82. PMID:22928789.
30. Task Force for Third Molar Summary. Summary of the third molar clinical trials; report of the AAOMS task force for third molar summary. J Oral Maxillofac Surg. 2012 Sep;70(9):2238-2248. PMID: 2290711.
31. Arce RM, Caron KM, Barros SP, Offenbacher S. Toll-like receptor 4 mediates intrauterine growth restriction after systemic Campylobacter rectus infection in mice. Mol Oral Microbiol. 2012 Oct;27(5):373-381. PMID:22958386.
32. Bencharit S, Altarawneh SK, Baxter SS, Carlson J, Ross GF, Border MB, Mack CR, Byrd WC, Dibble CF, Barros S, Loewy Z, Offenbacher S. Elucidating role of salivary proteins in denture stomatitis using a proteomic approach. Mol Biosyst. 2012 Oct 30;8(12):3216-3223. PMID: 23041753.
33. Wehmeyer MMH, Kshirsagar AV, Barros SP, Beck JD, Moss K, Preisser J, Offenbacher S. A randomized controlled trial of intensive periodontal therapy on metabolic and inflammatory markers in patients with ESRD: results of an exploratory study.
34. Al-Tarawneh SK, Bencharit S, Mendoza L, Curran AE, Barrow DA, Barros SP, Preisser J, Offenbacher S, Loewy Z, Gendreau L. Clinical and histological findings of denture stomatitis as related to intraoral colonization patterns of C.albicans, salivary flow and dry mouth. J Prosthodont. 2012 Oct 25. [Epub ahead of print]. PMID: 23107189.
35. Zhang S, Barros SP, Moretti AJ, Yu N, Zhou J, Preisser JS, Offenbacher S. Epigenetic regulation of TNFA expression in periodontal disease. J Periodontol. 2012 Nov 25. [Epub ahead of print].
36. Barros SP, Al-Tarawneh SK, Bencharit S, Loewy Z, Gendreau L, Offenbacher S. Salivary cytokine and levels in denture stomatitis: an exploratory case-control study. Open J Stomatology, 2012 Dec.
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MEMO

Periodontal Infections and Cardiovascular Disease : Biological Plausibility and Epidemiologic Evidence

Panos N. Papapanou, D.D.S., Ph.D.

Professer and Chair,
Section of Oral and Diagnostic Sciences,
Columbia University College of Dental Medicine

One of the key features of periodontal diseases is the intimate contact between the biofilm of the microbial plaque and the ulcerated epithelium of the periodontal pocket. This allows the subgingival bacteria, some of which have tissue-invading properties, to gain direct access to the underlying connective tissue and gingival microvasculature through the disrupted epithelial barrier. As a result, bacteremias are fairly common in patients with periodontitis and are triggered by mechanical stimulation of the gingival tissues. In addition, inflammatory mediators that are abundantly produced locally in the inflamed gingiva through cellular innate and adaptive immunity pathways can enter the blood stream, reach distant organs and also 'excite' the vascular endothelium. These phenomena have been shown to be important in the context of atherogenesis. The presentation will give an overview of the potential biologically plausible mechanisms through which periodontal infection/inflammation may lead to extra-oral pathology, and summarize the available epidemiologic evidence from cross-sectional, cohort and intervention studies that have investigated the association of periodontitis and cardiovascular/cerebrovascular disease. The public health implications of these findings will be discussed.

CURRICULUM VITAE

Education

1979-1984	School of Dentistry, University of Athens, Greece D.D.S, awarded July 1984
1985-1989	Ph.D Program, Faculty of Odontology, Göteborg University, Sweden Ph.D. in Periodontics, awarded December 1989 Thesis title: Patterns of alveolar bone loss in the assessment of periodontal treatment priorities. Sponsor: Prof. Jan L. Wennström Swedish Dental Journal, Supplement 66, 1989
2001	Columbia University School of Dental and Oral Surgery, New York, NY D.D.S., awarded May 2001

Position

1992-1995	Associate Professor Department of Periodontology, Göteborg University
1995-1998	Associate Professor Department of Oral Microbiology, Göteborg University
1997-1998	Assistant Dean, Research Graduate Curriculum Faculty of Odontology, Göteborg University
1998-2003	Associate Professor of Dentistry Columbia University, School of Dental and Oral Surgery
1999-present	Director, Division of Periodontics, Columbia University College of Dental Medicine
2003-present	Professor of Dental Medicine Columbia University College of Dental Medicine
2003-present	Chairman, Section of Oral and Diagnostic Sciences, Columbia University College of Dental Medicine
2005	University Tenure

Award and Honors

1996	The 1st Anthony A. Rizzo Young Investigator Award; Periodontal Research Group; International Association for Dental Research
1998	The Walther-Engel Prize; Academy of Graduate Dental Education, Karlsruhe, Germany
2007	Clinical Research Award; American Academy of Periodontology
2007	Educator Award for Outstanding Teaching and Mentoring in Periodontics; American Academy of Periodontology
2009	Sunstar World Periodontal Research Award Sunstar Foundation for Oral Health Promotion
2012	Special Citation, American Academy of Periodontology

Publications

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5. Noble, J.M., Borrell, L.N., Papapanou, P.N., Elkind, M., Scarmeas, N., Wright, C. (2009) Periodontitis is associated with cognitive impairment among older adults: analysis of NHANES III Journal of Neurological and Neurosurgical Psychiatry 80: 1206-1211.
6. Papapanou, P.N. , Behle, J.H., Kebschull, M., Celenti, R., Wolf, D.L., Handfield, M., Pavlidis, P., Demmer, R., (2009) Subgingival bacterial colonization profiles correlate with gingival tissue gene expression. BMC Microbiology Oct 18, 9(1): 221.
7. Michalowicz, B.S., Novak, M.J., Hodges, J.S., DiAngelis, A.J., Buchanan, W., Papapanou, P.N., Mitchell, D.A., Ferguson, J.E., Lupo, V.R., Bofill, J., Matseoane, S., Steffen, M., Ebersole, J.F. (2009) Serum inflammatory mediators in pregnancy: Changes following periodontal treatment and association with pregnancy outcomes. Journal of Periodontology 80: 1731-1741.
8. Demmer, R.T., Papapanou, P.N., Jacobs, D.R. Jr., Desvarieux, M. (2009) Evaluating clinical periodontal measures as surrogates for bacterial exposure: The Oral Infections and Vascular Disease Epidemiology Study (INVEST). BMC Medical Research Methodology, Jan 7;10:2.
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10. Demmer, R.T., Papapanou, P.N. (2010) Epidemiologic patterns of chronic and aggressive periodontitis. Periodontology 2000 53: 28-44.
11. Desvarieux, M., Demmer, R.T., Jacobs, D.R., Rundek, T.,

Boden-Albala, B., Sacco, R.L., Papapanou, P.N. (2010) Periodontal microbiota and hypertension. The Oral Infections and Vascular Disease Epidemiology Study (INVEST). Journal of Hypertension 28: 1413-1421.

