Tokyo Medical and Dental University
The 7th 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 ~Autumn Seminar~

東京医科歯科大学

第7回 グローバルCOE 国際シンポジウム

November 12th~14th, 2012
Tokyo Medical and
Dental University

http://www.tmd.ac.jp/cmn/gcoe/index.html

Fifth Retreat Meeting

Organizing Chairs of The 7th Global COE International Symposium

Yuichi Izumi, Professor and chairman, Dept. of Periodontology

Keiji Moriyama, Professor and chairman, Dept. of Maxillofacial Orthognathics

Molecular Science in Oral-Systemic Medicine
- Autumn Seminar -

November 12th~14th, 2012

2012.11.12（Mon）

13：00 − 13：10　President Address
Takashi Ohyama

Session 1　**chairpersons : Irma Thesleff, Keiji Moriyama**

13：10 − 14：10　**Martha J. Somerman**
NIDCR/NIH: Today's Discovery, Tomorrow's Cure

14：10 − 15：10　**Peter A. Mossey**
A global approach to the challenge of orofacial clefting

15：10 − 15：40　Poster Session 1（Coffee Break）

Session 2　**chairpersons : Peter A. Mossey, Masaki Noda**

15：40 − 16：40　**Kenjiro Kosaki**
Clinical molecular diagnostics of congenital malformation syndrome using in-solution hybridization-based enrichment and massively parallel sequencing

16：40 − 17：40　**Lynda F. Bonewald**
The Osteocyte as a Regulator of Bone Remodeling

17：40 − 18：40　**Keiji Moriyama**
New biological insights of tooth movement in response to mechanical stress

19：00 −　Reception

2012.11.13（**Tue**）

Session 3	**chairpersons : Martha J Somerman, Akira Yamaguchi**
9：00 − 10：00	**Irma Thesleff** Mechanisms of tooth renewal
10：00 − 11：00	**Satoshi Fukumoto** Role of dental epithelium- stem cell interactions during dental cell differentiation
11：00 − 11：10	Coffee Break

Session 4	**chairpersons : Linda F. Bonewald, Satoshi Fukumoto**
11：10 − 12：10	**Takashi Tsuji** Tooth Regenerative Therapy as a Future Dental Treatment
12：10 − 12：40	**Naoto Haruyama** Amelogenins: Multifaceted enamel matrix proteins in hard tissue biology

Session 5	**chairpersons : Young Ku, Kazuhisa Yamazaki**
13：40 − 14：40	**Gregory J. Seymour** The periodontal - systemic connection: Molecular mechanisms and their significance in overall health care
14：40 − 15：40	**Nawarat Wara-aswapati** Oral - Systemic Connection : Roles of the Host Factors
15：40 − 16：10	Poster Session 2（Coffee Break）

Session 6	**chairpersons : Nawarat Wara-aswapati, Yuichi Izumi**
16：10 − 17：10	**Young Ku** The biologic effect of oligopeptides derived from fibronectin and its application to biomimetics
17：10 − 18：10	**Kazuhisa Yamazaki** Periodontal disease and atherothrombotic diseases: Lessons from clinical and basic studies

2012.11.14（**Wed**）

Session 7	**chairpersons : Young–Chel Park, Takashi Ono**
10：00 − 11：00	**Tetsu Takahashi** Paradigm shift of orhthognathic surgery in diagnosis, simulation, and guided surgery
11：00 − 12：00	**Seung-Hak Baek** Recent Paradigm Change in Three-Dimensional Imaging and CAD-CAM Technology for Virtual Orthodontic Treatment and Orthognathic Surgery

Session 8	**chairpersons : Seung–Hak Baek, Tetsu Takahashi**
13：00 − 14：00	**Young-Chel Park** Clinical and biomechanical considerations for correction of the dento-facial deformities
14：00 − 15：00	**Kiyoshi Harada** Orthognathic Surgery :The Considerations for its Accuracy and Safety
15：00	Closing Remark　Yuichi Izumi Adjourn

C O N T E N T S

NIDCR/NIH: Today's Discovery, Tomorrow's Cure

Martha J. Somerman D.D.S., Ph.D.

Director NIDCR,
NIH and Chief Laboratory for Oral Connective Tissue Biology,
NIAMS, NIH. Bethesda, Maryland

This presentation will focus on research supported by National Institute of Dental and Craniofacial Research/ National Institutes of Health, with an emphasis on advances made toward improvements in treatment of dental-oral-craniofacial pathologies/conditions. Research topics, from basic to translational to clinical, will include: a) current and planned genomic analysis/genomic wide association studies applied to analysis of dental-oral-craniofacial pathologies/anomalies/disorders and will include cleft lip/palate, caries and periodontal diseases and Sjogren's Syndrome; b) salivary diagnostics for oral-systemic diseases; c) oral cancer from the oral cancer genome project to assays for diagnosis and early detection of head and neck cancer; d) public health challenges, e.g., acute/chronic pain linked to temporomandibular joint disorders and associated co- morbidities and human papilloma virus-related oral cancers; e) The microbiome project, where data have been obtained by sampling 6 sites (nasal passages, gastrointestinal tract, urogenital tract, skin and oral cavity (9 sites)) and are being analyzed for the role of these microbes in human health and disease; and f) clinical research within the clinical research center at NIH and also nationally/internationally. The emphasis will be on advances in research supported by NIDCR /NIH that have and will continue to improve the quality of health for all communities.

CURRICULUM VITAE

Education

1968 New York University, Arts and Science; BA
1972 Hunter College, Institute of Environmental Health Sciences, New York, NY; MS
1975 New York University, College of Dentistry, New York, NY; DDS
1978 Eastman Dental Research Center, Rochester, NY; Certificate in Periodontology
1980 Department of Pharmacology & Toxicology, University of Rochester Medical Center & Dental School, Rochester, NY; PhD

Position

2001 - 2002 Associate Dean for Research, University of Michigan, School of Dentistry
2002 - 2011 Professor, University of Washington School of Dentistry, Department of Periodontics
2002 - 2011 Dean, University of Washington School of Dentistry
2003 - 2011 Adjunct Professor, University of Washington School of Dentistry, Department of Oral Biology
2004 - 2011 Associate Medical Staff, University of Washington Medical Center
2004 - 2011 Medical Staff, Seattle Cancer Care Alliance
2004 - 2011 Associate Medical Staff, Harborview Medical Center
2011–present Affiliate Professor, University of Washington School of Dentistry, Department of Periodontics
2011–present Dean Emeritus, University of Washington, School of Dentistry

Award and Honors

2000 President-Elect, AADR
2001 President, AADR
2001 Fellow, American Association for the Advancement of Science
2003 William J. Gies Award in Periodontology
2005 IADR Distinguished Scientist - Research in Oral Biology Award
2005 Fellow, Pierre Fauchard Academy
2006 Fellow, American College of Dentists
2006 Fellow, International College of Dentists
2008 Advocacy Award, Seattle Local Chapter, American Student Dental Association
2010 Honorary Professor of West China College of Stomatology, Sichuan University
2010 IADR/Straumann Award in Regenerative Periodontal Medicine
2011 Paul Goldhaber Award, Harvard School of Dental Medicine
2012 New York University, College of Dentistry Distinguished Scientist Award

Publications

1. Popowics T, Foster BL, Swanson EC, Fong HK, Somerman MJ. Defining the roots of cementum formation. Cells Tissues Organs 181(3-4):248-57, 2005.
2. Foster BL, Somerman MJ. Regenerating the Periodontium: Is there a magic formula? Orthodontics and Craniofacial Research 8(4):285-91, 2005.
3. Berry JE, Ealba EL, Pettway GJ, Datta NS, Swanson EC, Somerman MJ, McCauley LK. JunB as a downstream mediator of PTHrP actions in cementoblasts. Journal of Bone and Mineral Research 21(2):246-257, 2006.
4. Hakki SS, Wang D, Franceschi RT, Somerman MJ. Bone Sialoprotein Gene Transfer to Periodontal Ligament Cells May Not Be Sufficient to Promote Mineralization In Vitro or In Vivo. J Periodontol, 77:167-173, 2006.
5. Foster BL, Nociti FH, Swanson EC, Matsa-Dunn D, Berry JE, Cupp CJ, Zhang P, Somerman MJ. Regulation of Cementoblast Gene Expression by Inorganic Phosphate, In Vitro. Calcif Tissue Int. 78:103-112, 2006.
6. Swanson EC, Fong HK, Foster BL, Paine ML, Gibson CW, Snead ML, Somerman MJ. Amelogenins regulate expression of genes associated with cementoblasts in vitro. Eur J Oral Sci 114 Suppl 1:239-43, 2006.
7. Rutherford R, Foster BL, Bammler T, Beyer D, Sato S, Somerman MJ. Extracellular Phosphate Alters Cementoblast Gene Expression. Journal of Dental Research 85(6):505-509, 2006.
8. Woo KM, Jun JH, Chen VJ, Seo J, Baek JH, Ryoo HM, Kim GS, Somerman MJ, Ma PX. Nano-fibrous scaffolding promotes osteoblast differentiation and biomineralization. Biomaterials 28:335-343, 2006.
9. Nemoto E, Darveau RP, Foster BL, Nogueira-Filho GR, Somerman MJ. Regulation of cementoblast function by P. gingivalis lipopolysaccharide via TLR2. Journal of Dental Research 85(8):733-738, 2006.
10. Mada Y, Miyauchi M, Oka H, Kitagawa M, Sakamoto K, Iizuka S, Sato S, Noguchi K, Somerman MJ, Takata T. Effects of endogenous and exogenous prostaglandin E2 on the proliferation and differentiation of a mouse cementoblast cell line (OCCM-30). J. Periodontol. 200677(12):2051-8, Dec 2006.
11. Zhang H, Somerman MJ, Berg J, Cunningham ML, Williams B. Dental anomalies in a child with craniometaphysial dysplasia. Pediatr Dent. 2007 Sep-Oct;29(5):415-9.
12. Noguchi K, Miyauchi M, Oka H, Komaki M, Somerman MJ, Takata T. Cyclooxygenase-2-dependent prostaglandin E(2) upregulates interleukin (IL)-1alpha-induced IL-6 generation in mouse cementoblasts. J Periodontol. 2007 Jan;78(1):135-40.
13. Oka H, Miyauchi M, Sakamoto K, Moriwaki S, Niida S, Noguchi K, Somerman MJ, Takata T. PGE2 activates cementoclastogenesis by cementoblasts via EP4. J Dent Res. 2007 Oct;86(10):974-9.
14. Sato S, Kitagawa M, Sakamoto K, Iizuka S, Kudo Y,

Ogawa I, Miyauchi M, Chu EY, Foster BL, Somerman MJ, Takata T. Enamel matrix derivative exhibits anti-inflammation properties in monocytes. J Periodontol 79(3) 535-540, 2008.

