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顎骨疾患プロジェクト国際シンポジウム

Tokyo Dental College Research Branding Project
Asian Rising Star Symposium 2021Identification of periodontal stem cells and niche regulated by
GPCR and Hedgehog signaling

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How the complex periodontal tissue is maintained is always our central question in the dental field. Although it is speculated that stem cells are involved in periodontal tissue homeostasis and regeneration, and their abnormal regulation is involved in the pathogenesis of the disease, *in vivo* analysis of periodontal microenvironment is not thoroughly performed yet. Periodontal cervical region, designated “crescent region” is a unique place for maintaining the periodontal tissue integrity. Here, we identified stem cell populations in the periodontal crescent region and their regulating mechanisms by using genetic lineage tracing technology. Stem cells identified in the crescent region show self-renew and have differentiation ability into all kinds of periodontal cells through GPCR and Hedgehog signaling. The *Gnas* gene, which encodes $G\alpha_s$ that transduces GPCR signaling, had an essential role to keep balance of ossification and fibrosis in the periodontal crescent region. We revealed that *Gnas* gene mutations altered periodontal tissue cell lineage determination and cellular plasticity. Loss of *Gnas* promoted osteogenic cell fate determination of periodontal stem cells by activating the CXCL12 and Hedgehog signaling, while gain of *Gnas* function led to fibrosis and caused periodontitis. Pharmacological intervention was able to rescue periodontal diseases caused by *Gnas* gene mutations. Thus, this study demonstrates that a novel stem cell population in the crescent region is regulated by unique niches, which provide new insights into selective lineage determination of periodontal stem cells.

Curriculum Vitae

2011 DDS, Tokyo Dental College, Japan

2017 PhD, Keio University, Japan

2011 – 2013 Intern, Department of Dentistry and Oral Surgery, Keio University School of Medicine, Japan

2017 – 2018 Instructor, Department of Dentistry and Oral Surgery, Keio University School of Medicine, Japan

2019 – 2021 Research Fellow, Department of Developmental Biology, Harvard University, USA

2021 – Assistant Professor, Department of Physiology, Tokyo Dental College, Japan

Honors

2016 : Ikeda Rika, Regenerative Medicine Research Award

2020 : The Japanese Stomatological Society, Best Poster Award

2020 : Keystone Symposia, Scholarship Award

Research Fields of Interest

In my research life, the underlying motivation and the first priority are to proceed with study from clinical aspects for patients. To achieve that, I enjoy understanding cellular signaling, niche regulation, and systemic regulation in homeostasis and pathogenesis based on multiple perspectives including stem cell biology, developmental biology, genetics, anatomy, neuroscience, microbiology, angiology, and cancer biology. Plus, I deeply believe that the most important thing is to enjoy such a diversity of oral science and curiosities with my wonderful colleagues.

Selected Publications

1. Morikawa S, **Ouchi T (Equal contribution)**, Shibata S, Fujimura T, Kawana H, Okano H, Nakagawa T. Applications of mesenchymal stem cells and neural crest cells in craniofacial skeletal research. *Stem Cells Int.* 2016 ; 2016 : 2849879.
2. **Ouchi T**, Morikawa S, Shibata S, Fukuda K, Okuno H, Fujimura T, Kuroda T, Ohyama M, Akamatsu W, Nakagawa T, Okano H. LNGFR⁺THY-1⁺ human pluripotent stem cell-derived neural crest-like cells have the potential to develop into mesenchymal stem cells. *Differentiation.* 2016 Dec ; 92(5) : 270 – 280.
3. **Ouchi T**, Morikawa S, Shibata S, Takahashi M, Yoshikawa M, Soma T, Miyashita H, Muraoka W, Kamayama K, Kawana H, Arima Y, Saya H, Okano H, Nakagawa T, Asoda S. Recurrent Spindle Cell Carcinoma Shows Features of Mesenchymal Stem Cells. *J Dent Res.* 2018 Jul ; 97(7) : 779 – 786.
4. Kimura H, **Ouchi T (Equal contribution)**, Shibata S, Amemiya T, Nagoshi N, Nakagawa T, Matsumoto M, Okano H, Nakamura M, Sato K. Stem cells purified from human induced pluripotent stem cell-derived neural crest-like cells promote peripheral nerve regeneration. *Sci Rep.* 2018 Jul 3 ; 8(1) : 10071.
5. **Ouchi T (Correspondence)**, Nakagawa T. Mesenchymal stem cell-based tissue regeneration therapies for periodontitis. *Regen Ther.* 2020 Jan 15 ; 14 : 72 – 78.