12. Vlachojannis, C., Dye, B.A., Herrera-Abreu, M., Pikdöken, L., Lerche-Sehm, J., Pretzl, B., Celenti, R., Papapanou, P.N. (2010) Determinants of serum IgG responses to periodontal bacteria in a nationally representative sample. Journal of Clinical Periodontology 37: 685-696.
13. Kebschull, M., Demmer, R.T., Papapanou, P.N. (2010) "Gum bug leave my heart alone" -Epidemiologic and mechanistic evidence linking periodontal infections and atherosclerosis. Journal of Dental Research 89: 879-902.
14. Kebschull, M., Papapanou, P.N. (2010) The use of gene arrays in deciphering the pathobiology of periodontal diseases. Methods in Molecular Biology In: Molecular techniques and applications in Oral Biology, 666: 385-393.
15. Demmer R.T., Pavlidis, P., Papapanou. P.N. (2010) Bioinformatics techniques in microarray research: Applied microarray data analysis using R and SAS software. Methods in Molecular Biology In: Molecular techniques and applications in Oral Biology, 666: 395-417.
16. Pollreisz, A., Hudson, B.I., Chang, J.S., Qu, W., Cheng, B., Papapanou, P.N., Schmidt, A.M., Lalla E. (2010) Receptor for advanced glycation end products mediates pro-atherogenic responses to periodontal infection in vascular endothelial cells. Atherosclerosis 212: 451-456.
17. Albert, D.A., Begg, M.D., Andrews, H.F., Williams, S.Z., Ward, A., Conicella, M.L., Rauh, V., Thomson, J.L., Papapanou, P.N. (2011) An examination of periodontal treatment, dental care, and pregnancy outcomes in an insured population in the United States. American Journal of Public Health 101: 151-156.
18. Kebschull, M., Papapanou, P.N. (2011) Periodontal microbial complexes associated with specific cell and tissue responses. Journal of Clinical Periodontology 38: supplement 11: 17-27.
19. Michalowicz, B., Hodges, J., Lussky, R., Bada, H., Rawson, T., Buttross, L., Chiriboga, C., DiAngelis, A., Novak, M., Buchanan, W., Mitchell, D., Papapanou, P.N. (2011) The influence of maternal periodontitis on infant neurodevelopment. Pediatrics127: e1212-1220.
20. Jönsson, D., Ramberg, P., Demmer, R.T., Kebschull, M., Dahlén, G., Papapanou, P.N. (2011) Gingival tissue transcriptomes in experimental gingivitis. Journal of Clinical Periodontology 38: 599-611.
21. Lalla, E. & Papapanou, P.N. (2011) Diabetes mellitus and periodontitis: a tale of two common interrelated diseases. Nature Reviews Endocrinology 7: 738-748.
22. Messier, M.D., Emde, K., Stern, L., Radhakrishnan, J., Vernocchi, L., Cheng, B., Angelopoulos. C. Papapanou, P.N. (2012) Radiographic periodontal bone loss in chronic kidney disease. Journal of Periodontology 83: 602-611.
23. Albert, D.A., Ward, A., Allweiss, P., Graves, D.T., Knowler, W.C., Kunzel, C., Leibel, R.L., Novak, K.F., Oates, T.W., Papapanou. P,N., Schmidt, A,M,, Taylor, G.W., Lamster, I.B., Lalla. E. (2012) Diabetes and oral disease: implications for health professionals Annals of the New York Academy of Sciences 1255: 1-15.
24. Lockhart, P.B , Bolger, A.F., Papapanou, P.N., Osinbowale, O., Trevisan, M., Levison, M.E., Taubert, K.A., Newburger, J.W., Gornik, H.L., Gewitz, M.H., Wilson, W.R., Smith, S.C. Jr., Baddour, L.M. (2012) Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association?: A Scientific Statement From the American Heart Association. Circulation 125: 2520-2544.
25. Papapanou, P.N. (2012) The prevalence of periodontitis in the US: Forget what you wre told. Journal of Dental Research 91: 907-908.
26. Stoecklin-Wasmer, C., Guarnieri, P., Celenti, R., Demmer, R.T., Kebschull, M., Papapanou, P.N. (2012) MicroRNAs and their target genes in gingival tissues. Journal of Dental Research 91: 934-940.
27. Papapanou, P.N., Trevisan, M. (2012) Periodontitis and atherosclerotic vascular disease: What we know and why it is important. Journal of the American Dental Association 143: 826-828.
28. Demmer, R.T, Squillaro, A., Papapanou, P.N, Rosenbaum, M., Friedewald, W.T., Jacobs, D.R.Jr., Desvarieux, M. (2012) Periodontal infection, systemic inflammation and insulin resistance: Results from the Continuous National Health and Nutrition Examination Survey (NHANES) 1999-2004. Diabetes Care 35: 2235-2242.
29. Papapanou, P.N. (2012) The prevalence of periodontitis in the US: forget what you were told. Journal of Dental Research 91: 907-908.
30. A comparison of periodontal status in two regional, population-based studies of SHIP and INVEST (2012) Holfreter, B., Demmer, R.T., Bernhardt, O., Papapanou, P.N., Schwahn, C., Kocher, T., Desvarieux, M. Journal of Clinical Periodontology 39: 1115-1124.
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32. Krämer, B., Kebschull, M., Nowak, M., Demmer, R.T., Haupt, M., Körner, C., Perner, S., Jepsen, S., Nattermann, J., Papapanou, P.N. (2013) Role of the NK cell-activating receptor CRACC in periodontitis Infection and Immunity 81: in press.
33. Bostanci, N., Ramberg, P., Wahlander, Å., Grossman, J., Jönsson, D., Barnes, V., & Papapanou, P. N. (2013) Label-free quantitative proteomics reveals differentially regulated proteins in experimental gingivitis. Journal of Proteome Research 12: in press.

MEMO

The Role of Host Response Variations in Oral and Systemic Disease Interactions

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Professor of Pathology and Periodontology
University of Pennsylvania, School of Dental Medicine

Variations in host response amongst humans are critical in determining who gets disease and who remains healthy given the same environmental challenges. Clearly initiating and environmental challenges are necessary in any disease, and in periodontal disease the subgingival biofilm and challenges such as smoking can fulfill these roles. This lecture will explore the relationship between oral disease, specifically periodontal disease, and other chronic inflammatory diseases such as diabetes, heart disease and pre-term pregnancies. The central role of the chronic inflammatory burden as a linking feature between these diseases and the specific potential effect of the periodontal biofilm as the major etiological agent will be addressed. Mechanistic links, particularly for cardiovascular disease, and the concept of shared risk factors will be covered also. The gatekeeper role of our surface epithelial layer and its variations will be explored in both its molecular variations and functions. Stimulation of TLRs by periodontal bacteria typically produces either a hyper-inflammatory response or an anti-microbial peptide response. These responses are understood to be regulated by epigenetic modifications. Likewise the changes in cellular receptor expression are mediated by micro RNAs which may also have a role in apoptotic responses. Features such as the lipid raft cellular receptors, in particular the TLR family as well as GPCRs will be reviewed as will the potential for signaling through these receptors in producing cytokine, and other cellular inflammatory and anti-inflammatory responses. The importance of genetics, specifically by SNP carriage, and the regulation of inflammation by both micro RNA affects and by chromatin remodeling and other epigenetic changes will be mentioned. The central role of chronic inflammation and how it contributes and is worsened in a variety of states will be considered. The audience should achieve an understanding and a realistic perspective of the interactions of these chronic diseases and knowledge on their prevention.