15. Osathanon T, Linnes ML, Rajachar RM, Ratner BD, Somerman MJ, Giachelli CM. Microporous nanofibrous fibrin-based scaffolds for bone tissue engineering. Biomaterials 29 4091-4099, 2008.
16. Fatherazi S, Matsa-Dunn D, Rutherford B, Foster B, Somerman MJ, Presland R. Phosphate regulates osteopontin gene transcription. J Dent Res 88(1):39-44, January 2009.
17. Nagatomo KJ, Tompkins KA, Fong H, Zhang H, Foster BL, Chu EY, Murakami A, Stadmeyer L, Canalis E, Somerman MJ. Transgenic overexpression of gremlin results in developmental defects in enamel and dentin in mice. Journal Connective Tissue Research 49:6,391-400, 2008.
18. Fong H, Foster BL, Sarikaya M, Somerman MJ. Structure and mechanical properties of Ank/Ank mutant mouse dental tissues – An animal model for studying periodontal regeneration. Arch Oral Biol. 54(6):570-576, 6/09.
19. Nemoto E, Koshikawa Y, Kanaya S, Tsuchiya M, Tamura M, Somerman MJ, Shimauchi H. Wnt signaling inhibits cementoblast differentiation and promotes proliferation. Bone 44:805-812, 2009.
20. Osathanon T, Giachelli CM, Somerman MJ. Immobilization of Alkaline Phosphatase on Microporous Nanofibrous Fibrin Scaffolds for Bone Tissue Engineering. Biomaterials 30 4513-4521, 2009
21. Fong H, Chu EY, Tompkins KA, Foster BL, Nociti FH, Sitara D, Lanske B, and Somerman MJ. Aberrant cementum phenotype associated with hypophoshphatemic Hyp mouse. J Periodontol, 80: 1348-54, 2009.
22. Lee M, Chu E, El-Abbadi M, Foster B, Tompkins K, Giachelli C, Somerman M. Characterization of Mandibular Bone in a Mouse Model of Chronic Kidney Disease. J Periodotol, 81: 300-309, 2010.
23. Chu EY, Fong H, Blethen FA, Tompkins KA, Foster BF, Yeh KD, Nagatomo KJ, D. Matsa-Dunn D, Sitara D, Lanske B, Rutherford RB, and Somerman MJ. Ablation of systemic phosphate regulating gene fibroblast growth factor 23 (Fgf23) compromises the dentoalveolar complex Anatomical Record, 293: 1214-1226, 2010.
24. Zhang H, Tompkins K, Garrigues J, Snead ML, Gibson C, Somerman MJ. Full Length Amelogenin Binds to Cell Surface LAMP-1 on Tooth Root/Periodontium Associated Cells. Arch Oral Bio, 55(6): 417-425 2010.
25. Kanaya S, Nemoto E, Ebe Y, Somerman M, and Shimauchi H. Elevated extracellular calcium increases fibroblast growth factor-2 gene and protein expression levels via a cAMP/PKA dependent pathway in cementoblasts. Bone, Sep;47(3):564-72, 2010.
26. Hakki SS, Foster BL, Nagatomo KK, Bozkurt SB, Hakki EE, Somerman MJ, and Nohutcu RM. Bone morphogenetic Protein-7 enhances cementoblast function, in vitro. J Periodotol, 81(11): 1663-1674, 2010.
27. Ballweg R, Berg J, DeRouen T, Fiset L, Mouradian W, Somerman M. Dental Education in the United States: Expanding our partnerships beyond the Four Walls. J Dent Educ. 75:300-309, 2011.
28. Somerman MJ. Growth Factors and Periodontal Engineering-where next? J Dent Res, 90(1): 7-8, 2011.
29. Foster BL, Nagatomo KJ, Bamashmous SO, Tompkins KA, Fong H, Dunn D, Chu EY, Guenter C, Kingsley DM, Rutherford RB and Somerman MJ. The Progressive Ankylosis Protein Regulates Cementum Apposition and Extracellular Matrix Composition. Cells Tissues Organs, 194(5): 382-405, 2011.
30. Tada H, Nemoto E, Foster BL, Somerman MJ, and Shimauchi H. Phosphate increases bone morphogenetic protein-2 expression through cAMP-dependent protein kinase and ERK1/2 pathways in human dental pulp cells. J Bone Mineral Res, 48(6):1409-1416, 2011.
31. Rodrigues TL, Nagatomo KJ, Foster BL, Nociti FH, Jr., and Somerman MJ. Modulation of phosphate/pyrophosphate metabolism to regenerate the periodontium. A novel in vivo approach. J Periodontol, 82:1757-1766, 2011.
32. Rodrigues, TL, Foster BL, Silverio KG, Luciane, M, Casati MZ, Sallum EA, Somerman MJ, Nociti FH. Correction of hypophospatasia (Hpp) associated mineralization deficiencies in vitro by phosphate/prophosphate modulation in periodontal ligament cells. J Periodontol. 83(5):653-663, 2012.
33. Silverio K, Davidson K, James R, Adams A, Foster BL, Nociti F, Somerman MJ, and Moon R. The Wnt/ β -catenin pathway regulates Bmp2-mediated differentiation of dental follicle cells along a cementoblast / osteoblast pathway. Journal of Periodontal Research, 47(3):309-312, 2012.
34. Cao Z, Zhang H, Zhou X, Han X, Ren Y, Gao T, Xiao Yin, de Crombrugghe B, Somerman MJ, and Feng JQ. Genetic Evidence for the Vital Function of Osterix in Cementogenesis. J Bone and Mineral Research: 5, 1080-1092, 2012.
35. Sun J, Orapin H, Bumgarner R, Lakely B, Somerman MJ and Zhang H. Laser capture microdissection (LCM) enables cellular and molecular studies of tooth root development. International Journal of Oral Sciences, 4, 7-13, 2012.
36. Foster BL, Nagatomo KJ, Nociti FH, Fong H, Dunn D, Tran AB, Wang W, Narisawa S, Millán JL, and Somerman MJ. Central role of pyrophosphate in acellular cementum., PLoS ONE, 7(6), e38393, 2012.
37. Rodrigues TL, Foster BL, Silverio KG, Martins L, Casati MZ, Sallum EA, Somerman MJ, Nociti FH. Hypophosphatasia-associated deficiencies in mineralization and gene expression in cultured dental pulp cells obtained from human teeth.. J Endodontics: 38(7):907-912, 2012.

MEMO

A global approach to the challenge of orofacial clefting

Peter A. Mossey, B.D.S., Ph.D.

Professor of Craniofacial Development and Dentofacial Orthopaedics,
University of Dundee

Background : Birth defects in general and craniofacial anomalies, the most common of which is non syndromic cleft lip and /or palate CL/P, have emerged as a component part of the World Health Organisation's Non Communicable Diseases (NCD) agenda; and it was agreed at the 63rd World Health Assembly in May 2010 that due to the rising tide of birth defects, these should be prioritised in health policy by member states around the world. This has led to the inclusion of CL/P in the subsequent Global Burden of Disease (GBD) agenda and it has become apparent that in the absence of intervention there is a very high neo-natal mortality associated with cleft lip and palate in the developing world. There is also convincing evidence that death and disability due to congenital malformations has been grossly under represented in the GBD hitherto and this issue requires concerted global attention.

Global epidemiology : in consensus meetings co-ordinated by the WHO between 2000 and 2004, efforts to co-ordinate the descriptive epidemiology of CL/P around the world has resulted in a meta analytic approach co-ordinated by the International Clearing House for birth defects (ICBD) based in Rome, Italy. This has collected information from registries around the world in a format that allows data comparison and an estimate of global birth prevalence of CL/P; and also establishes an infrastructure that facilitates the planning of health services to meet the burden imposed by orofacial cleft care.

Global oral health inequalities research network (GOHIRN) : The IADR have established a new overarching network that identifies the importance of oral diseases as a major public health issue and that major inequalities in oral health exist both within and between countries. This group will work with major international stakeholders to address issues such as the Millennium Development Goals and work to address oral health inequalities using a "common risk factor" approach alongside other major non-communicable diseases such as cardiovascular disease, cancers, diabetes, obesity and respiratory disorders. The objectives will be to influence clinicians, educators, policy makers, researchers and research funders around the world.

European cleft research : for the last decade significant advances have been made around the world in (a) improving the evidence base for best treatment protocols in the management of infants born with CL/P and (b) significant advances in knowledge of genetic and environmental aetiology. A series of European initiatives from SCANDCleft, EUROCleft, the European Science Foundation (ESF), EUROCRAN and now EUROCleftNet have made a significant contribution and present future opportunities in the co-ordination of global research efforts and aim towards establishing standardised research protocols which will ultimately allow inter-centre comparisons.

Genomics approach : This presentation will provide the compelling evidence for a strong genetic component in non-syndromic CL/P and will describe the genetic approaches for the identification of causative genes. This will include selected candidate gene association studies, linkage studies, genome wide association studies (GWAS), array comparative genomic hybridisation (CGH) and informative animal models. Unique insights into the molecular pathogenesis of CL/P through candidate gene pathways will include interferon regulatory factor 6 (IRF6), ventral anterior homeobox 1 (VAX 1) and the MSX1 and BMP signalling pathways.

In the context of determining the genetic aetiology of clefts, it is also important to consider the implications of heterogeneity, cleft sub-phenotypes, inter-population differences and gene / environment interaction and strategies for future studies to enhance understanding of the molecular pathogenesis of CL/P through functional genomics, epigenetics, gene expression and considering an array of approaches to identify rarer missense mutations in the pathogenesis of common, complex diseases.

The clinical implications of an improved characterisation of genetic aetiology in terms of prevention will be discussed.

CURRICULUM VITAE

Education

- BDS 1983 Dentistry, University of Dundee
- PhD University of Glasgow 1994 Craniofacial Genetics
- FDS, RCS Royal College of Surgeons of Edinburgh 1987 Dentistry
- D Orth, RCS Royal College of Surgeons of Edinburgh 1987 Orthodontics
- M Orth, RCS Royal College of Surgeons of England 1988 Orthodontics
- FFD RCSI, Royal College of Surgeons in Ireland, 1988 Orthodontics
- FDS RCPS, Royal College of Physicians and Surgeons of Glasgow, 2005 Dentistry
- ILTM 2001, Membership of the Higher Education Academy

Position

1983 - 1983	Associate General Dental Practice Fermanagh, Northern Ireland
1984 - 1984	House Officer Orthodontics, Dundee Dental Hospital Dundee, Scotland
1984 - 1985	Senior House Officer Oral Surgery, Dundee Dental Hospital. (Resident) Dundee, Scotland
1985- 1987	Registrar, Orthodontics Victoria Hospital Kirkcaldy, Fife, Scotland
1987 - 1989	Registrar, Orthodontics Edinburgh Dental Hospital Edinburgh, Scotland
1989 - 1989	Senior Registrar (Locum), Orthodontics, Royal Victoria Hospital Bournemouth
1989 - 1994	Lecturer/Hon. Senior Registrar Orthodontics, Glasgow Dental Hospital and School Glasgow, Scotland
1994 – 1997	Lecturer in Orthodontics Dundee University Dental School Dundee, Scotland
1997 – 2000	Senior Lecturer Dundee University Dental School Dundee, Scotland
2000 – 2003	Reader Dundee University Dental School Dundee, Scotland
2003 – present	Professor of Craniofacial Development and Dentofacial Orthopaedics Dundee University Dental School Dundee, Scotland

Publications

1. Mossey, P.A. (1997)
   Chapter: "Clinical skills assessment in Dentistry"
   In "Guide to Assessment of Students Progress and Achievements" Editors: Godfrey, J and Heylings, D.
   Publication produced by the Medical and Dental Education Network as a Study Guide for circulation to all UK Medical and Dental Schools in March 1997.
2. Mossey, P.A. (1997)
   Chapter: "Structured Clinical Operative Tests"
   Accepted for publication in "Innovations in Clinical Teaching"
   Dennick, R.G.(Ed.) SEDA Publications, Birmingham, March 1997.
3. Mossey, P.A. and Gilmour, M. (Eds) (1998)
   Report of proceedings of European Science Foundation Exploratory conference, Dundee, September 1997.
   "Interaction of genes and maternal nutrition in orofacial clefting: aetiology, pathogenesis and exploration of preventive strategies". University of Dundee, Dental Health Services Research Unit. ISBN 1899809 171.
4. Mossey, P.A. and Stirrups, D. R. Eds (1998)
   Core competencies in Dentistry: Exploring the issues
   Report of proceedings of MADEN meeting and the first meeting in UK to discuss clinical competencies in the Dental curriculum
   Publication produced by the Medical and Dental Education Network (June 1998) ISBN 0 9531025 13
5. Mossey, P. A., Newton, J.P., Mason, A. and Stirrups, D. R. Eds (1999)
   Clinical competencies in Dentistry: "Assessing in competence"
   (Report of proceedings of December 1998 Medical and Dental Education Network (MADEN) conference)
   Publication produced by Queen Mary and Westfield College (September 1999) ISBN 0 9531025 48
6. Ball, G., McLennan, G., McManners, J., Mossey, P.A., Raine, P. and Reynolds, B. (1999)
   Scottish Needs Assessment Programme (SNAP) document entitled "Cleft Lip and Palate" submitted to the Scottish Office in November 1998. Recommendations currently being implemented in the Managed Clinical Network for Orofacial Clefts in the Scottish National Health Service.
   SNAP Reports, Scottish Office, Nov. 1998
7. Mossey, P.A., Trindade, I.E.K., Shaw, W.C., and de Souza Freitas, J.A. Eds. (1999)
   International Task Force on Craniofacial Anomalies Conference Report "Developing strategies for cost effective treatment and preventive interventions for Cleft Lip and palate". Conference held in Bauru, Sao Paulo, Brazil, October 2-5, 1998. ISBN No. 85-87666-01-0
8. Mossey, P.A. Ed. (1999)
   European Science Foundation (ESF), 2nd International Collaborative Workshop, Strasbourg 20th/21st February,

1999 "Development of methods to investigate the interaction between nutritional, environmental and genetic factors in early human development: demonstration project in orofacial clefts" Conference Report, University of Dundee, 2000. ISBN 1899809 194

