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The future of cytokine and stem cell therapies for
periodontal regeneration

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Enhancing the biological potentials of mesenchymal stem cells (or periodontal tissue stem cells) within periodontal ligament and stimulating the periodontal regeneration are recognized as being clinically possible. In fact, it has been demonstrated that both GTR and Enamel Matrix Derivative (EMD) treatments induce the statistically significant periodontal regeneration in a clinical field. However, there is still the necessity to develop more effective treatment procedures to enhance biological activities of periodontal tissue stem cells and further improve the outcome of periodontal regeneration. Basic Fibroblast Growth Factor (FGF-2) is known to stimulate the proliferation, migration and differentiation of a variety of cell types and to strongly induce angiogenesis. In randomized controlled double-blinded clinical trials conducted in Japan, a significant difference in % increase in alveolar bone height at 2-or 3-walled intrabony defects was demonstrated by standardized radiographs between Placebo Group and 0.3% human recombinant FGF-2-applied Group at 9 months after the treatment. This FGF-2 medicine has finally approved by Ministry of Health, Labor and Welfare and become commercially available (Regroth®) in Japan. Interestingly, we have also revealed that auto-transplantation of adipose-tissue derived multilineage progenitor cells (ADMPC) together with fibrin gel into periodontal-tissue defects stimulates the periodontal regeneration at 9 months after the transplantation. These results suggest that both cytokine and stem cell therapies are promising options to stimulate periodontal regeneration. It is also expected that these therapies can be also applied for dental implant treatment. If we can successfully merge all three elements of tissue engineering (stem cells, signaling molecule and scaffold) for periodontal regeneration in an orchestrated manner in the future, we may be able to maximize the outcome.

Curriculum Vitae

- 1984 DDS Osaka University Faculty of Dentistry, Japan
 1988 PhD Osaka University Graduate School of Dentistry, Japan
 1988 Visiting Fellow, National Cancer Institute, National Institutes of Health, USA
 1990 Instructor, Osaka University Faculty of Dentistry
 1992 Assistant Professor, Osaka University Dental Hospital
 2000 Associate Professor, Osaka University Graduate School of Dentistry
 2002 Professor and Chair,
 Department of Periodontology, Osaka University Graduate School of Dentistry
 2016 Director of Osaka University Dental Hospital
 2019 President of the Japanese Society of Periodontology

Honors

- 1998 Anthony Rizzo Periodontal Research Award
 (IADR Periodontal Research Group(PRG))
 2009 AAP R. Earl Robinson Periodontal Regeneration Award
 2012 IADR/AADR William J. Gies Award
 2013 IADR Distinguished Scientist Award for Basic Research in Periodontal Disease.
 2018 IADR/PRG Regenerative Periodontal Medicine Award

Research Fields of Interest

Periodontology, Regenerative Medicine

Selected Publications

1. Iwayama T, Okada T, Ueda T, Tomita K, Matsumoto S, Takedachi M, Wakisaka S, Noda T, Ogura T, Okano T, Fratzl P, Ogura T, Murakami S : Osteoblastic lysosome plays a central role in mineralization. *Sci Adv.* 3 : 5 : eaax0672, 2019.
2. Fujihara C, Kanai Y, Masumoto R, Kitagaki J, Matsumoto M, Yamada S, Kajikawa T, Murakami S : Fibroblast growth factor-2 inhibits CD 40-mediated periodontal inflammation. *J Cell Physiol.* 234 : 7149 – 7160, 2019.
3. Kitagaki J, Miyauchi S, Asano Y, Imai A, Kawai S, Michikami I, Yamashita M, Yamada S, Kitamura M, Murakami S : A Putative Association of a Single Nucleotide Polymorphism in GPR126 with Aggressive Periodontitis in a Japanese Population. *PLOS ONE.* 10 : 11(8) : e0160765, 2016.
4. Kitamura M, Akamatsu M, Kawanami M, Furuichi Y, Fujii T, Mori M, Kunimatsu K, Shimauchi H, Ogata Y, Yamamoto M, Nakagawa T, Sato S, Ito K, Ogasawara T, Izumi Y, Gomi K, Yamazaki K, Yoshie H, Fukuda M, Noguchi T, Takashiba S, Kurihara H, Nagata T, Hamachi T, Maeda K, Yokota M, Sakagami R, Hara Y, Noguchi K, Furuuchi T, Sasano T, Imai E, Ohmae M, Koizumi H, Watanuki M, Murakami S : Randomized placebo-controlled and controlled non-inferiority phase III trials comparing trafermin, a recombinant human fibroblast growth factor 2, and enamel matrix derivative in periodontal regeneration in intrabony defects. *J Bone Miner Res.* 31 : 806 – 814, 2016.
5. Fujihara C, Yamada S, Ozaki N, Takeshita N, Kawaki H, Takano-Yamamoto T, Murakami S : Role of Mechanical stress-induced glutamate signaling-associated molecules in cytodifferentiation of periodontal ligament cells. *J Biol Chem.* 285 : 28286 – 28297, 2010.