CURRICULUM VITAE

Education

1980 BDS University of Edinburgh
1983 PhDDepartment of Microbiology, University of Edinburgh, Medical School
1986 FDS RCS Royal College of Surgeons Edinburgh
1993 FDS RCPS Royal College of Physicians and Surgeons Glasgow

Position

1980 - 1983	Research Fellow, Microbiology Department, Edinburgh University Medical School
1983 - 1983	House Office in Oral Medicine/Periodontology, Edinburgh Dental Hospital and School
1983 - 1987	Lecturer in Periodontology, Dundee Dental Hospital and School
1988 - 1994	Senior Lecturer, Honorary Consultant and Coordinator of the Periodontal Unit, University of Glasgow Dental Hospital and School.
1994	Additional - Professor in Periodontology and Oral Immunology
1995	Additional – Director, Oral Immunology Research Group (top ranked, 2001 RAE)
2000	Additional - Associate Dean for Research and Enterprise
2002 - 2009	Associate Dean Research, Endowed Professor, Dept. Periodontology, Professor, Dept. Microbiology & Immunology. University of Louisville Dental School, Kentucky.
Since 2009	Morton Amsterdam Dean, Professor of Pathology and Periodontology, University of Pennsylvania School of Dental Medicine, Philadelphia, Pennsylvania, USA

Award and Honors

1. EuroPerio I Research Award: Adonogianaki, Wennstrom, Kinane. 1994
2. British Society of Periodontology, Research prize: Apatzidou, Kinane. 2001
3. 'B' merit award holder (NHS). 2000
4. Delta Endowed Chair, University of Louisville. 2002
5. Honorary Member of the Swiss Society of Periodontology. 2001
6. KY HEROS Award to enhance scientific appreciation in the community. 2004
7. Chair- Elect of the Gordon Conference on Periodontology 2003-2008.
8. Councillor for the Periodontal Research Group of the Int. Assoc. Dental Research.
9. Basic Science Award of the International Association for Dental Research 2012.

Publications

1. IL-6, tPA, PAI-2, albumin levels following initial periodontal treatment in chronic periodontitis patients with or without type 2 diabetes. Inflamm Res. 2011 Feb;60(2):143-51. Epub 2010 Sep 17. PubMed PMID: 20845058. Kardeşler L, Buduneli N, Çetinkalp S, Lappin D, Kinane DF. Gingival crevicular fluid
2. Ozçaka O, Başoğlu OK, Buduneli N, Taşbakan MS, Bacakoğlu F, Kinane DF. Chlorhexidine decreases the risk of ventilator-associated pneumonia in intensive care unit patients: a randomized clinical trial. J Periodontal Res. 2012 Feb 29. doi: 10.1111/j.1600-0765.2012.01470.x
3. Kinane JA, Benakanakere MR, Zhao J, Hosur KB, Kinane DF. Porphyromonas gingivalis influences actin degradation within epithelial cells during invasion and apoptosis. Cell Microbiol. 2012

MEMO

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The Periodontal Host Response with Type 2 Diabetes

Fusanori Nishimura, D.D.S., Ph.D.

Professer and Chair,
Department of Dental Science for Health Promotion,
Hiroshima University Institute of Biomedical and Health Sciences

In the past decade, periodontal disease has been recognized as not merely a local infectious disease, but as chronic, subclinical, inflammatory disease for the host. The subjects with type 2 diabetes appear to respond to bacterial challenge in an exaggerated manner as compared with the subjects without diabetes through several possible mechanisms, and develop severer forms of inflammatory periodontal disease. Severe periodontal disease in such subjects, in turn, acts to reduce insulin sensitivity known as insulin resistance, thereby contributing to the induction of hyperglycemia as well as hyperinsulinemia, important risk factors for vascular complications. Additionally, recent studies suggested that such subclinical inflammatory state also promotes renal dysfunction, all of which are important risk factors for atherosclerosis. Finally, all such conditions act to increase the risk for coronary heart diseases, one of the leading causes of mortality and morbidity in subjects with diabetes. Thus, it is very important to elucidate molecular mechanisms as to why local periodontal inflammation is amplified to the level of influencing our overall systemic health.

Recently, macrophages have been suggested to infiltrate into adipose tissues, and to interact with adipocytes, thereby exacerbating adipose tissue inflammation. Furthermore, both cell types appear to express toll-like receptor-4 (TLR4), and free fatty acids have been found to act as endogenous ligand for TLR4. Based on these findings, we hypothesized that, in cases of infectious diseases such as severe periodontal disease and gut infection, classical exogenous ligand for TLR4 may further exacerbate inflammatory responses in adipose tissue, thereby contributing to the induction of many unwanted side effects such as insulin resistance. To prove this, we established co-culture system between adipocytes and macrophages and stimulated these cells with bacterial lipopolysaccharide (LPS). We found that stimulation of the cells with LPS markedly up-regulated inflammatory gene expression in adipocytes as well as protein productions from co-cultures. Some of these effects were confirmed in vivo model by using both genetically induced and environmentally induced obese model mice as well. Hence, our results suggest that, although the prevalence of extremely obese subjects as seen in western societies is very low in eastern Asia including Japan, once they develop severe periodontal diseases, the disease may up-regulate adipose tissue inflammation, especially in subjects with newly diagnosed type 2 diabetes who are slightly more obese than the subjects without diabetes. Current understanding on these mechanisms will be discussed in the context of developing new "order-made" diagnostic strategies to avoid such unwanted side effects.

CURRICULUM VITAE

Education

1985 DDS, Kyushu University Faculty of Dentistry

Position

1988 Assistant, Okayama University Dental School
1990 Post-Doctoral Research Fello, Columbia University School of Dental and Oral Surgery
1993 Associate Research Scientist, Columbia University School of Dental and Oral Surgery
1995 Assistant, Okayama Univesity Dental School
1997 Assistant Professor Okayama University Hospital
2003 Assocate Professor, Okayama University Graduate School of Medicine and Dentistry
2006 Professor, Hiroshima University Graduate School of Biomedical Sciences

Award and Honors

1999 Young Investigator Award, Japanese Society Of Conservative Dentistry
1999 The First Award In Basic Research Category Of 7th Meeting Of The International Academy Of Periodontology
2005 Lion Award, Japanese Society Of Periodontology

Publications

1. Iwata H, Soga Y, Meguro M, Yoshizawa S, Okada Y, Iwamoto Y, Yamashita A, Takashiba S, Nishimura F. High glucose up-regulates lipopolysaccharide-stimulated inflammatory cytokine production via c-jun N-terminal kinase in monocytic cell line THP-1. J Endotoxin Res, 13:227-234, 2007.
2. Yamashita A, Soga Y, Iwamoto Y, Yoshizawa S, Iwata H, Kokeguchi S, Takashiba S, Nishimura F. Macrophage-adipocyte interaction: Marked IL-6 production by co-cultures stimulated with LPS. Obesity, 15:2549-2552, 2007.
3. Yamashita A, Soga Y, Iwamoto Y, Asano T, Li Y, Abiko Y, Nishimura F. DNA microarray analyses of genes expressed differentially in 3T3-L1 adipocytes co-cultured with murine macrophage cell line RAW 264.7 in the presence of the toll-like receptor 4 ligand bacterial endotoxin. Int J Obese, 32: 1725-1729, 2008.
4. Nakarai H, Yamashita A, Nagayasu S, Iwashita M, Kumamoto S, Ohyama H, Hata M, Soga Y, Kushiyama A, Asano T, Abiko Y, Nishimura F. Adipocyte-macrophage interaction may mediate LPS-induced low-grade inflammation: potential link with metabolic complications. Innate Immunity, [E-pub ahead of print: 2010]18: 164-170, 2012.