9. Mossey, P.A. Ed. (2000)
European Science Foundation 3rd International Collaborative Workshop, Dundee, 19th-20th May 2000. Gene-environment interaction in early human development: demonstration project on orofacial clefts. Conference Report, University of Dundee, 2001. ISBN 1899809 216
10. Mossey, P.A. and Little, J. (2002)
Chapter 12: "Epidemiology of oral clefts: an international perspective". In Wyszynski DF (Ed) Cleft lip and palate. From origin to treatment. pp127-158. Oxford University Press (August 2002) ISBN: 0-19-513906-2
11. NOTE: This book has won the 2003 AAP/PSP award for excellence in scholarly publishing within clinical medicine. Those initials stand for American Association of Publishers/Professional and Scholarly Publishing.
12. Authors/Eds Mossey, P.A., Munger, J. C. and Shaw, W.C. Eds (2002)
Global Strategies Towards Reducing the Health Care Burden of Craniofacial Anomalies
WHO Reports, Human Genetics Programme: Management of Noncommunicable Diseases: International Collaborative Research on Craniofacial Anomalies, WHO publications, Geneva, Switzerland. ISBN 92 4 159038 6
13. Authors/Eds: Mossey, P.A. and Castillia, E. (2003)
Global Registry and Database on Craniofacial Anomalies
WHO Reports, Human Genetics Programme: International Collaborative Research on Craniofacial Anomalies, WHO publications, Geneva, Switzerland. ISBN 92 4 159110 2
14. Authors/Eds: Mossey, P.A., Holsgrove, G., Stirrups, D.R., and Davenport, E. (2006)
Essential Skills for the New Dentist – Oxford University Press (OUP) Published April 2006 ISBN 0-19-852619-9
15. Chief Editor: Mossey, P.A. (2006)
Addressing the global challenges of craniofacial anomalies
WHO Reports, Human Genetics Programme: Management of Noncommunicable Diseases: International Collaborative Research on Craniofacial Anomalies, WHO publications, Geneva, Switzerland. ISBN 92 4 159490 X
16. Bearn, D. R. and Mossey, P. A. (2011)
Chapter 3: "Aetiology and Malocclusion". In Orthodontics, Principles and Practice. Editors: Gill, D. S., Naini, F. B. and Dental Update. Wiley-Blackwell, ISBN-13: 978-1-4051-8747-3
17. Mossey, P.A., and Modell, B. (2012)
Chapter 1: "Epidemiology of Oral Clefts 2012: An International Perspective". In "Cleft Lip and Palate. Epidemiology, Aetiology and Treatment" Editor Cobourne, M.T. Frontiers of Oral Biology, Vol. 16, p1-18. ISBN 978-3-318-02107-3

MEMO

Clinical molecular diagnostics of congenital malformation syndrome using in-solution hybridization-based enrichment and massively parallel sequencing

Kenjiro Kosaki, M.D., Ph.D., F.A.C.M.G.

Center for Medical Genetics,
Keio University School of Medicine

As catalogued in genetic textbooks like "Smith's Recognizable Patterns of Human Malformation" and "Inborn Errors of Development" several hundreds of genes have been shown to cause human congenital disorders. The identification of these causative genes has offered us a wonderful opportunity to delineate the molecular basis of these disorders. Molecular diagnosis offers valuable information to the patients and their families in terms of prognosis, preventing complications, and providing accurate genetic counseling. Theoretically, any gene can be tested by the direct sequencing of PCR products amplified from the patient's genomic DNA. However, identifying pathogenic mutations has been difficult when the causative gene has a large number of exons. In such cases, direct sequencing is expensive, technically demanding, and time consuming. Recently, next generation sequencing [NGS] has been introduced. We are currently developing a sensitive and specific mutation analysis system covering most of the genes enlisted in the Smith's textbook with targeted enrichment and massively parallel sequencing. In this symposium, we would like to share our strategies with the audience.

Generally speaking, there are two NGS approaches for diagnostic sequencing in genetic disorders: PCR-based targeted enrichment followed by long-read sequencing and in-solution hybridization-based enrichment followed by short-read sequencing. In-solution hybridization-based enrichment was adopted because PCR method does not allow multiplex enrichment of thousands of sequences. A proof-of-principle experiment was performed on thirty patients with neurofibromatosis type was performed and the ability of NGS protocol to identify likely disease-causing mutations was demonstrated in comparison with the current methodology, Sanger sequencing. Our diagnostic protocol illustrates a drastic change in the clinical molecular diagnostics of congenital malformation syndromes and provides a paradigm for other genetic conditions.

CURRICULUM VITAE

Education

Undergraduate	Keio University, 1985, Tokyo Japan
Graduate	Keio University, M.D., 1989, Tokyo Japan
	Keio University, Doctor of Medical Science (D.M.Sc.), 1998, Tokyo, Japan
Licensure	Physician's license in Japan, No.326408
	ECFMG Certificate, No. 0-434-038-6
Board Certification	Japan Pediatric Society, 1993
	American Board of Medical Genetics (M.D. Clinical Genetics), 1996

Position

1989 - 1993	Resident in Pediatrics Keio University Hospital, Tokyo Japan
1993 - 1997	Fellow in Genetics/Dysmorphology University of California, San Diego San Diego, CA, USA
1997 - 1998	Fellow in Developmental Pathology Baylor College of Medicine Houston, TX, USA
1998 - 1999	Instructor of Medical Genetics Department of Pediatrics Keio University School of Medicine Tokyo, Japan
1999 - 2003	Chief, Division of Medical Genetics and Dysmorphology Assistant Professor of Pediatrics Keio University School of Medicine Tokyo, Japan
2003 - 2011	Chief, Division of Medical Genetics and Dysmorphology Associate Professor of Pediatrics Keio University School of Medicine Tokyo, Japan
2012 - Present	Director, Center for Medical Genetics Professor of Medical Genetics Keio University School of Medicine Tokyo, Japan

Award and Honors

1993	Japan-North America Medical Exchange
1994	Foundation Fellowship Award.
1995	San Diego Children's Hospital Research Award.
1998	Howard Hughes Medical Institute Postdoctoral Research Fellowship for Physicians

Publications

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MEMO

The Osteocyte as a Regulator of Bone Remodeling

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As the skeleton matures, the ratio of osteocytes to other bone cells such as osteoblasts and osteoclasts increases to approximately 90-95% osteocytes in the adult skeleton. The osteocyte is a terminally differentiated cell localized within mineralized matrix thereby unable to divide while within this environment. Osteocytes can remain viable for decades in the bone matrix. To remain viable, these cells are exposed to bone fluid which provides nutrients but also allows the osteocyte to send molecular messages to other cells. Osteocytes are connected to each other and cells on the bone surface and the marrow space via their dendritic processes representing another mode of osteocyte communication. The morphology and other properties allow this cell to be exquisitely sensitive to mechanical loading and unloading which is translated into signals such as sclerostin or RANKL to regulate osteoblastic bone formation and osteoclastic bone resorption. Many of the effects of osteotropic factors such as parathyroid hormone are mediated through osteocytes. Therefore, the osteocyte is a major regulator of bone modeling and remodeling. Effects of aging on the skeleton may be through changes in the osteocyte. Maintaining or optimizing osteocyte function may abrogate bone loss and maintain bone mass.

CURRICULUM VITAE

Education

1973 B.A . (Biology) University of Texas, Austin, TX,
1984 Ph.D. (Immunology/Microbiology) Medical University of South Carolina, Charleston, SC.

Position

1993-1998	Associate Professor, Department of Biochemistry; University of Texas Health Science Center, San Antonio, Texas
1992-1998	VA Research Investigator, Audie Murphy Veterans Administration, Medical Center Hospital, San Antonio, TX
1992-1998	Associate Professor, Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, TX
1992-1998	Associate Professor of Medicine, Department of Medicine; University of Texas Health Science Center, San Antonio, TX
1998-2001	Professor of Medicine, Departments of Medicine, Biochemistry, and Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, TX
2001-present	Lefkowitz Professor of Oral Biology and Director of the Bone Biology Research Program, School of Dentistry, University of Missouri at Kansas City, Kansas City, MO.
2009-present	Director, UMKC Center of Excellence in the Study of Dental and Musculoskeletal Tissues
2009-present	UMKC Vice Chancellor for Research and Economic Development Interim

Award and Honors

1996-1999	Council Member, American Society for Bone and Mineral Research
1997-2001	Executive Board, Association of Biomolecular Resource Facilities
1998-2000	President, Association of Biomolecular Resource Facilities
1999-2004	NIH NIDCR Board of Scientific Counselors
2001-2004	Chair, NIDCR Board of Scientific Counselors
2001-2004	FASEB Board of Directors, non-voting
2001- 2004	Vice-Chair, National Osteoporosis Foundation, Scientific Advisory Board
2004-2005	International Osteoporosis Foundation
2005	University of Missouri Curator’ s Professor
2006	Distinguished Scientist Award in Mineralized Tissue IADR/AADR
2006	“RIB” Award, Sun Valley Workshop
2011-present	NIH NIAMS Council
2011	President-elect, American Society for Bone and Mineral Research

Publications

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MEMO

New biological insights of tooth movement in response to mechanical stress

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Orthodontic tooth movement is a dynamic biological phenomenon, which is triggered by the loss of equilibrium in the mechanical environment surrounding the tooth upon orthodontic force application. To date, it is widely accepted that periodontal tissue, including cementum, periodontal ligament (PDL) and alveolar bone, play indispensable roles in tooth movement due to its unique biomechanical, cellular, and molecular natures, although the precise underlying mechanisms are yet to be fully elucidated.

To investigate the involvement of periodontal tissue in mechanical stress, we prepared an experimental tooth movement model in vivo and demonstrated that the forced mechanical stress stimulated the transcription of periostin, which is a 90 kDa secreted extracellular matrix (ECM) implicated in cellular adhesion and migration. In contrast, occlusal hypofunction decreases the expression of both periostin and twist, a basic helix-loop-helix transcription factor, which binds to periostin promoter to stimulate its transcription.

On the other hand, osteocytes are thought to be the major bone cell type responsible for sensing mechanical strain and coordinating signals of bone resorption and formation. Recently it has been reported that targeted deletion of osteocytes by diphtheria-toxin (DT) injection into the mice expressing DT receptor specifically in osteocytes results in bone loss, whereas the bone mass does not decrease in response to unloading experiment by tail suspension of these mice. To further elucidate the roles of osteocytes in bone remodeling triggered by mechanical loading/unloading, we conducted tooth movement in the osteocyte-ablated mice and compared the distance of tooth movement as well as the histological changes between the groups with or without intraperitoneal DT injection. The distance of tooth movement in DT-injected mice was significantly smaller than that in DT-uninjected mice on day 12. Interestingly, the number of TRAP-positive osteoclasts decreased in DT-injected mice after day 8, compared with that in DT-uninjected mice. These results suggest that osteocytes are involved in osteoclast formation in response to the change of mechanical environment, and that osteocytes play a crucial role in mechanical stress-induced bone remodeling during tooth movement.

CURRICULUM VITAE

Education

1980-1986	Tokyo Medical and Dental University
1986	D.D.S. (Doctor of Dental Surgery)
1986-1990	Tokyo Medical and Dental University Graduate School, 2nd. Department of Orthodontics
1990	Ph.D. (Doctor of Philosophy, Tokyo Medical and Dental University)

Position

1990-1992	Senior resident, 2nd Department of Orthodontics, Tokyo Medical and Dental University, Tokyo, Japan
1992-1994	Post Doctoral Fellow, Department of Medicine, Division of Endocrinology and Metabolism, University of Texas Health Science Center at San Antonio, San Antonio Texas, U.S.A.
1994-1997	Instructor, 2nd. Department of Orthodontics, Tokyo Medical and Dental University, Tokyo, Japan
1997	Junior Associate Professor, 2nd Department of Orthodontics, Tokyo Medical and Dental University
1998- 2007	Professor and Chairman, Department of Orthodontics and Dentofacial Orthopedics, The University of Tokushima
2007–present	Professor and Chairman, Department of Maxillofacial Orthognathics, Graduate School, Tokyo Medical and Dental University
2011–present	Director of Dental School, Tokyo Medical and Dental University

Award and Honors

1993 Young Investigator Award, Fifteenth Annual Meeting of the American Society for Bone and Mineral Research, Tampa, Florida

Publications

1. Izawa, T., Ishimaru, N., Moriyama, K., Kohashi, M., Arakaki, R., Hayashi, Y.: Crosstalk between RANKL and Fas signaling in dendritic cells controls immune tolerance. Blood 110(1): 242-250 (2007)
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6. Sato-Wakabayashi M, Inoue-Arai MS, Ono T, Honda E, Kurabayashi T, Moriyama, K. Combined fMRI and MRI movie in the evaluation of articulation in subjects with and without cleft lip and palate. Cleft Palate Craniofac J. 45(3): 309-14, 2008
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9. Okudaira M, Ono T, Kawamoto T, Moriyama, K. Three-dimensional analysis of lower lip movement during articulation in subjects with mandibular prognathism. Orthod Waves. 67(3): 93-103, 2008
10. Okudaira M, Kawamoto T, Ono T, Moriyama, K. Soft-tissue changes in association with anterior maxillary osteotomy: a pilot study. Oral Maxillofac Surg. 12(3):131-8, 2008
11. Miraoui H, Oudina K, Petite H, Tanimoto Y, Moriyama K, Marie PJ. Fibroblast growth factor receptor 2 promotes osteogenic differentiation in mesenchymal cells via ERK1/2 and protein kinase C signaling. J Biol Chem. 284(8): 4897-904. 2009
12. Inoue-Arai MS, Ono T, Honda E, Kurabayashi T, Moriyama K. Motor coordination of articulators depends on the place of articulation. Behav Brain Res. 199(2): 307-16. 2009
13. Yagi Y, Suda N, Yamakoshi Y, Baba O, Moriyama K. In vivo application of amelogenin suppresses root resorption.