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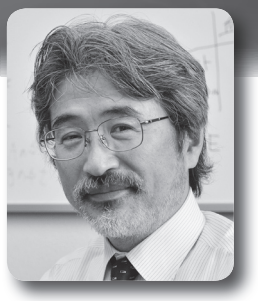
Periodontal Medicine
– Prediction of Systemic Diseases on Periodontal Infection –



Shogo Takashiba, D.D.S., Ph.D.
Professer and Chair,
Department of Pathophysiology - Periodontal Medicine,
Okayama University Graduate School of Medicine,
Dentistry and Pharmaceutical Sciences

Epidemiological studies have suggested the relations among many systemic diseases and periodontitis. In those studies, clinical indices have been used as parameter to show severity of periodontitis. What is really involved in the pathogenicity of the systemic diseases that periodontitis relates? Direct pathogenicity of periodontal bacteria seems to be a small portion of the pathogenicity between these diseases. Host responses to the bacteria or denatured host proteins must be a large portion of pathogenicity such as immune responses to molecules mimicked to the bacterial antigens or involved in inflammation.

For further understanding the severity of periodontitis, we have been used both bacterial DNA to identify specific periodontal bacteria and immunoglobulin G (IgG) to determine the degree of sensitization by bacterial antigens. Increased IgG antibody level means activated acquired immune response and further host response that may cause failure of homeostasis, resulting tissue or organ damages. Real pathogenicity has not been well documented.

However, using these two parameters, we can understand the host responses of periodontitis patients. There are three groups; 1) major group with regular IgG response reflecting the severity of periodontal infection, 2) minor group with hypo-response (low IgG level) to severe periodontal infection, 3) minor group with hyper-response (high IgG level) to less periodontal infection.

In the first group, IgG antibody level changes according to the amount of bacterial DNA detected from periodontal lesion. Thus, it is easy to infer about the sensitization of host from these laboratory examinations. Furthermore, this group may be close to those whose periodontal conditions related to the some systemic diseases. Studies using this assumption have been conducted, suggesting relations between periodontitis and systemic disease somehow. In the second group, IgG antibody level stays lower level even though a lot of amount of bacterial DNA detected from periodontal lesion. The host may be in immuno-compromised condition. Bacteremia or aspiration pneumonia must be considered. In the third group, IgG v\level stays higher level even though very low amount of bacterial DNA detected from periodontal lesion. Hyper-immunoglobulinemia that may relate to injury of glomerulus must be considered. In addition, excessive immunoreaction may exist and injure tissues or organs. Because few studies using this assumption have been conducted, further studies must be performed for these systemic diseases.

In this lecture, I will show our recent studies as examples for the idea mentioned above. The definition of threshold of IgG titer against *Porphyromonas gingivalis*, utilization of the IgG titer test to explain chronic obstructive pulmonary disease, preliminary study to reveal the relation of the IgG titer and atherosclerosis related to diabetes.

CURRICULUM VITAE

Education

1986 Okayama University Dental School
1990 Okayama University Graduate School of Dentistry

Position

1990 Assistant Professor
Okayama University Hospital of Dentistry
1992 Visiting Scientist
Eastman Dental Center (Rochester, NY, USA)
1994 Assistant Professor
Okayama University Dental School
1995 Associate Professor
Okayama University Dental School
2001 Associate Professor
Okayama University Graduate School of Medicine and Dentistry
2002 Professor
Okayama University Graduate School of Medicine and Dentistry
2005 Professor
Okayama University Graduate School of Medicine, mDentistry and Pharmaceutical Sciences

Award and Honors

1997 IADR Travel Award
2001 Japanese Society of Periodontology Science Award

Publications

1. Myokai F, et al. A novel lipopolysaccharide-induced transcription factor regulating tumor necrosis factor alpha gene expression: molecular cloning, sequencing, characterization, and chromosomal assignment. Proc Natl Acad Sci U S A. 1999 Apr 13;96(8):4518-23.
2. Omori K, et al. High glucose enhances interleukin-6-induced vascular endothelial growth factor 165 expression via activation of gp130-mediated p44/42 MAPK-CCAAT/enhancer binding protein signaling in gingival fibroblasts. J Biol Chem. 2004 Feb 20;279(8):6643-9.
3. Yamazaki K, et al. Relationship of periodontal infection to serum antibody levels to periodontopathic bacteria and inflammatory markers in periodontitis patients with coronary heart disease. Clin Exp Immunol. 2007 Sep;149(3):445-52.
4. Martinez ZR, et al. Gene profiles during root canal treatment in experimental rat periapical lesions. J Endod. 2007 Aug;33(8):936-43.
5. Yamaguchi T, et al. IL-6/sIL-6R enhances cathepsin B and L production via caveolin-1-mediated JNK-AP-1 pathway in human gingival fibroblasts. J Cell Physiol. 2008 Nov;217(2):423-32.
6. Kitamura M, et al. Periodontal tissue regeneration using fibroblast growth factor-2: randomized controlled phase II clinical trial. PLoS One. 2008Jul 2;3(7):e2611.
7. hematopoietic stem cell transplantation ward. Support Care Cancer. 2010 Feb;19(2):303-7.
8. Soga Y, et al. Progress of oral care and reduction of oral mucositis--a pilot study in a
9. Kitamura M, et al. FGF-2 stimulates periodontal regeneration: results of a multi-center randomized clinical trial. J Dent Res. 2011 Jan;90(1):35-40.
10. Sugi N, et al. Prognosis of periodontitis recurrence after intensive periodontal treatment using examination of serum IgG antibody titer against periodontal bacteria. J Clin Lab Anal. 2011;25(1):25-32.
11. Tsuge S, et al. Specific in situ visualization of plasma cells producing antibodies against Porphyromonas gingivalis in gingival radicular cyst: application of the enzyme-labeled antigen method. J Histochem Cytochem. 2011 Jul;59(7):673-89.
12. Nakao R, et al. Outer membrane vesicles of Porphyromonas gingivalis elicit a mucosalimmune response. PLoS One. 2011;6(10):e26163.
13. Tomikawa K,et al. Smad2 decelerates re-epithelialization during gingival wound healing. J Dent Res. 2012 Aug;91(8):764-70.
14. Takahashi T, et al. Relationship between periodontitis-related antibody and frequent exacerbations in chronic obstructive pulmonary disease. PLoS One. 2012;7(7):e40570.
15. Kudo C, et al. Assessment of the plasma/serum IgG test to screen for periodontitis. J Dent Res. 2012 Dec;91(12):1190-5.

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Association between Periodontal Disease and Adverse Pregnancy Outcome

Yasushi Furuichi, D.D.S., Odont.Dr.
Professer and Chair,
Division of Periodentology & Endodontology,
Department of Oral Rehabilitation,
School of Dentistry, Health Sciences University of Hokkaido

Periodontal disease is an infectious disease with a certain extent of inflammatory lesion in the periodontium where numbers of microorganisms and inflammatory cells are in contact and varieties of inflammatory mediators are produced and/or infiltrated in. Chronic periodontitis becomes prominent at later ages of adulthood, but gingivitis proceeds at their younger ages. Adverse pregnancy outcome includes pre-term birth (PB: delivery earlier than 37 weeks of gestation) and low birth-weight (LBW: delivery weight less than 2,500 g). Incidence rate of PLBW (PB and /or LBW) are reported to be 4~15 % and varies among different countries and districts. PLBW is the main cause of mortality and morbidity of the new-born and be an ineligible burden not only from familial but also from socioeconomic aspects.

Both periodontal disease and adverse pregnancy outcome are multi-factorial in its pathogenesis and possess common risk factors such as smoking. Since the middle of 1990`s, a number of epidemiological and experimental studies have been performed on the topic of the association between periodontal disease and PLBW and the results were reported in the literature. Such studies can be categorized into three groups according to the aims of the studies, i.e. analyzing the association between the both events, analyzing the mechanisms behind the association, and evaluating the effects of periodontal intervention on the association. Although there have been somewhat large discrepancies in the results of the association studies, significant positive associations have been reported in more than half of the large scaled epidemiological studies. Mechanisms of the association have been analyzed with employing microbiological, immune-pathological, and genomic methods. So far, there have been several studies showing interesting findings which may in part explain the mechanisms of the association. It could be concluded that the biggest controversies were found in the periodontal intervention studies and that periodontal treatments would not be recommended during the pregnancy in order to reduce the incidences of PLBW according to the results of the large scaled RCTs. However, it has also been claimed that periodontal treatment during the pregnancy in itself is beneficial in order to treat periodontal disease and maintain healthier periodontium of the pregnant women. It was also demonstrated that unsuccessful periodontal treatments resulted in higher risks of PLBW than successful periodontal treatments in a study.

In this presentation, association between periodontal disease and adverse pregnancy outcome will be discussed from the three aspects mentioned above.

CURRICULUM VITAE

Education

He graduated from the Faculty of Dentistry, Kagoshima University in 1985. He received Licentiate degree in Odontology in 1992, and Odont Dr degree in 1998, at the Faculty of Odontology, Gothenburg University in Sweden,.

Position

He is a professor and chair of the Division of Periodontology and Endodontology, Department of Oral Rehabilitation, School of Dentistry, Health Sciences University of Hokkaido since 2004, and is a director of the Dental and Medical Clinic of the same university since 2009. He was a private practitioner at Sakuma Dental Clinic in Ibaraki, Japan between 1985-1988 and 1993-1993, and a research assistant at the Department of Periodontology, Faculty of Odontology, University of Gothenburg, Sweden between 1988-1991 and 1993-1998. He was an assistant professor between 1998-2000, a lecturer between 2000-2002, and an associate professor between 2002-2004 at the Department of Periodontology, Faculty of Dentistry, Kagoshima University, Japan.

Publications

1. Furuichi Y, Shimotsu A, Ito H, Namariyama Y, Yotsumoto Y, Hino Y, Mishige Y, Inoue M, Izumi Y. Associations of periodontal status with general health conditions and serum antibody titers for Porphyromonas gingivalis and Actinobacillus actinomycetemcomitans. J Periodontol. 2003;74(10):1491-7.
2. Hasegawa K, Furuichi Y, Shimotsu A, Nakamura M, Yoshinaga M, Kamitomo M, Hatae M, Maruyama I, Izumi Y. Associations between systemic status, periodontal status, serum cytokine levels, and delivery outcomes in pregnant women with a diagnosis of threatened premature labor. J Periodontol. 2003;74(12):1764-70.
3. Nakajima Y, Furuichi Y, Biswas KK, Hashiguchi T, Kawahara K, Yamaji K, Uchimura T, Izumi Y, Maruyama I. Endocannabinoid, anandamide in gingival tissue regulates the periodontal inflammation through NF-kappaB pathway inhibition. FEBS Lett. 2006;580(2):613-9.
4. Shirakata Y, Setoguchi T, Machigashira M, Matsuyama T, Furuichi Y, Hasegawa K, Yoshimoto T, Izumi Y. Comparison of injectable calcium phosphate bone cement grafting and open flap debridement in periodontal intrabony defects: a randomized clinical trial. J Periodontol. 2008;79(1):25-32.
5. Yonamine Y, Matsuyama T, Sonomura T, Takeuchi H, Furuichi Y, Uemura M, Izumi Y, Noguchi K. Effectable application of vascular endothelial growth factor to critical sized rat calvaria defects. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109(2):225-31.
6. Nagasawa T, Noda M, Katagiri S, Takaichi M, Takahashi Y, Wara-Aswapati N,Kobayashi H, Ohara S, Kawaguchi Y, Tagami T, Furuichi Y, Izumi Y. Relationship between periodontitis and diabetes - importance of a clinical study to prove the vicious cycle. Intern Med. 2010;49(10):881-5.
7. Hidaka T, Nagasawa T, Shirai K, Kado T, Furuichi Y. FGF-2 induces proliferation of human periodontal ligament cells and maintains differentiation potentials of STRO-1(+)/CD146(+) periodontal ligament cells. Arch Oral Biol. 2012;57(6):830-40.
8. Komatsu T, Nagano K, Sugiura S, Hagiwara M, Tanigawa N, Abiko Y, Yoshimura F, Furuichi Y, Matsushita K. E-selectin mediates Porphyromonas gingivalis adherence to human endothelial cells. Infect Immun. 2012;80(7):2570-6.
9. Kato S, Nakashima K, Nagasawa T, Abiko Y, Furuichi Y. Involvement of Toll-like receptor 2 in apoptosis of Aggregatibacter actinomycetemcomitans-infected THP-1 cells. J Microbiol Immunol Infect. 2012.
10. Yamada Y, Nakamura S, Ito K, Umemura E, Hara K, Nagasaka T, Abe A, Baba S, Furuichi Y, Izumi Y, Klein OD, Wakabayashi T. Injectable Bone Tissue Engineering Using Expanded Mesenchymal Stem Cells. Stem Cells. 2012.

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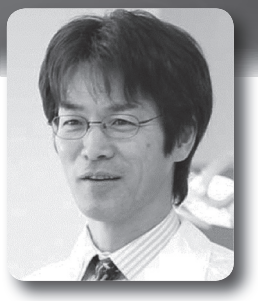
Interrelationships between Systemic Osteoporosis and Periodontal Disease : Association and Mechanisms



Koji Inagaki, D.D.S., Ph.D.

Professor,
Department of Dental Hygiene,
Aichi Gakuin University Junior College

Many studies have attempted to define the relationship between postmenopausal osteoporosis and periodontal disease. Most studies support a positive association between these common diseases; however, many are cross-sectional in nature, include relatively small sample sizes, and have inadequate control of potential confounding factors, such as age, gender, hormone intake, race, and smoking, limiting our understanding of the nature of the relationship between these diseases. Clinical conditions causing low estrogen environments in postmenopausal women allow T- and B-cell abnormalities, increased local production of the bone-active cytokines (i.e., Interleukin-1, -6 and -8, tumor necrosis factor- (TNF-) and a rise in prostaglandin E_2, resulting in the progression of periodontitis. In post-menopausal osteoporosis, lack of estrogen will affect the remodeling of the bone tissue in such a way that, in most patients with periodontitis, the amount of bone resorbed exceeds that being formed, resulting in net bone loss. Osteoporosis can be treated by a variety of methods, the hormone replacement therapy (HRT), the selective estrogen receptor modulators (SERM) and the bisphosphonates. The HRT or bisphosphonates treatments improve the clinical outcome of periodontal disease and may be an adjunctive treatment to preserve periodontal bone mass. This presentation reviews the current evidence on the mechanism of periodontal breakdown after menopause with long-term follow-up cases and the benefit to oral health by treatments for osteoporosis.