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14. Hiasa M, Abe M, Nakano A, Oda A, Amou H, Kido S, Takeuchi K, Kagawa K, Yata, Hashimoto T, Ozaki S, Asaoka K, Tanaka E, Moriyama K, Matsumoto T. GM-CSF and IL-4 induce dendritic cell differentiation and disrupt osteoclastogenesis through M-CSF receptor shedding by up-regulation of TNF- α converting enzyme (TACE). Blood, 114(20): 4517-4526. 2009.
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17. Aoki A, Moriyama K, Kawamoto T, Aoki K, Inokuchi T, Kudoh A, Nagahama K, Baba Y, Suzuki S, Ohya K. Amount of bone lengthening affects blood flow recovery and bone mineralization after distraction osteogenesis in a canine cleft palate model. Cleft Palate Craniofac J. 47(3): 303-313 2010.
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35. Qiu L, Haruyama N, Suzuki S, Yamada D, Obayashi N, Kurabayashi T, Moriyama K. Accuracy of orthodontic miniscrew implantation guided by stereolithographic surgical stent based on cone-beam CT-derived 3D images. Angle Orthod. 2011 (in press)
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MEMO

Mechanisms of tooth renewal

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The capacity for tooth renewal is quite limited in mammals. The major mechanism of tooth renewal in vertebrates is tooth replacement and in fish and reptiles teeth can be replaced continuously. However, in mammals the deciduous dentition, or part of it, can be replaced by a second set of functional teeth, and there is maximally one round of tooth replacement. The mechanisms of tooth replacement have remained largely unknown mainly because mice do not replace their teeth. We have used the ferret as a model animal and performed morphological and molecular analyses of tooth replacement. The replacement teeth are formed successionally from their deciduous predecessors. They develop from the so called dental lamina associated with the outer enamel epithelium of the preceding tooth. We have recently localized putative stem/progenitor cells in the dental lamina epithelium during tooth replacement. These observations have also indicated that there may be a capacity for continued tooth replacement in mammals.

In addition to replacement, some mammalian teeth can be renewed by continuous growth which compensates for tooth wear. We have examined the mechanisms of the continuous growth of the mouse incisor. Our results together with work from other laboratories have indicated that there is a stem cell niche in the proximal end of the incisor in the so called labial cervical loop. The maintenance and differentiation of the epithelial stem and progenitor cells is regulated by a complex network of stimulatory and inhibitory molecules affecting Fgf, Tgfbeta, Bmp, Wnt and Hh signal pathways. The stem cells responsible for tooth renewal have been identified in the cervical loop. We have recently demonstrated that these cells express the stem cell marker Sox2 and that the Sox2 positive cells contribute to all epithelial cell lineages of the incisor. Taken together, the current data indicate that tooth renewal is based on epithelial stem and progenitor cells which seem to have a conserved common genetic signature in different types of tooth renewal, and that their maintenance and differentiation is regulated by a network of same conserved signal pathways that regulates tooth morphogenesis.

CURRICULUM VITAE

Education

1972 Graduation from Dental School (DDS), Medical Faculty University of Helsinki
1975 Doctor of Odontology (Dr.Odont , PhD) University of Helsinki
1978-1979 Visiting Associate (postdoc), Laboratory of Developmental Biology and Anomalies, NIDR, Bethesda, MD, USA1980 Docent (Lecturer) in Developmental Biology University of Helsinki
1983 Specialist's rights in orthodontics Finland

Position

1973-1976 Research Associate, the Academy of Finland
1976-1978 Instructor, Dept. of Pedodontics and Orthodontics, University of Helsinki
1979-1983 Instructor, Dept. Pedodontics and Orthodontics, Univ. Helsinki
1983-1990 Scientist, Academy of Finland
1990-2004 Professor and Chairman, Department of Pedodontics and Orthodontics, University of Helsinki

Award and Honors

1987 Pohjola Prize, Finnish Dental Society and Finnish Dental Association
1993 Distinguished Scientist Award in Craniofacial Biology, Int.Assoc.Dent.Res.(IADR)
1994 Finnish Academy of Science and Letters (Suom. Tiedeakat.), invited member
1995 Thuréusprize , Umeå university
1997 City of Helsinki Science Award
1997 Honorary Doctor in Odontology, University of Göteborg
1997 International Prize, Swedish Dental Society
1998-2003 Academy Professor, Academy of Finland
1999 Anders Jahre Prize in Medicine, Oslo University
2000 Acta Odontologica Scandinavica Prize for " Excellent contribution to dental research"
2000 EMBO, invited member
2002 Honorary Doctor in Odontology, University of Copenhagen
2004 Honorary Doctor in Science, McGill University, Montreal
2005 Professor of the Year, Finnish Association of University Professors
2005 Sheldon Friel Memorial Lecturer, European Orthodontic Society
2005 Finnish Society of Sciences and Letters (Suom. Tiedeseura), invited member
2005 Honorary Doctor, Katholieke Universiteit Leuven, Belgium
2005-2010 Honorary Professor in Craniofacial and Dental Genetics, University of Copenhagen
2006 William J. Gies Award for best paper in J.Dent.Res., IADR/AADR
2008 Chair, Gordon Conference on "Craniofacial Morphogenesis & Tissue Regeneration
2008-2009 President, European Orthodontic Society
2008 Honorary Doctor, University of Debrecen, Hungary
2008 Isaac Schour Memorial Award, IADR
2008 Honorary Doctor, University of Oslo
2009 AAAS Fellow
2009 Valkhof Chair (Visiting Professor), Radboud University Nijmegen, The Netherlands
2009 Apollonia Prize, Finnish Dental Society
2010 Paul Goldhaber Award, Harvard School of Dental Medicine
2010 Honorary Doctor, Karolinska Institutet, Stockholm
2011 Professor EJ Nyström Award, Finnish Society of Sciences and Letters

Publications

199 original articles in peer reviewed journals
105 review articles and book chapters
h index: 71

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Role of dental epithelium- stem cell interactions during dental cell differentiation

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Division of Pediatric Dentistry,
Tohoku University Graduate School of Dentistry

Tooth morphogenesis is characterized by reciprocal interactions between the dental epithelium and mesenchymal cells derived from the cranial neural crest, which result in the formation of the proper number and shapes of teeth. Multiple extracellular signaling molecules, including BMPs, FGFs, WNTs, and Shh, have been implicated in these interactions for tooth development. The epithelial cells then subsequently give rise to enamel-forming ameloblasts, while the dental pulp stem cells (DPSCs) form dentin-forming odontoblasts and dental pulp cells. Epithelial-mesenchymal interactions regulate the growth and morphogenesis of ectodermal organs such as teeth. The interactions between DPSCs and the epithelium have not yet been clearly elucidated. Dental pulp stem cell line (SP) that was comprised of enriched side population cells and that displayed a multipotent capacity to differentiate into odontogenic, osteogenic, adipogenic, and neurogenic cells. We then analyzed interactions between SP cells and cells from the rat dental epithelial cell line (SF2). SP cells differentiated into odontoblasts that expressed dentin sialophosphoprotein when cultured with SF2 cells. This differentiation was regulated by BMP-2 and -4 and was inhibited by the BMP antagonist Noggin.

Stem cell research has identified and established several types of stem cells, including induced pluripotent stem (iPS) cells, which are generated from a variety of somatic cell types via introduction of transcription factors that mediate pluripotency and has great potential for tissue-specific regenerative therapies. Further, ameloblasts secrete enamel-specific extracellular matrices, including ameloblastin (AMBN), and these are lost upon tooth eruption following transformation and apoptosis. This makes it impossible to repair or replace damaged enamel in an erupted tooth. Since ameloblasts are lost upon tooth eruption, identifying alternative sources of these cells becomes important. Since dental epithelial cells, which differentiate into enamel secreting ameloblasts, disappear in adults after tooth development, our strategy to create ameloblasts from mouse iPS cells may have direct application in regenerative tooth medicine. We found that mouse iPS cells cultured with mitomycin-C treated SF2 cells displayed an epithelial cell-like morphology. These cells expressed the epithelial cell markers p63 and cytokeratin-14, and the ameloblast markers AMBN, but did not express the endodermal cell marker Gata6 or the mesodermal cell marker brachyury. This is the first demonstration of differentiation of iPS cells into ameloblasts through interactions with the dental epithelium.

A number of factors are thought to give iPS cells the capacity for direct or indirect differentiation into ameloblasts. Possible direct effectors include gap junctions, intercellular binding molecules, adhesion factors and extracellular matrices secreted by dental epithelium. Growth factors might also be involved, because conditioned medium from SF2 cells induced AMBN expression in iPS cells. AMBN is also a candidate factor for dental cell differentiation of iPS cells, as SF2 cells expressing low levels of AMBN did not induce the differentiation of iPS cells. AMBN has diverse functions in various cellular physiologies, such as cell growth, differentiation, cell polarization and attachment, although the detailed mechanisms of AMBN signaling require additional investigation. AMBN-null mice display severe enamel hypoplasia due to impaired dental epithelial cell proliferation, polarization and differentiation into ameloblasts, as well as loss of cell attachment activity with immature enamel matrix. These results suggest that AMBN is necessary for both in vivo and in vitro ameloblast differentiation.

Co-culturing with dental epithelial cells appears to induce stem cell differentiation that favors an odontogenic cell fate and this might be a useful approach in tooth bioengineering.

CURRICULUM VITAE

Education

1988 Graduated from Kurashiki-Amaki High School (Okayama)
1994 D.D.S. Nagasaki University School of Dentistry
2000 Ph.D. (Dr. of Dental Science) Nagasaki University School of Dentistry

Position

1994-1997 Instructor, Nagasaki University School of Dentistry (Department of Pediatric Dentistry)
1997-2000. Research fellow of the Japanese Society for the Promotion of Science
2000–2003 Instructor, Nagasaki University School of Dentistry (Department of Pediatric Dentistry)
2000-2002 Visiting Fellow, Molecular Biology Section, Craniofacial Developmental Biology and Regeneration Branch, National Institute of Dental and Craniofacial Research (NIDCR), National Institute of Health (NIH) (Chief. Yoshihiko Yamada)
2003-2004 Assistant professor, Nagasaki University School of Dentistry (Department of Pediatric Dentistry)
2004-2007 Associate professor, Kyushu University, Faculty of Dental Science (Section of Pediatric Dentistry)
2007- Professor, Tohoku University Graduate School of Dentistry (Division of Pediatric Dentistry)

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Tooth Regenerative Therapy as a Future Dental Treatment

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Graduate School of Innovation Studies (Intellectual Property Management),
Tokyo University of Science

Oral functions such as enunciation, mastication and occlusion, are an important aspect of good health and quality of life. These oral functions are achieved in harmony with the teeth, masticatory muscles and the temporomandibular joint under the control of the central nervous system. Damage, loss and the onset of disease in teeth, including dental caries and periodontal disease, thus cause fundamental problems for oral functions and associate health issues. Various therapies for these dental disorders have been established using artificial materials such as root canal treatments and prosthesis procedures. Furthermore, after the loss of a tooth, the tooth functions are traditionally restored by replacement with an artificial tooth, the use of a bridge, and also osseo-integrated dental implants.

To restore the partial loss of organ functions and to repair damaged tissues, an attractive concept in regenerative therapy is stem cell transplantation into various tissues and organs. Dental tissue-stem cells have been identified and will have utility for the development of stem cell transplantation therapy to restore the partial loss of organ function and thereby achieve dental tissue repair such as caries and periodontal diseases. The ultimate goal of regenerative therapy is to develop fully functioning bioengineered organs that can replace lost or damaged organs following disease, injury or aging. For the success of tooth replacement regenerative therapy, a bioengineered tooth must be capable of erupting in the lost tooth region in an adult oral environment and achieve full functionality, including sufficient masticatory performance, biochemical cooperation with the periodontal tissues and proper responsiveness to noxious stimulations via neurons in the maxillofacial region.