CURRICULUM VITAE

Education

1976 - 1982 Aichi-Gakuin University Nagoya
DDS
1982 - 1986 Aichi-Gakuin University
(graduate course in Periodontology)
PhD

Position

1. Professor, Department of Dental Hygiene, Aichi Gakuin University Junior College
2. Associate Professor, Department of Periodontology, Aichi Gakuin University
3. Diplomate of the Japanese Board of Periodontology
4. Diplomate of the Japanese Board of Tobacco Control
5. Diplomate of the Japanese Board of Conservative Dentistry
6. Diplomate of the Japanese Board of Occlusion & Health
7. Caretaker of Aichi Association for Tobacco-free Kids and Research Group on Smoke-Free Psychology
8. Director of Diplomate, Japanese Society of Periodontology

Award and Honors

2003 The Incentive Award of the Japan Osteoporosis Society
2009 The Incentive Award of the Tokai School Health Association

Publications

1. Morita I, Nakagaki H, Taguchi A, Kato K, Murakami T, Tsuboi S, Hayashizaki J, Inagaki K, Noguchi T.: Relationships between mandibular cortical bone measures and biochemical markers of bone turnover in older Japanese men and women. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 108(5):777-783, 2009
2. Otani T, Yoshii C, Kano M, Kitada M, Inagaki K, Kurioka N, Isomura T, Hara M, Okubo Y, Koyama H.: Validity and reliability of Kano test for social nicotine dependence (KTSND). Ann Epidemiol, 19(11):815-822, 2009
3. Yoshii S, Tsuboi S, Morita I, Takami K, Inukai J, Inagaki K, Nakagaki H.: Temporal association of elevated C-reactive protein and periodontal disease in men. J Periodontol, 80(5):734-739, 2009
4. Katagiri S, Nitta H, Nagasawa T, Uchimura I, Izumiyama H, Inagaki K, Kikuchi T, Noguchi T, Kanazawa M, Matsuo A, Chiba H, Nakamura N, Kanamura N, Inoue S, Ishikawa I, Izumi Y.: Multi-center intervention study on glycohemoglobin (HbA1c) and serum, high-sensitivity CRP (hs-CRP) after local anti-infectious periodontal treatment in type 2 diabetic patients with periodontal disease. Diabetes Res Clin Pract, 83(3):308-315, 2009
5. Dumitrescu AL, Inagaki K.: Interrelationships between periodontal disease and mortality, cardiovascular disease, metabolic syndrome, diabetes mellitus, Dumitrescu AL. Etiology and Pathogenesis of Periodontal Disease, 1st ed, Springer, Germany, 2010, 125-157, 159-190, 215-244, 265-278, 279-293, 295-306, 307-318.
6. Huang B, Inagaki K, Yoshii C, Kano M, Abbott PV, Noguchi T, Takahashi K, Bessho K.: Social nicotine dependence in Australian dental undergraduate students. Int Dent J, 61(3):152-156, 2011
7. Nomura Y, Shimada Y, Hanada N, Numabe Y, Kamoi K, Sato T, Gomi K, Arai T, Inagaki K, Fukuda M, Noguchi T, Yoshie H.: Salivary biomarkers for predicting the progression of chronic periodontitis. Arch Oral Biol, 57(4):413-420, 2012
8. Morita I, Inagaki K, Nakamura F, Noguchi T, Matsubara T, Yoshii S, Nakagaki H, Mizuno K, Sheiham A, Sabbah W.: Relationship between periodontal status and levels of glycated hemoglobin. J Dent Res, 91(2):161-166, 2012
9. Noguchi T, Kikuchi T, Inagaki K.: Periodontitis and diabetes, Yoshie H, At the forefront: illustrated topics in dental research and clinical practice, 1st ed, Quintessence Publishing Co Inc, Germany, 2012, 43-46.

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Is There a Role for Stem Cells in Periodontal Regeneration?

Mark Bartold, D.D.S., Ph.D.

Professor of Periodontics & Director Colgate Australian
Clinical Dental Research Center
University of Adelaide

Although stem cells have received considerable attention in recent years, clonogenic bone marrow stromal stem cells (also know as mesenchymal stem cells) were first isolated and characterized almost 40 years ago. Since then considerable effort has been made in determining the therapeutic applications of mesenchymal stem cells. Mesenchymal stem cell properties such as multipotency and immunomodulation make these cells ideal candidates for tissue regeneration and tissue engineering. Most of us are familiar with the concept of embryonic stem cells and their potential use in tissue regeneration. Over the past 10 years, reports have appeared characterizing mesenchymal stem cells isolated from the periodontal tissues (periodontal ligament and gingiva) and their potential use in periodontal regeneration. More recently reports of isolation of induced pluripotent stem (iPS) cells from gingiva and periodontal ligament have appeared. Both mesenchymal stem cells and iPS cells from periodontal tissues provide an attractive source of cells for periodontal tissue engineering. It is now clear that in order for tissue engineering to reach its full regenerative potential an appropriate scaffold for cell delivery together with the incorporation of supplemental cytokines and growth factors will be necessary for the regenerative process to proceed both spatially and temporally. The precise roles of mesenchymal stem cells in tissue regeneration still need to be elucidated. For example, it is still unclear whether these cells act via direct differentiation in situ or through paracrine mediated processes leading to recruitment of local progenitor cells to enable tissue regeneration. In this presentation the biology and potential for clinical use of periodontal stem cells for periodontal regeneration will be explored.

CURRICULUM VITAE

Education

1. BDS, University of Adelaide
2. BScDent(Hons) university of Adelaide
3. PhD, University of Adelaide
4. FRACDS(Perio), Royal Australasian College of Dental Surgeons
5. DDSc, University of Adelaide

Position

Professor of Periodontics
Director Colgate Australian Clinical Dental Research Center

Award and Honors

1992 Who's Who in Australia
First listed in Who's Who in Australia from 1992 - present
Published by Information Australia (ISBN 0810-8226)

1995 Academy of Dentistry International
Elected Fellow of the Academy of Dentistry International

1995 Australian Dental Association
Appointed "Guest Lecturer" to the Northern Territory" for 1995

1996 Alan Docking IADR Science Award
Awarded for outstanding contributions to dental science
International Association for Dental Research
Australian & New Zealand Division
Sydney, September 1996

1998 International College of Dentists
Elected Fellow of the International Academy of Dentists

2002 Royal Australasian College of Dental Surgeons
Meritorious Service Award

2003 Pierre Fauchard Academy
Elected Fellow

2004 Order of Australia
Member of the Order of Australia

2005 Indian Society of Periodontology
Honorary Life Membership

2008 Meritorious Service Award, Australian Dental Association
Awarded for outstanding service to dentistry, dental education and the ADA in Australia in an extraordinary manner for 30 years.

2012 Ray Williams Prize, Australian Society of Periodontology
For the most significant series of papers published in periodontal research for the triennium 2009-2011.

Publications

1. Goss AN, Bartold PM, Sambrook P, Hawker P. The nature and frequency of bisphosphonate associated osteonecrosis of the jaws in dental implant patients in South Australia. Journal of Oral and Maxillofacial Surgery 68: 237-243; 2010.
2. Fitzsimmons TR, Sanders AE, Bartold PM, Slade GD. Local and systemic biomarkers in gingival crevicular fluid increase odds of periodontitis. Journal of Clinical Periodontology 37: 30-36; 2010.
3. Bartold PM, Cantley MD, Haynes DR. Mechanisms and control of pathologic bone loss in periodontitis. Periodontology 2000 53: 55-69; 2010.
4. Mrozik K, Zilm PS, Bagley CJ, Hack S, Hoffman P, Gronthos S, Bartold PM. Proteomic characterization of mesenchymal stem cell-like populations derived from periodontal ligament, dental pulp and bone marrow: analysis of differentially expressed proteins Stem Cells and Development 19: 1485-1499; 2010
5. Kataria NG, Bartold PM, Dharmapatni AASK, Atkins GJ, Holding CA, Haynes DR. Expression of tumor necrosis factor like weak inducer of apoptosis (TWEAK) and its receptor FN14 in healthy and periodontitis tissues. Journal of Periodontal Research 45: 564-573; 2010
6. Bartold PM, Marino, V, Cantley, M, Haynes, DR. Effect of P. gingivalis-induced inflammation on development of rheumatoid arthritis. Journal of Clinical Periodontology 37: 405-411; 2010
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MEMO

Periodontal Tissue Engineering
– The Future Perspective of Cytokine Therapy and Cell Therapy –

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It has been demonstrated that mesenchymal stem cells and progenitor cells of osteoblasts or cementoblasts can be identified within periodontal ligament (PDL). Thus, improving the biological potential of these cells and stimulating the periodontal regeneration are recognized as being clinically possible. One of the most physiologically efficient methods to stimulate these cells is the use of cytokines.