To generate whole tooth, the approach is to recreate organogenesis through the epithelial-mesenchymal interactions that occur in the developing embryo and thereby develop fully functioning bioengineered organs from the resulting bioengineered organ germ generated via three-dimensional cell manipulation using immature stem cells in vitro. We previously developed a bioengineering method for forming a three-dimensional organ germ in the early developmental stages, termed the 'bioengineered organ germ method' (Nature Methods 4, 227-230, 2007). This method was adoptable to generate various organ germs such as tooth, hair follicles (Nature Commun. 3, 784, 2012, Sci. Rep. 2, 424, 2012), salivary gland and lacrimal gland. Recently, we reported fully functioning bioengineered tooth replacements after the transplantations of a bioengineered tooth germ (PNAS 106, 13475-13480, 2009) or mature tooth unit comprising the bioengineered tooth and periodontal tissues such as periodontal ligament and alveolar bone (PLoS ONE, 6, e21531, 2011) into a lost tooth region. The bioengineered molar tooth germ could erupt and reach occlusion with an opposing tooth after transplantation in the mouse adult oral environment. The bioengineered tooth unit, which was controlled for length and shape, was successfully transplanted into a properly-sized bony hole in the alveolar bone through bone integration by recipient bone remodeling. These bioengineered teeth displayed physiological tooth functions such as mastication, periodontal ligament function for bone remodeling and responsiveness to noxious stimulations. Tooth regenerative therapy has the potential to provide essential functional recovery and ultimately replace the current artificial materials used in dental treatments.

In this presentation, I would like to talk and discuss about the strategies and recent progress of the research and development for the establishment of tooth regenerative therapies.

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Education

1984	BSc, Faculty of Science, Niigata University, Japan
1986	MSc, Graduate School of Science, Niigata University, Japan
1989-1992	Graduate School of Science, Kyushu University, Japan
1993	PhD, Graduate School of Science, Niigata University, Japan

Position

1986-1989	Researchers, Central Research Laboratories, Yamanouchi Pharmaceutical Co Ltd.
1993-2000	Senior Researcher, Pharmaceutical Frontier Research Laboratory, JT Inc.
2000-2007	Associate Professor, Faculty of Industrial Science and Technology, Tokyo University of Science
2008	Visiting Professor, Louis Pasteur University, French
2007-Present	Professor, Graduate School of Industrial Science and Technology, Tokyo University of Science
2009-Present	Professor, Research Institute of Science and Technology, Tokyo University of Science
2009-Present	Visiting Professor, Tokyo Dental College, Japan
2010-Present	Professor, Graduate School of Innovation Studies (Intellectual Property Management), Tokyo University of Science

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Amelogenins: Multifaceted enamel matrix proteins in hard tissue biology

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Amelogenins are the most abundant extracellular matrix proteins secreted by ameloblasts during tooth development and are important for enamel formation. Recently, amelogenins have been detected not only in ameloblasts, which are differentiated from the epithelial cell lineage, but also in other tissues, including mesenchymal tissues at low levels, suggesting that amelogenins possess other functions in these tissues.

In the first part of this presentation, the emerging evidences for the additional roles of full-length amelogenin (M180) and leucine-rich amelogenin peptide (LRAP) in mesenchymal cells, such as chondrocytes and osteoblasts, will be introduced.

Experiments utilizing a chondrogenic cell line, ATDC5, revealed that the supplement of recombinant mouse M180- or LRAP-protein into chondrogenesis-stimulating medium increased alkaline phosphatase (ALP) activity and glycosaminoglycan secretion at 14 and 21 days of culture, respectively, as compared with the control. Quantitative PCR (Q-PCR) analysis indicated that LRAP increased the gene expression levels of Runx2, Col2a1, and Aggrecan at 7 days of differentiation. Moreover, both M180 and LRAP significantly increased the gene expression levels of ALP, Aggrecan, Col10a1, and Osteopontin at 28 days of culture. BrdU assay and Q-PCR analysis for Wnt signalling indicated that both M180 and LRAP reduced the cell proliferation, but induced the cell differentiation possibly through altered non-canonical Wnt signalling.

Interestingly, amelogenin null mice showed increased osteoclastogenesis and root resorption in periodontal tissues. Recombinant amelogenin proteins suppress osteoclastogenesis in vivo and in vitro, suggesting that amelogenin, especially LRAP, was involved in preventing idiopathic root resorption by regulating osteoclastogenesis (odontoclastogenesis). To identify extended functions of LRAP in bone formation and resorption, we then engineered transgenic (TgLRAP) mice using a murine 2.3kb α 1(I)-collagen promoter to drive expression of LRAP. Although LRAP expression did not affect bone structure in these mice, the ovariectomized (OVX) TgLRAP mice resisted bone loss induced by ovariectomy resulting in higher bone mineral density compared to OVX wild type (WT) mice. The quantitative analysis of calcein intakes indicated that the OVX TgLRAP mice had increased bone formation compared to sham operated WT mice. The parameters for bone resorption in tissue sections showed increased number of osteoclasts in OVX WT, but not in OVX TgLRAP compared to sham operated WT or TgLRAP mice. in vitro calvarial cell cultures isolated from the TgLRAP mice showed increased ALP activity and increased formation of mineralization nodules. The TgLRAP calvarial cells also showed inhibitory effects on osteoclastogenesis in vitro. Gene expression comparison by Q-PCR in calvarial cells indicated that bone formation makers such as Runx2, ALP and Osteocalcin were increased in TgLRAP, compared to WT cells. Meanwhile, Rankl expression was decreased in TgLRAP cells in vitro, supporting the bone phenotypes in OVX mice. These results suggest that the LRAP have distinct roles to maintain the bone metabolism.

Although amelogenins are implicated in tissue-specific epithelial-mesenchymal or mesenchymal-mesenchymal signaling, the precise molecular mechanism has not been characterized. To obtain a clue for the mechanism, the results of a yeast two-hybrid assay aimed at identifying protein-binding partners for LRAP will be introduced in the last part of this presentation.

The therapeutic application of an enamel matrix derivative (EMDOGAIN®) rich in amelogenins resulted in the regeneration of cementum, alveolar bone, and periodontal ligament in the treatment of experimental or human periodontitis, indicating the attractive potential of amelogenin in hard tissue formation. Gaining further insights into the cell functions modulated by the multifunctional amelogenin proteins will lead to the development of new therapeutic approaches for treating dental diseases and disorders.

CURRICULUM VITAE

Education

1992-1998 D.D.S., Tohoku University, School of Dentistry, Sendai, Miyagi, Japan
Passed the Examination of National Board (1998)

1998-2002 Ph. D., Tohoku University Graduate School of Dentistry, Sendai, Miyagi, Japan
Major: Orthodontics

Position

2002-2002 Clinical doctor in Tohoku University Hospital (Orthodontics)

2002-2003 Assistant professor in Tohoku University, Graduate School of Dentistry (Division of Orthodontics and Dentofacial Orthopedics)

2003-2009 Assistant professor in Tohoku University, Graduate School of Dentistry
(Division of Oral Dysfunction Science)

2004-2007 Visiting fellow, Functional Genomics Section, Laboratory of Cell and Developmental Biology, NIDCR, NIH, Bethesda, MD, USA

2009-present Research associate professor in Tokyo Dental and Medical University, GCOE program
(Section of Maxillofacial Orthognathics)

Award and Honors

2004 Fogarty International Center fellowship award for post-doctoral training at the NIH

2007 Best presentation awards at the annual meeting of Japanese Orthodontic Society

Publications

1. Haruyama N, Igarashi K, Saeki S, Otuka-Isoya M, Shinoda H, Mitani H.
   Estrous-cycle-dependent Variation in Orthodontic Tooth Movement. J Dent Res. 2002 Jun;81(6): 406-10
2. Liu L, Igarashi K, Haruyama N, Saeki S, Shinoda H, Mitani H.
   Effects of local administration of clodronate on orthodontic tooth movements in rats.
   Eur J Orthod. 2004 Oct;26(5):469-73.
3. Kanzaki H, Chiba M, Takahashi I, Haruyama N, Nishimura M, Mitani H.
   Local OPG gene transfer to periodontal tissue inhibits orthodontic tooth movement.
   J Dent Res. 2004 Dec;83(12):920-5.
4. Kanzaki H, Chiba M, Arai K, Takahashi I, Haruyama N, Nishimura M, Mitani H.
   Local RANKL gene transfer to the periodontal tissue accelerates orthodontic tooth movement.
   Gene Ther. 2006 Apr;13(8):678-85.
5. Hatakeyama J, Philp D, Hatakeyama Y, Haruyama N, Shum L, Aragon MA, Yuan Z, Gibson CW, Sreenath T, Kleinman HK, Kulkarni AB. Amelogenin-mediated Regulation of Osteoclastogenesis, and Periodontal Cell Proliferation and Migration. J Dent Res. 2006 Feb;85(2):144-9.
6. Haruyama N, Thyagarajan T, Skobe Z, Wright JT, Septier D, Sreenath TL, Goldberg M, Kulkarni AB.
   Overexpression of transforming growth factor-beta1 in teeth results in detachment of ameloblasts and enamel defects. Eur J Oral Sci. 2006 May;114 S1:30-4.
7. Verdelis K, Ling Y, Sreenath T, Haruyama N, Macdougall M, van der Meulen MC, Lukashova L, Spevak L, Kulkarni AB, Boskey AL.
   DSPP effects on in vivo bone mineralization.
   Bone. 2008 Dec; 43(6):983-90
8. Choi SJ, Roodman GD, Feng JQ, Song IS, Amin K, Hart PS, Wright JT, Haruyama N, Hart TC.
   In vivo impact of a 4 bp deletion mutation in the DLX3 gene on bone development. Dev Biol. 2009 Jan; 325(1):129-37.
9. Sato S, Tsuchiya M, Komaki K, Kusunoki S, Tsuchiya S, Haruyama N, Takahashi I, Sasano Y, Watanabe M.
   Synthesis and intracellular transportation of type I procollagen during functional differentiation of odontoblasts. Histochem Cell Biol. 2009 May;131(5):583-91. [Epub 2009 Jan 21]
10. Hatakeyama J, Fukumoto S, Nakamura T, Haruyama N, Suzuki S, Hatakeyama Y, Shum L, Gibson CW, Yamada Y, Kulkarni AB. Synergistic Roles of Amelogenin and Ameloblastin. J Dent Res. 2009 Apr;88(4):318-322.
11. Haruyama N*, Sreenath TL*, Suzuki S, Yao X, Wang Z, Wang Y, Honeycutt C, Iozzo RV, Young MF, Kulkarni AB.
    * Authors equally contributed.
    Genetic evidence for key roles of decorin and biglycan in dentin mineralization. Matrix Biol. 2009 Apr;28(3):129-136.

12. Suzuki S, Sreenath T, Haruyama N, Honeycutt C, Terse A, Cho A, Kohler T, Müller R, Goldberg M, Kulkarni AB. Dentin sialoprotein and dentin phosphoprotein have distinct roles in dentin mineralization. Matrix Biol. 2009 May;28(4):221-9.
13. Sato K, Haruyama N, Shimizu Y, Hara J, Kawamura H. Osteogenesis by gradually expanding the interface between bone surface and periosteum enhanced by bone marrow stem cell administration in Rabbits. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010 July;110(1):32-40.
14. Choi SJ, Song IS, Feng JQ, Gao T, Haruyama N, Gautam P, Robey PG, Hart TC. Mutant DLX 3 disrupts odontoblast polarization and dentin formation. Dev Biol. 2010; Aug 15;344(2):682-92.
15. Cho A, Suzuki S, Hatakeyama J, Haruyama N, Kulkarni AB. A Method for Rapid Demineralization of Teeth and Bones. Open Dent J. 2010 Dec 15;4:223-229.
16. Ma D, Zhang R, Rios HF, Haruyama N, Sun Y, Xie Y, Kulkarni AB, Qin C, Feng JQ. A novel role of Periostin in postnatal tooth formation and mineralization. J Biol Chem. 2011 Feb 11;286(6):4302–09 Epub 2010 Dec 3.
17. Terao F, Takahashi I, Mitani H, Haruyama N, Sasano Y, Suzuki O, Takano-Yamamoto T. Fibroblast growth factor 10 regulates Meckel's cartilage formation during early mandibular morphogenesis in rats. Dev Biol. 2011 Feb 15;350(2):337-47. Epub 2010 Dec 11.
18. Haruyama N, Hatakeyama J, Moriyama K, Kulkarni AB. Amelogenins: Multi-functional enamel matrix proteins and their binding partners. J Oral Biosci. 2011 Aug;53(3):257-66.
19. Qiu L, Haruyama N, Suzuki S, Yamada D, Obayashi N, Kurabayashi T, Moriyama K. Accuracy of orthodontic miniscrew implantation guided by stereolithographic surgical stent based on cone-beam CT derived 3D images. Angle Orthod. 2012 Mar;82(2):284-93.
20. Tokugawa Y, Kubota M, Nishimura M, Haruyama N, Igarashi K Bone regeneration of canine artificial alveolar clefts using bone-marrow-derived mesenchymal stromal cells and β -tricalcium phosphate: A preliminary study Orthod Waves. 2012 June;71(2):51–58
21. Suzuki S, Haruyama N, Nishimura F, Kulkarni AB. Dentin sialophosphoprotein and dentin matrix protein-1: Two highly phosphorylated proteins in mineralized tissues. Arch Oral Biol. in press.
22. Mitani K*, Haruyama N*, Hatakeyama J, Igarashi K. * Authors equally contributed. Amelogenin splice isoforms stimulate chondrogenic differentiation of ATDC5 cells. Oral Dis. in press.

MEMO

The periodontal - systemic connection: Molecular mechanisms and their significance in overall health care

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University of Otago, New Zealand

The relationship between poor oral health and systemic diseases has, over the last two decades, been increasingly recognized. A large number of epidemiological studies have now clearly established the link between poor oral health and cardiovascular diseases, poor glycaemic control in diabetics, as well as a number of other diseases. The vast majority of studies investigating the relationship between periodontal disease and cardiovascular disease show a significant positive association even after adjusting for confounders, such that the focus is now on the biological mechanisms which under pin this relationship as well as on the role of periodontal treatment in reducing the risk of further cardiovascular events. A number of hypotheses have been postulated to explain the association between periodontal disease and atherosclerosis. These include (i) common susceptibility which may involve a common susceptibility gene(s) but where there is no direct link between the two diseases, (ii) direct infection of the arterial wall by oral organisms, including the recognised periodontal pathogens, following bacteraemia, (iii) systemic inflammation and increased levels of circulating cytokines with atherogenic potential and finally (iv) molecular mimicry between stress proteins expressed on the periodontal bacteria and heat shock protein 60 (HSP60) expressed on stressed endothelial cells. With respect to this final mechanism, antibodies to both Porphyromonas gingivalis GroEL antigen and human HSP60, which cross-react with one another, have been identified in the serum of patients with cardiovascular disease, the levels of which are significantly correlated with the extent of periodontal disease and with the numbers of periodontal pathogens. In addition, cross-reactive P. gingivalis GroEL and HSP60 specific T cell have been identified in the peripheral blood, as well as in the atherosclerotic plaques of patients with atherosclerosis. These data, together with the observation that enhanced atherosclerosis in P. gingivalis infected Apo-E deficient mice is associated with increased levels of anti- P. gingivalis GroEL antibodies, provide strong support for the role of molecular mimicry contributing to the association between periodontal disease and cardiovascular disease.

Although a number of studies have shown an improvement in endothelial function following periodontal therapy, there is a distinct lack of evidence showing that the treatment of periodontal disease impacts on clinical cardiovascular outcomes. Such studies, by necessity, need to involve several thousand subjects followed over a long period of time – up to ten years and are probably too expensive and too difficult to undertake.

Overall however, the relationship between poor oral health and systemic diseases has become a significant issue, and despite the lack of direct clinical evidence, there is sufficient strong basic biological evidence to explain the underlying mechanism, such that these associations can no longer be ignored in overall health strategies.

CURRICULUM VITAE

Education

1971 BDS (honours) , University of Sydney
1974 MDSc (periodontology) , University of Sydney
Thesis : Gingival fluid : its nature and measurement.
1978 PhD, University of London
Thesis : The immunopathogenesis of chronic inflammatory perio¬dontal disease in man: Phenotypic chacterization of lymphoid cell subpopulations in situ using enzyme and surface antigen markers.
1984 MRCPath, The Royal College of Pathologists, England
1996 FRCPath, The Royal College of Pathologists, England
1996 FFOP (RCPA) , The Royal College of Pathologists Australasia
2004 FRACDS (Perio) , The Royal Australasian College of Dental Surgeons

Position

1997-2003 Head, School of Dentistry, Faculty of Health Sciences, The University of Queensland.
1999 -2001 Director of Research, Faculty of Health Sciences, The University of Queensland
2002-2008 Professor of Oral Biology & Periodontology, The University of Queensland
2004-2005 Guest Professor, Faculty of Dentistry, The University of Berne, Switzerland
2004-2005 Consultant Periodontist, Logan Hospital, Brisbane
2005-present Dean Faculty of Dentistry and Professor of Periodontology, University of Otago, New Zealand
2008 Visiting Professor, Department of Periodontology, University of Nebraska, Lincoln, Nebraska, U.S.A.
2009-2010 Deputy Pro Vice-Chancellor, Division of Health Sciences, University of Otago, New Zealand

Award and Honors

2003 Fellowship of the Pierre Fauchard Academy FPFA
2003 Honorary life membership of the British Society for Periodontology
2003 Member in the General Division of the Order of Australia for services to dentistry through immunology and periodontal research and through dental and oral health education and administration AM
2004 Honorary life membership of the Australian Dental Association (Queensland branch) for long and distinguished service to dentistry
2005 Fellowship of the Academy of Dentistry International FADI
2008 Fellowship of the Royal Society of New Zealand for outstanding contribution to New Zealand science. FRSNZ

Publications

Books

1. SEYMOUR GJ, SAVAGE NW, and WALSH LJ: Immunology: An Introduction for the Health Sciences. McGraw Hill. 1995.
2. SEYMOUR GJ, CULLINAN MP, HENG N Eds; Oral Biology Molecular Techniques and Applications. Methods in Molecular Biology 666– Humana Press Totowa, NJ USA 2010

Edited Journal

1. SEYMOUR GJ & TAYLOR JJ Eds; Immunoregulation in periodontal disease. Periodontology 2000 Volume 35: 2004
2. ARMITAGE GC , CULLINAN MP, SEYMOUR GJ Eds; Comparative Biology of Chronic and Aggressive Periodontitis. Periodontology 2000 Volume 53: 2010

Book Chapters

1. GREAVES MF, WILLIAMS RC and SEYMOUR GJ: Assay for human lymphocyte subpopulations. In 'Current Research in Rheumatoid Arthritis and Allied Diseases' Ed. D.C. Dumonde and R.M. Maini. Medical and Technical Publications Press Ltd. England, 1978.
2. POULTER LW, CHILOSI M, SEYMOUR GJ, HOBBS S and JANOSSY G: Immunofluorescence Membrane Staining and Cytochemistry, Applied in Combination for Analyzing Cell Interactions in situ. In: Polak, J. and van Noorden, S. eds. Immunocytochemistry Practical Applications in Pathology and Biology 1983; pp. 233 48. Bristol, Wright PSG.
3. SEYMOUR GJ: Chronic inflammatory periodontal disease in total oral health care. In Current Aspects of Dental Health - a Scientific Approach, 1983; pp. 110 5. Oral B Foundation, Australia.
4. WALSH LJ, SEYMOUR GJ and POWELL RN: Interleukin-1 and an Interleukin-1 inhibitor modulate CD1 antigen expression on a putative intraepithelial Langerhans cell precursor population. In: "The Langerhans Cell". Eds. J. Thivolet & D. Schmitt. John Libbey Eurotext 1988; 172: 231-239.
5. SEYMOUR GJ and FORD PJ. The oral cavity. In: Mucosal Immunology. Ed. A.W. Cripps. Newey & Beath, Newcastle. pp. 143-148.
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8. SEYMOUR GJ, CULLINAN MP, WESTERMAN B and GEMMELL E. Risk factors for periodontal disease in an Australian population. in "Risk Factors in Asian Pacific Populations". 1996. Ed. P Mark Bartold. Proceedings of the Asian Pacific Society of Periodontology. Chapter 11, 92-103.
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10. ASHMAN RB, SEYMOUR GJ. General Immunology. In 'Oxford Handbook Of Applied Dental Sciences' Ed. C Scully. Oxford University Press, Oxford England, 2002; pp 434-447
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13. ASHMAN RB, SEYMOUR GJ. Clinical Immunology. In 'Oxford Handbook Of Applied Dental Sciences' Ed. C Scully. Oxford University Press, Oxford England, 2002; pp 470-480.
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10. SINON SH, RICH AM, HUSSAINI HM, YOON H-S, FIRTH NA, SEYMOUR GJ Metastases to the oral region from pleural mesothelioma. Head & Neck 2011; (in press)
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MEMO

Oral - Systemic Connection: Roles of the Host Factors

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Periodontitis is an inflammatory disease caused by gram-negative periodontopathic bacteria which can induce the production of host inflammatory mediators, eventually leading to the breakdown of tooth-supporting tissues. Emerging evidence has suggested the association of periodontal diseases with several systemic diseases such as diabetes mellitus (DM), cardiovascular diseases (CVDs), adverse pregnancy outcomes, respiratory diseases, Alzheimer's disease and cancer. Host immune responses play a vital role in the periodontal-systemic connection.

In this lecture, we will discuss the association of host factors, Wnt5a and trefoil factors (TFFs), with periodontitis. Wnt5a is secreted by activated antigen-presenting cells and Wnt5a signaling is essential for the general inflammatory response of human macrophages during sepsis. TFFs are secreted molecules involved in cytoprotection against tissue damage and immune response. Recently, we have investigated the mechanisms by which P. gingivalis modulates Wnt5a expression. In addition, we determined if TFF expression in saliva and gingival tissues was associated with periodontal pathology. Our results suggested that Wnt5a and TFF3 may be involved in the pathogenesis of periodontal disease and play a role in the periodontal-systemic connection.

CURRICULUM VITAE

Education

1987-1993 D.D.S. (1st Class Honors)
Faculty of Dentistry, Khon Kaen University
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1994-1998 Doctor of Medical Sciences (DMSc) in Oral Biology
Certificate in Periodontology
Harvard School of Dental Medicine
Harvard University
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2003-present Diplomate, The Thai Board of Periodontology, Thailand

2003-present Diplomate, The American Board of Periodontology, USA

Position

2001-2004 Assistant Professor of Periodontology
Faculty of Dentistry, Khon Kaen University,
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2003-present Assistant to the President-International Affairs
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2005-present Associate Professor of Periodontology
Faculty of Dentistry, Khon Kaen University,
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2005-2006 Acting Director (Founded Acting Director)
Language Institute, Khon Kaen University,
Thailand

2006 - 2007 Director (Founded Director)
Confucius Institute at Khon Kaen University
Khon Kaen University, Thailand

2008 - 2009 Visiting Professor
Department of Hard Tissue Engineering (Periodontology)
Faculty of Dentistry, Tokyo Medical and Dental University Japan

Award and Honors

2002 The JSPS-NRCT scholarship
For research at Tokyo Medical and Dental University Japan

2004 The short-term visiting lecturer grant
Center for Excellence Program for Frontier Research on Molecular Destruction and Reconstruction of Tooth and Bone Tokyo Medical and Dental University, Japan

2005 "Paper of the week" Journal of Biological Chemistry

2008 JSPS Invitation Fellowship Program for Research in Japan (Long Term)

2009 Distinguished Alumni Award
Faculty of Dentistry, Khon Kaen University, Thailand

Publications

1. Zhang P, Behre G, Pan J, Iwama A, Wara-aswapati N, Radomska HS, Auron PE, Tenen DG, and Sun Z. Negative Cross-Talk Between Hematopoietic Regulations: GATA proteins repress PU.1. Proc. Natl. Acad. Sc. USA 1999; 96: 8705-8710
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3. Wara-aswapati N, Koyama Y, Waterman WR, Tetradis S, Choy BK, Webb AC, and Auron PE. Human Cytomegalovirus IE2 Protein Upregulates Human Prointerleukin 1 β Gene Expression via Protein-Tethered Transactivation. Mol. Cell Biol. 1999; 19:6803-6814
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28. Su J, Sripanidkulchai B, Sripanidkulchai K, Piyachaturawat P, Wara-Aswapati N. Effect of Curcuma comosa and estradiol on the spatial memory and hippocampal estrogen receptor in the post-training ovariectomized rats. J Nat Med. 2011 Jan;65(1):57-62.
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MEMO

The biologic effect of oligopeptides derived from fibronectin and its application to biomimetics

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Fibronectin(FN) is a major glycoprotein in the extracellular matrix (ECM) and regulates various cellular events. It is consisted of disulfide-linked 235 kDa monomers, which are composed of three domains; types I, II and III. The Arg-Gly-Asp (RGD) and Pro-His-Ser-Arg-Asn (PHSRN) in 10^{th} and 9^{th} type III domain, respectively, are important cell adhesion. Oligopeptides based on FN are regarded as attractive biomolecules for biomaterials. We synthesized FN type III 7-10, 8-10 and 9-10 fragments and analyzed their biologic activities. We also synthesized PHSRN and RGD containing short oligopeptides with linkers and also via recombinant DNA technology and investigated their biological effects. Recently we evaluated the oligopeptides from fibrin binding domain based on FN and found that these peptides have enhancing biologic activities in some cell lines. We hypothesized that these peptides can be used as biomaterial surface modifiers which could enhance biocompatibility and wound healing.