Basis Fibroblast Growth Factor (FGF-2) is known to be deeply involved in the proliferation, migration and differentiation of a variety of cells and to strongly induce angiogenesis. Utilizing beagle dogs and non-human primates, we revealed that topical application of recombinant FGF-2 induced statistically significant periodontal tissue regeneration in the experimentally-prepared intraosseous bone defects. Recently, a human clinical trial was conducted using FGF-2 in Japan. This was a randomized controlled double-blinded clinical trial of dose responses including placebo comparison. As a result, a significant difference in % increase in alveolar bone height at 2- or 3-walled intrabony defects of the patients was demonstrated by standardised radiographs between Placebo Group and 0.3% -FGF-2 Group at 9 months after the treatment. This suggests that topical application of FGF-2 can be efficacious in regeneration of periodontal tissue of periodontitis patients.

Based on the results of a series of *in vitro* analyses, we have suggested the following mode of action of FGF-2 to induce periodontal regeneration. During the early stages of periodontal tissue regeneration, FGF-2 stimulates the proliferation and migration of PDL cells while maintaining their multipotent nature, inducing differentiation into hard tissue-forming cells such as osteoblasts and cementoblasts. Furthermore, FGF-2 induces angiogenesis and increases extracellular-matrix production such as osteopontin, hyaluronan from PDL cells, thus leading to a local environment suitable for the periodontal regeneration. These results in the enhanced periodontal tissue regeneration are shown at the FGF-2-applied sites.

For ideal periodontal regeneration, it is crucial to fully introduce the concept of "tissue engineering". If we need to treat severe bony defects or horizontal bone destruction with FGF-2, it is essential to introduce the concept of a "scaffold" into the carrier of FGF-2 drug. An FGF-2 carrier that could provide a formable and osteoconductive scaffold for undifferentiated progenitor cells within PDL would dramatically increase both the dental and craniofacial applications of FGF-2 drug.

Furthermore, researchers, including our group, have found that mesenchymal stem cells can be obtained from various tissues such as bone marrow and adipose tissues. By using beagle dog models, we recently revealed that transplantation of adipose-tissue derived stem cells enhances periodontal regeneration at applied sites. The combined effects of 'cell therapy' and 'cytokine therapy' need to be assessed in the future, to allow the establishment of 'periodontal tissue engineering'.

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Education

1978-1984 D.D.S.
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1984-1988 Ph.D.
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Position

1988 - 1988 Research Fellow, Department of Periodontology and Endodontology, Osaka University Faculty of Dentistry, Japan
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
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2002 -present Professor and Chairman, Department of Periodontology, Osaka University Graduate School of Dentistry
2008 -present Vice Director of Osaka University Dental Hospital

Award and Honors

1984 Yumikura Award: Osaka Univ. Faculty of Dentistry
1998 Anthony Rizzo Periodontal Research Award (IADR Periodontal Research Group)
2009 AAP R. Earl Robinson Periodontal Regeneration Award
2012 IADR/AADR William J. Gies Award

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J. Cell. Physiol.227: 2622-2631, 2012.

MEMO

Clinical Application of Er:YAG Laser in Periodontal and Peri-implant Therapy

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Recently, various lasers have been used for a wide range of oral conditions. Lasers have numerous advantageous physical properties such as ablation, hemostasis, bactericidal effect as well as photo-bio-modulation, making it suitable for treating inflammatory and infectious conditions. Thus, the use of lasers is considered safe and effective for treating oral diseases such as periodontitis and peri-implantitis.

Among various laser systems, in particular, the recent development of the Er:YAG laser has expanded the application of lasers to hard tissue treatment in periodontics since the 2.94 μm wavelength can be applied on both dental soft and hard tissues. The Er:YAG laser has various characteristics advantageous for soft and hard tissue management, such as easy and precise ablation, cutting, debridement and recontouring with minimal thermal damage to the surrounding tissues under water irrigation. Nowadays, the Er:YAG laser is effectively being used for various tissue managements such as gingival tissue ablation, dental root and implant fixture surface debridement, and osseous surgery.

In periodontal and peri-implant applications, the Er:YAG laser is capable of treating alveolar bone tissue either directly or indirectly during osseous management. Animal studies reported faster wound healing in bone tissue following Er:YAG laser ablation compared to bur cutting, as well as significantly enhanced and favorable new bone formation following surgical treatment of periodontitis or peri-implantitis using an Er:YAG laser compared to mechanical instrumentation. These positive results are considered to be due to the high decontamination and detoxification effects of the Er:YAG laser on the diseased site, the pronounced bleeding from the laser-treated bone surface, as well as the production of characteristic microstructures on the ablated bone and root surfaces, which possibly enhances fibrin and blood clot retention. In addition, potential photo-bio-modulation effects of low-level laser effect which induces a variety of biological responses may be partly involved in the increased bone formation. Given these observations and evidences, the Er:YAG laser has been recently established as one of the most promising laser systems for periodontal and peri-implant therapy.

In this presentation, the current clinical applications of Er:YAG laser for various treatments such as soft tissue management, non-surgical and surgical periodontal treatment, osseous surgery and peri-implant therapy will be discussed, based on scientific evidence from currently available basic and clinical studies as well as clinical cases.

CURRICULUM VITAE

Education

1979 D.D.S. degree: Tokyo Medical and Dental University, Faculty of Dentistry
1983 Ph.D. degree: Tokyo Medical and Dental University, Graduate School, Periodontology in Dental Research Division
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1983 - 1992 Instructor, Department of Periodontology, Tokyo Medical and Dental University
1987 - 1989 Maître Assistant, Department of Oral Physiopathology and Periodontology, University of Geneva
1992 - 1999 Associate Professor, Department of Periodontology, Kagoshima University Dental School
1999 - 2003 Professor and Chair, Department of Periodontology, Kagoshima University Dental School
2003 - 2007 Professor and Chair, Department of Periodontology, Field of Oral and Maxillofacial Rehabilitation, Course for Developmental Therapeutics, Kagoshima University Graduate School of Medical and Dental Sciences
Vice President, Kagoshima University Medical and Dental Hospital
2007 - Present Professor and Chair, Department of Periodontology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University
2008 - Present Assistant Director, Tokyo Medical and Dental University Hospital of Dentistry

Award and Honors

1. R Earl Robinson Periodontal Regeneration Award, American Academy of Periodontology. (2009.9.15. Boston)
2. William J. Gies Award Clinical Research Category, International Association of Dental Research / American Association of Dental Research. (2012.6.20. Iguaçu Falls, Brazil

Publications

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26. Taniguchi Y, Aoki A, Mizutani K, Takeuchi Y, Ichinose S, Takasaki A A, Schwarz F, Izumi Y. Optimal Er:YAG laser irradiation parameters for debridement of microstructured fixture surfaces of titanium dental implants. Lasers Med Sci, in press
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MEMO