CURRICULUM VITAE

Education

1980-1982 Predental course, College of Natural Science, Seoul National University(S.N.U.)
1982-1986 D.D.S.: College of Dentistry, S.N.U.
1988-1993 M.S. : Graduate School, S.N.U.
1994-1997 Ph. D : Graduate school, S.N.U.

Position

1996-2009 Full time instructor, Assistant professor, Associate professor, School of Dentistry, S.N.U.
2009-present Professor and Chairman, Department of Peridontology, School of Dentistry, S.N.U.
1999-2000 Visiting Professor, Department of Periodontology, School of Dentistry, University of North Carolina at Chapel Hill, N.C., U.S.A.
2004 Visiting Professor, Department of Periodontology, Royal College of Dentistry, Aarhus University, Denmark
2004 Director, Implant Center, Seoul National University Dental Hospital
2005-present Adjunct Professor, Department of Periodontology, University of Pennsylvania
2005-2006 Associate Dean of Student Affairs and Planning, School of Dentistry, Seoul National University
2008-2010 Associate Dean of Student Affairs, Seoul National University
2010-2010 Visiting Professor, Department of Periodontology, Tokyo Medical and Dental University, Japan

Publications

1. Seol YJ, Lee JY, Park YJ, Lee YM, Young-Ku, Rhyu IC, Lee SJ, Han SB, Chung CP. Chitosan sponges as tissue engineering scaffolds for bone formation. Biotechnol Lett. 2004 Jul;26(13):1037-41.
2. Yang SM, Kim SY, Lee SJ, Lee YK, Lee YM, Ku Y, Chung CP, Han SB, Rhyu IC. Tissue response of calcium polyphosphate in beagle dog, Part II; 12 months result. Key Eng Mat 2004;254-256:245-248.
3. Kim Y, Jang JH, Ku Y, Koak JY, Chang IT, Kim HE, Lee JB, Heo SJ Microarray-based expression analysis of human osteoblast-like cell response to anodized titanium surface.. Biotechnol Lett. 2004 Mar;26(5):399-402
4. Lee JY, Lee YM, Shin SY, Seol YJ, Ku Y, Rhyu IC, Chung CP, Han SB. Effect of subantimicrobial dose doxycycline as an effective adjunct to scaling and root planning. J Periodontol. 2004 Nov;75(11):1500-8
5. Y Ku, CP Chung, JH Jang. The effect of the surface modification of titanium using a recombinant fragment of fibronectin and vitronectin on cell behavior. Biomaterials 2005; 26(25):5153-5157
6. Park YJ, Kim KH, Lee JY, Ku Y, Lee SJ, Min BM, Chung CP. Immobilization of bone morphogenetic protein-2 onto a nanofibrous chitosan membrane for enhanced guided bone regeneration. Biotechnol Appl Biochem. 2006 Jan;43(Pt1):17-24
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12. Kim TI, Lee G, Jang JH, Chung CP, Ku Y. Influence of RGD-containing oligopeptide-coated surface on bone formation in vitro and in vivo. Biotechnol Lett. 2007

Mar;29(3):359-363.
13. Park JB, Lee JY, Park YJ, Rhee SH, Lee SC, Kim TI, Seol YJ, Lee YM, Ku Y, Rhyu IC, Han SB, Chung CP. Enhanced Bone Regeneration in Beagle Dogs With Bovine Bone Mineral Coated With a Synthetic Oligopeptide. J Periodontol. 2007 Nov;78(11):2150-2155.
14. Kim HY, Lee SW, Cho SI, Patton L, Ku Y. Associations between teeth with unmet needs and socioeconomic status among South Korean dentate government employees. J Public Health Dent. 2007 Summer;67(3):174-178.
15. Seol YJ, Kim KH, Park YJ, Lee YM, Ku Y, Rhyu IC, Lee SJ, Han SB, Chung CP. Osteogenic effects of bone morphogenetic protein-2 plasmid gene transfer. Biotechnol Appl Biochem. 2008 Jan. 49:85-96.
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17. Hwang YJ, Fien MJ, Lee SS, Kim TI, Seol YJ, Lee YM, Ku Y, Rhyu IC, Chung CP, Han SB. Effect of Scaling and Root Planing on Alveolar Bone as Measured by Subtraction Radiography J Periodontol. 2008 Sep. 79(9):1663-1669.
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19. Park OJ, Shin SY, Choi Y, Kim MH, Chung CP, Ku Y, Kim KK.The association of osteoprotegerin gene polymorphisms with periodontitis. Oral Dis. 2008 Jul;14(5):440-444
20. Kim SH, Kim DY, Kim KH, Ku Y, Rhyu IC, Lee YM. The efficacy of a double-layer collagen membrane techinique for overlaying block graft in a rabbit calvarium model. Clin Oral Implnats Res. 2009 Oct;20(10):1124-1132.
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MEMO

Periodontal disease and atherothrombotic diseases: Lessons from clinical and basic studies

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Over the past two decades, the relationship between poor oral health and systemic diseases has been increasingly recognized. There is considerable epidemiological evidence to support the concept that poor oral health may put patients at a significant risk for a variety of systemic conditions such as coronary heart disease (CHD). CHD is the leading cause of death in Japan and other developed countries. The major pathway underlying CHD pathology is atherosclerosis. Several risk factors for atherosclerosis have been identified, including smoking, hypertension, hyperglycemia, hypercholesterolemia and genetic factors. However, atherosclerosis can develop in the absence of these classic risk factors. Recent epidemiological studies have suggested a link between atherosclerosis and infection/inflammation. Associations have been reported with Chlamydia pneumoniae, Helicobacter pylori, and cytomegalovirus, as well as with dental infections, particularly those associated with periodontitis. Several biologically plausible mechanisms have been presented to explain the association, such as bacteremia, elevated levels of inflammatory markers, generation of cross-reactive immune responses by chronic infections, and induction of imbalanced cholesterol metabolism. There is evidence demonstrating the direct effect of periodontopathic bacteria on host cells, increased levels of high-sensitivity C-reactive protein and elevated levels of cross-reactive antibody between human heat-shock protein 60 and its orthologue, GroEL of Porphyromonas gingivalis. We have demonstrated that P. gingivalis induces several atherosclerosis-related molecules in human coronary arterial endothelial cells, and that high-sensitivity C-reactive protein (hs-CRP) and interleukin (IL)-6 protein levels are higher in cases of periodontitis and that successful treatment of periodontitis decreases the levels of both mediators. In addition, periodontitis patients have lower anti-atherogenic HDL cholesterols than periodontally healthy subjects. However, since the two disorders share several common risk factors, including cigarette smoking, age, and diabetes mellitus, and moreover, current research does not yet provide evidence of a causal relationship between the two diseases, media claim about an association between periodontitis and heart disease. Nevertheless, several animal studies aimed at clarifying the effect of periodontopathic bacterial infection on atherogenesis have successfully shown the formation of atheromatous plaque and the elevation of systemic inflammatory markers. Recently, we have shown by using mouse model that periodontal infection itself does not cause atherosclerosis, but it accelerates it by inducing systemic inflammation and deteriorating lipid metabolism, particularly when underlying hyperlidemia or susceptibility to hyperlipidemia exists. In this presentation, an update on the current understanding of the contribution of poor oral health to atherosclerosis and the possible mechanisms involved will be presented and discussed based mainly on our studies.

CURRICULUM VITAE

Education

1974-1980 Kanagawa Dental College
Awarded the degree of D. D. S.

1980-1985 Department of Periodontology, Niigata University Graduate School of Dentistry
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1985-1988 Assistant Professor, Niigata University Dental Hospital

1988-1999 Senior Lecturer, Niigata University Dental Hospital

1999-2004 Associate Professor, Division of Periodontology, Department of Oral Biological Science, Niigata University Graduate School of Medical and Dental Sciences

2004-2010 Professor, Department of Oral Health and Welfare, Niigata University Faculty of Dentistry

2006-present Professor, Center for Transdisciplinary Research, Niigata University

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Publications

1. Maeakawa T, Takahashi N, Honda T, Yonezawa D, Miyashita H, Okui T, Tabeta K, Yamazaki K. Porphyromonas gingivalis antigens and interleukin-6 stimulate the production of monocyte chemoattractant protein-1 via the up-regulation of early growth response-1 transcription in human coronary artery endothelial cells. J Vasc Res 47(4): 346-354, 2010.
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MEMO

Paradigm shift of orhthognathic surgery in diagnosis, simulation, and guided surgery

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The traditional planning for orthognathic surgery using tracing and dental plaster models has remained mostly unchanged over the past 50 years. They present significant limitations and are often inadequate for the treatment of patients with complex CMF deformities. My topic is 3D surgical simulation for orthognathic surgery based on the occlusal relationship to predict surgical outcomes.

Before taking CT scanning, impression of the bite and upper and lower dental arches was taken using special impression tray and silicon impression material. 3-D virtual skull model with detailed dental occlusal and intercuspidation date was created by triple CT scan procedure. First the patient was vertically scanned with wax bite wafer in place in a natural seated position using standardized CT scanning protocol. Second, the tray and impression material was placed in the patient's mouth in the correct position, and the patient was scanned with a smaller field of view centered on the occlusal plane. Finally, the special tray and impression material was scanned more precisely using high-resolution standardized CT scanning protocol. These three scanning dates were installed to Maxilim software (Ver. 2.2.2, Medicim NV, Mechelen, Belgium). Acquiring the 3D integrated augmented skull model with dentition, 3D cephalometric analysis, virtual osteotomy and segmentation of each bony segment were undergone. The surgical simulation was then performed at the position of final occlusion by use of virtual elastics between upper and lower teeth.

Next step from the simulation, we need some intraoperative guides to acquire the actual results same as simulated results. There are two possibilities to make such guide, one is template to set on the osteotomy gap to indicate the amount of movement and another is surgical splint that made as an intermediate splint same as conventional model surgery. We have used 3D virtual surgical splints made from a transparent polycarbonate material (Tecanat Polycarbonate, Eisigner Industries, US) processed using computeter-aided design and computer-aided manufacturing techniques during the actual surgery.

3D virtual orthognathic surgery planning has powerful potential as a communication tool because it offers the possibility to visualize an integrated treatment plan of the patient as a single virtual anatomic model including the hard and soft tissue and teeth. Furthermore, the surgical guides help surgeons to indicate appropriate 3D location of maxillary segment during bimaxillary surgery. However, to make the paradigm shift from conventional planning to 3D virtual planning, some problems such as time consuming, costs, irradiation and quality of care have to be overcome near future.

CURRICULUM VITAE

Education

1977-1983 Tohoku University School of Dentistry, Sendai Japan (D.D.S.)

1983-1987 Postgraduate course of Tohoku University School of Dentistry, Microbiology and Oral Surgery (Ph.D.)

Position

1990-1994 Assistant Professor, Department of Oral and Maxillofacial Surgery II, Tohoku University School of Dentistry, Sendai, Japan.

1994-1995 Assistant Professor, Division of Dentistry and Oral Surgery, Akita University School of Medicine, Akita, Japan. Lecturer, Division of Dentistry and Oral Surgery, Akita University School of Medicine, Akita, Japan.

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2012 Professor and Head,
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Recent Paradigm Change in Three-Dimensional Imaging and CAD-CAM Technology for Virtual Orthodontic Treatment and Orthognathic Surgery

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Current rapid change of paradigm in the diagnosis and treatment for patients with malocclusion and facial deformity give a new horizon to the orthodontic treatment and orthognathic surgery in terms of efficiency and effectiveness.

This presentation will give you the up-to-date information of 3D-Digital processes which are currently being used in the diagnosis and treatment planning, and real treatment in the orthodontic treatment and orthognathic surgery for both clinical practice and research.