Poster Session

Sixth Retreat 2013

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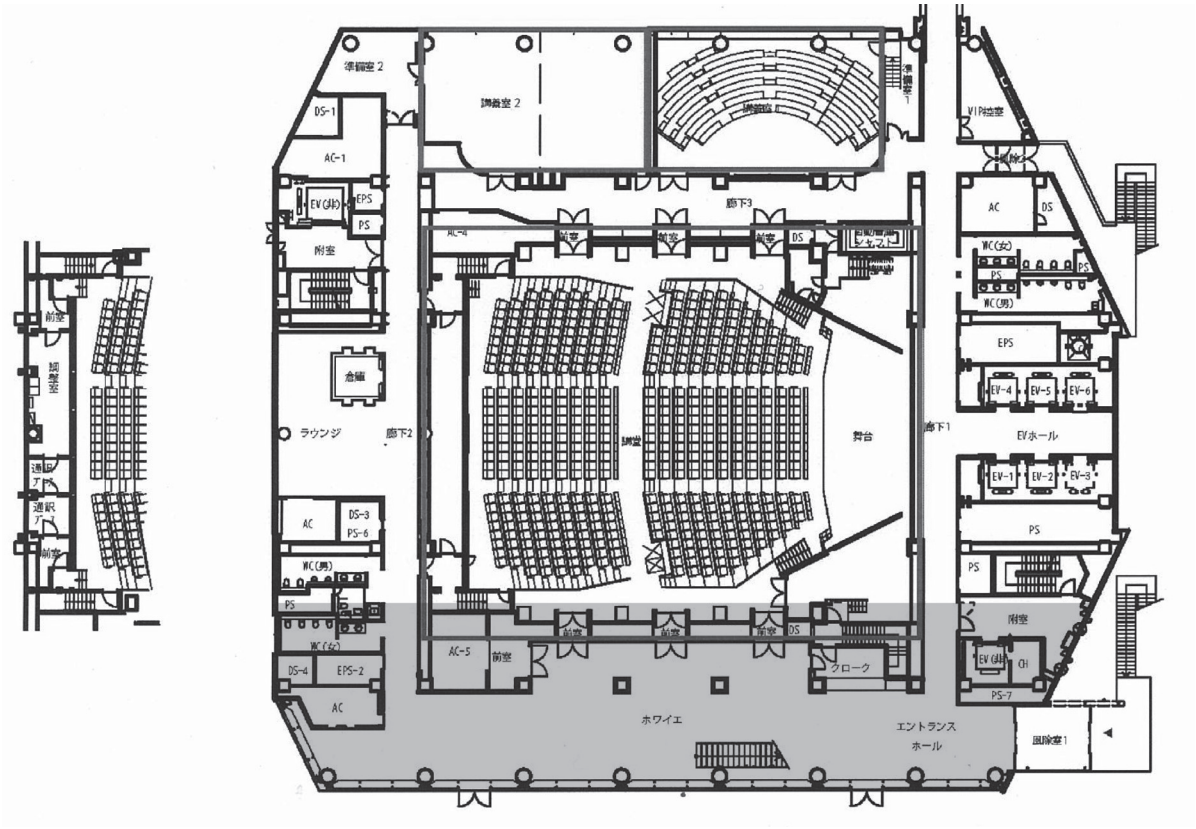
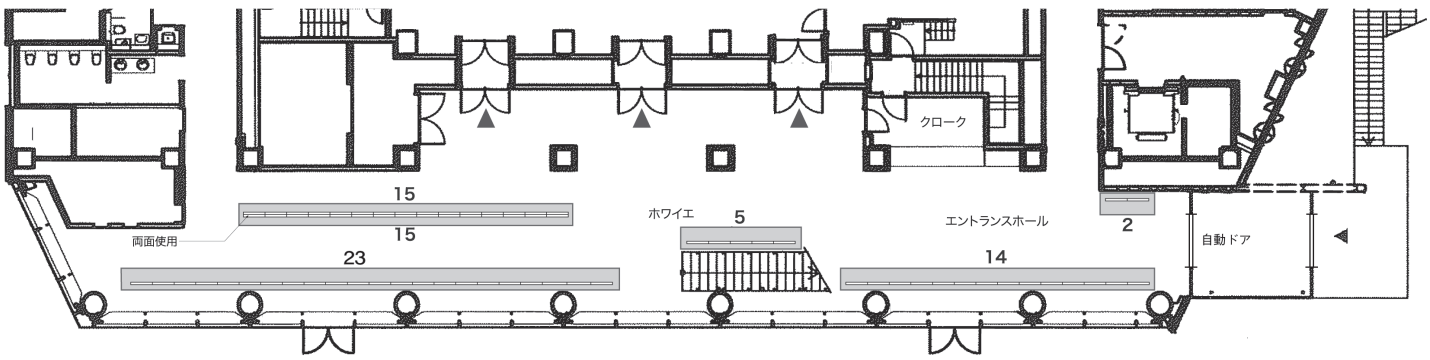
Marwa Madi	3
Ma Chengshan	3
Yuki Yamaguchi	3
Bijaya Haobam	3
Zayar Lin	3
Rumana Khanom	3
Duarte Puerto Carolina Lizeth	3
Ye ChangChang	3
Dawud Abduweli	3
Cheng Xu	3
Yuji Tsuchido	3
Norihiko Ashigaki	3
Junpei Shirakawa	3
Md.Sofiqul Islam	3
Masako Yoshizaki	3
Yukihiko Hashida	3
Thitthaweerat Suppason	3
Hisanori Hasegawa	3
Shin Fukuda	3
Tadashi Hosoya	3
Naoki Kimura	3

MEMO

Name	Grade
Masayoshi Uezono	3
Mandurah, Mona Mohammad M.	3
Mayumi Ogita	3
Warunee Pluemsakunthai	3
Nadila Wali	3
Gerardo Jose Joves Mendez	3
Nurmaa Dashzeveg	2
Suphanantachat Supreda	2
Rajapakshe Mudiyanselage Anupama Rasadari Rajapakshe	2
Kahaer Abula	2
Takehito Ono	2
Gu Jie	2
Lee Phenix	2
Surapornsawasd Thunyaporn	2
Thanit Prasitsak	2
Alaa Abdulahad Turkistani	2
Lodha Ena	2
Thanatvarakorn Ornnicha	2
Waka Yokoyama	2
Yusuke Matsuo	2
Yoko Nakazato	2
Maheswari Kuppusamy	2
Mohannad Issa Michael Nassar	2
Kenji Ogura	2
Takayuki Yamada	2
Uehara Daniela Tiaki	1
Nuylan, Michelle Loyola	1
Makiri Kawasaki	1
Hua Qiao	1
Khunkar, Sahar Jameel M	1
Natsuka Umezawa	1
Tetsuya Saito	1
Kenchi Takenaka	1
Alsayed, Ehab Zaki E	1
Kong Kalyan	1
Baba Bista	1

MEMO


準備室 2
講義室 2
講義室 1
VIP控室
DS-1
AC-1
EV(共)
EPS
PS
廊下3
附室
AC
DS
WC(女)
WC(男)
EPS
EV-4
EV-5
EV-6
前室
倉庫
ラウンジ
廊下2
講堂
舞台
廊下1
EVホール
EV-1
EV-2
EV-3
AC
DS-3
PS-6
WC(男)
WC(女)
DS-4
EPS-2
AC-5
クローク
EV(共)
CH
PS-7
ホワイエ
エントランス
ホール
風除室1


クローク
15
15
両面使用
23
ホワイエ
5
エントランスホール
14
2
自動ドア

MEMO