The purposes of this presentation are to discuss about the data acquisition from CT, intra-oral scanning, and surface scanning, the data manipulation including virtual segmentation of teeth, virtual diagnostic and final set-up of the models, virtual bracket positioning and jig fabrication, virtual orthognathic surgery, and virtual fabrication of surgical wafers, and the appliance fabrication and delivery for indirect bonding jig with customized base, and surgical wafers using CAD-CAM and SLA technology.

CURRICULUM VITAE

Education

1. College of Dentistry, Seoul National University, graduated February, 1988, with the degree of D.D.S..
2. Graduate School, Seoul National University, graduated February, 1991, obtained an M.S.D. (specialized in Orthodontics) for a thesis entitled : "A soft tissue analysis on facial esthetics of Korean young adults"
3. Graduate School, Seoul National University, graduated February, 1997, received a Ph.D. (specialized in Orthodontics) for a thesis entitled : "A study on the distribution of several growth factors in the artificially created cleft lip wound healing of rabbit fetuses "

Position

2003–present	Director of Academics, Secretary General, Vice President, Korean Cleft Lip and Palate Association
2003–present	Member. Editorial Review Board, Angle Orthodontist
2004–present	Director of Education, Director of Scientific Affairs, Director of Planning, Secretary General, Director, Korean Association of Orthodontists
2004–present	Director of PR and CRM, Director of Education and Research, Director of Planning and Budget, Seoul National University Dental Hospital
2005-2007	Assistant Dean, School of Dentistry, Seoul National University.
2005–present	Member. Editorial Review Board. American Journal of Orthodontics and Dentofacial orthopedics.
2006–present	Director and Head Coach, Seoul National University Rowing Team
2007-2010	Member, Committee of Dental Care Evaluation in Ministry of Health and Welfare, Korea
2009–present	Chair, Dept. of Orthodontics, School of Dentistry, Seoul National University
2010-present	Fellow of the International College of Dentists
2010–present	Member of the General Assembly, Korean Association of Orthodontists
2011–present	Member, Commission of the Ministry of Patriots and Veterans Affairs, Korea

Award and Honors

1. received a summa cum scholarship from Seoul National University in 1986, 1987
2. graduated as summa cum laude in Seoul National University in Feb 1988
3. The prize of President of Seoul National University, February, 1988
4. The prize of President of Korean Association of Orthodontists, September 1997
5. The 10th Beomho award for Young Scientific Researcher (Korean division of IADR), Jan 24, 1998.
6. Unilever travel award from IADR 1999, Vancouver, Canada
7. Award of 2007 Year' s Book, Natural Science, The National Academy of Sciences, Republic of Korea. "Baek SH, Nahn DS. New Paradigm of Craniofacial Distraction Osteogenesis. JeeSung Pub. Co. Seoul, Korea, 2006."
8. The 5th YeonSong Dental Award. Korean Academy of Dental Science. Feb 22, 2009
9. CDABO Case Report of the Year Award , AAO meeting. Boston, May 2, 2009

MEMO

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Clinical and biomechanical considerations for correction of the dento-facial deformities

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So far, the conventional orthognathic surgery has been widely used to treat the dentofacial deformity patient. However, some problems were found such as limited amount of movement in the skeletal tissue, high recurrence rate and difficulty to achieve the functional and esthetic balance. To minimize the limitation and side effects of the orthognathic surgery, orthopedic intervention has been widely used for the treatment of dento-facial deformities. As a result, orthopedic intervention such as distraction osteogenesis and rapid maxillary expansion has became an alternative option for treatment of hypoplasia in the patients with dento-facial deformity.

Biologic and biomechanical background of distraction osteogenesis for the treatment of maxillary hypoplasia in cleft lip and palate patient and in the hemi facial microsomia patient will be discussed with the clinical cases. Rapid maxillary expansion(RME) has been widely used to correct the vertical and transverse deficiency of the maxilla in the growing patients. It is possible to extend the indication of age and the range of maxillary expansion by using the surgically assisted RME and the mini screw assisted RME. The characteristics of surgically assisted RME and the mini screw assisted RME will also be discussed with the treated cases and related researches.

If the patient with dento-facial deformity was treated under accurate diagnosis and treatment planning with a proper biologic and biomechanical principles, accompanied with overcorrection and long term retention, it would be possible to improve the functional and esthetic balance

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Education

1975	Doctor of Dental Surgery (DDS), Yonsei University, Seoul / Korea
1978	Specialist in Orthodontics, Yonsei University, Seoul / Korea
1984	Doctor of Philosophy(PhD), Graduate school,Yonsei University
1984-1985	Visiting Assistant Professor, Dept. of Orthodontics University of Connecticut, U. S .A.
1998-1999	Visiting Professor, Dept. of Orthodontics University of British Columbia, Vancouber, CANADA
1992-2002	Professor and Chairman, Dept. of Orthodontics, College of Dentistry, Yonsei University
2002-2004	Director, Dental Hospital, Yonsei University
2004-2008	Dean, College of Dentistry, Yonsei University, Seoul, KOREA
1981-present	Professor, Dept. of Orthodontics, College of Dentistry, Yonsei University, Seoul, Korea

Position

1986-1990	Editor in Chief, Korean Journal of Orthodontists,
1986-present	International Member, American Association of Orthodontists
1993-present	Director, The Korean adult orthodontic research institute
1994-1995	Chairman, Organizing Committee The 2nd Asian Pacific Orthodontic Congress
1996	Member of Scientific Committee, VI International Symposium on Dentofacial Development and Function (Athens-Greece)
1996-present	Member, World Federation of Orthodontists
2000-2002	President, Korean Association of Orthodontists
2002	Chairman, The 1st Asian Implant- Orthodontic Conference
2004-present	Member, Editorial Review Board,, Angle Orthodontists
2005-present	Member, Editorial Review Board, American Journal of Orthodontics and Dentofacial Orthopedics
2007-2008	President, Dean's Counsil of the Korean Dental College
2008	Chairman, Organizing Committee, The1st world Implant Orthodontic Conference and the 7th Asian Implant Orthodontic Conference
2009-present	President, World Implant Orthodontic Association
2010-present	President, Korean association of orthodontic professors.

Publications

1. Angle Orthod, Obstructive Sleep Apnea Patients with the Oral Appliance Experience Pharyngeal Size and Shape Changes in Three Dimensions, 75(1):15-22, SH Kyung, YC Park, EK Pae, 2005
2. Journal of clinical Orthodontic, Extraction Space Closure with Vacuum-Formed Splints and Miniscrew Anchorage, 39(2): 76-79, YC Park, JS Lee, DH Kim, 2005
3. Journal of clinical Orthodontic, Bonding Orthodontic Attachments to Miniscrew Heads, JCO 39(6):348-353, SH Kyung, HW Choi, KH Kim, YC Park, 2005
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12. Quintessence book co., Applications of Orthodontic Mini-implants, JS Lee, JK Kim, YC Park, Robert L, Vanarsdall, Jr, 2007
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periornl soft tissue after bracket removal, 37(2)125-136, JS Lee, KC Choy, YC Park, KH Kim, 2007
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18. The Korean Journal of Orthodontics, Labial and buccal surface contours of Korean normalocclusion in a three-dimensional digital model, 38(2):95-103, SW Song, JY Cho, JS Choi, YC Park, JH Chae, 2008
19. The Korean Journal of Orthodontics, The effect of loading time on the stability of mini-implant, 38(3):149-158, SY Lee, JY Cha, TM Yoon, YC Park, 2008
20. Angle Orthodontist, Nasal Changes after Surgical Correction of Skeletel Class Ⅲ Malocclusion in Koreans, 78(3):427-432, CJ Chung, YB Lee, KH Park, SH Park, YC Park, KHo Kim, 2008
21. Angle Orthodontist, Open Bite Correction by Intrusion of Posterior Teeth with Miniscrew, 78(4):699-710, YC Park, HA Lee, NC Choi, DH Kim, 2008
22. Int'l J of Oral & maxilo facial implant, Influence of the Length of the Loading Period After Placement of Orthodontic Mini-implants on Changes in Bone Histomorphology:Microcomputed Tomographic and Histologic Analysis. 24:842-849, JY Cha, JK Lim,, JW Song, Daisuke Sato, Makoto Kenmotsu, Takashi lnoue, YC Park, 2009
23. Am J Orthod Dentofacial Ortho, Restotation of an alveolar bone defect caused by an ankylosed mandibular molar by root movement of the adjacent tooth with minisrew implants, 136:440-449, KJ Lee, E J, HS Yu, YC Park, 2009
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33. KH Kim, KJ Lee, JY Cha, YC Park, 2011
34. American Journal of Orthodontics and Dentofacial Orthopedics, Displacement pattern of the maxillary arch depending on miniscrew position in sliding mechanics 140(2):224-232, KJ Lee, YC Park, CJ Hwang, TH Choi, 2011
35. Am J Orthod Dentofacial Orthop, Total distalization of the maxillary arch in a patient with skeletal Class II malocclusion, 139(6):823-833, YJ Choi, SJ Lee, JY Cha, YC Park, 2011

MEMO

Orthognathic Surgery : The Considerations for its Accuracy and Safety

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Now orthognathic surgery is one of the most common surgical methods for the treatment of dento-facial deformity patients. Though there are many technique for orthognathic surgery, sagittal splitting of the mandibular ramus and Le Fort Ⅰ osteotomy of the maxilla are the most popular. Since these popular orthognathic surgeries have been well trained by oral surgeons, few major troubles have been reported during surgery recently. However, results of the orthognathic surgery should be based on the improvement of occlusal disharmony. The postoperative occlusal condition depends on accuracy of the surgical movement on the jaw bones. In addition, as a surgical basis, the techniques for accurate bone movement should be free from unexpected bleeding or jaw bone fracture. Since orthognathic surgery is becoming a common treatment method in the field of oral and maxillofacial surgery, safety must be guaranteed during surgery. In this lecture, several original techniques are introduced for accurate and safe movement of jaw bone during orthognathic surgery.

In the sagittal splitting of the mandibular ramus, the bilateral mandibular rami are split into the proximal and distal segments. The distal segment is moved posterior or anterior to improve the occlusal disharmony. However, the proximal segment must be maintained in its original position due to the presence of condyle. Improper positioning of the proximal segment, namely, condyle can cause various problems of temporomandibular joint and instability of the postoperative occlusion. Therefore, it is considered to be better that the pre-splitting position of the proximal segment should be recorded using a device. Even though beginners of the orthognathic surgery perform the sagittal splitting of the mandibular ramus, luxation of the temporomandibular joint can be prevented using this device during surgery.

In the maxillary osteotomy, accurate upward impaction is difficult because there are important blood vessels nourishing the maxilla in its posterior portion. Though some oral surgeons perform upward hammering of the maxilla for its upward movement, it' s very danger. The presence of inferior concha and, in the similar situation, nasal-intubated endotracheal tube also interferes during upward movement of the maxillary segment. To solve these problems of upward movement of the maxilla, additional osteotomy to Le Fort Ⅰ or application of resin replica is performed during surgery.

These techniques have not only advantages, but also some disadvantages. I hope the accuracy and safety of orthognathic surgery will be discussed through this lecture to increase the quality of lives of the patients undergoing orthognathic surgery.

CURRICULUM VITAE

Education

1985 Graduated from Tokyo Medical and Dental University, Faculty of Dentistry.
1985 Entered the Graduate School of Tokyo Medical and Dental University, Faculty of Dentistry, and joined the 2nd Department of Oral and Maxillofacial Surgery as a Graduate Student.
1989 Graduated from the Graduate School of Tokyo Medical and Dental University, Faculty of Dentistry, and Appointed to a Clinical Fellow of the 2nd Department of Oral and Maxillofacial Surgery.

Position

1. Appointed to a Clinical Fellow in 1989.
2. Transferred to the Department of Plastic Surgery, Faculty of Medicine, Kitasato University as an Assistant Professor (Instructor) in 1990.
3. Returned to the 2nd Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Tokyo Medical and Dental University as an Assistant Professor (Instructor) in 1992.
4. Appointed to an Assistant Professor (Lecturer) in 2003.
5. Appointed to an Associate Professor in 2004.
6. Appointed to a Professor and Chairman of the Department of Oral and Maxillofacial Surgery, University Hospital, Faculty of Medicine, University of Yamanashi in 2006.
7. Appointed to a Professor of the Department of Oral and Maxillofacial Surgery, Division of Medicine, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi in 2008.
8. Appointed to a Professor of the Section of Maxillofacial Surgery, Department of Maxillofacial/Neck Reconstruction, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University in 2012, and serving in that position up to this date.

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