## Division of Biochemistry Department of Oral Biology

### **Research Overview**

Our research primarily focuses on the following three topics related to aging and oral health:

- 1) Exploration and analysis of anti-aging components derived from natural plants,
- 2) Creation and analysis of genetically modified mice for using the GONAD method,
- 3) Functional analysis of SPP-1 (osteopontin) in the periodontal ligament.

The GONAD method is a new technique for creating genetically modified animals, such as knockouts. Unlike previous methods, it allows for the direct introduction of gene-editing vectors into fertilized eggs within the fallopian tube without extracting the eggs, making it possible to create genetically modified animals. This method has enabled us to easily and quickly create various genetically modified animals. We aim to validate and demonstrate the anti-aging effects of various components extracted from natural plants in vivo using this technology. Additionally, we aim to elucidate the unknown functions of various molecules acting in the periodontal ligament, by applying these techniques.

### **Research Staff**

Professor: Toshiya Arakawa, MBA, PhD

Assistant Professor: Ayuko Takada, DDS, PhD

Assistant Professor: Rie Takai, DDS, PhD

### **Collaborative Researcher**

Nattakarn Hosiriluck, *DDS*, *PhD* (Department of Masticatory Sciences, Faculty of Dentistry, Mahidol University, Bangkok Thailand)



T. Arakawa



A. Takada



R. Takai



N. Hosiriluck,

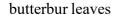
## The ongoing research topics:

- 1) Exploration of components with anti-aging effects found in the leaves of butterbur.
- 2) Creation and analysis of knockout mice using the GONAD method.
- 3) Production of SPP-1 knockout mice and functional analysis in the periodontal ligament.

GONAD Method









# **Published paper**

- \* Giri S, Uehara O, <u>Takada A</u>, Paudel D, Morikawa T, <u>Arakawa T</u>, Nagasawa T, Abiko Y, Furuichi Y.The effect of Porphyromonas gingivalis on the gut microbiome of mice in relation to aging. J Periodontal Res. 57(6):1256-1266, 2022. doi: 10.1111/jre.13062.
- \* Hosiriluck, N., Kashio, H., <u>Takada, A.</u>, Mizoguchi, I., & <u>Arakawa, T.</u> The profiling and analysis of gene expression in human periodontal ligament tissue and fibroblasts. *Clinical and Experimental Dental Research*, 8,658–672. 2022
- \* Kubota A, Terasaki M, <u>Takai R</u>, Kobayashi M, Muromoto R, Kojima H. 5-Aminosalicylic Acid, A Weak Agonist for Aryl Hydrocarbon Receptor That Induces Splenic Regulatory T Cells. *Pharmacology*. 107(1-2):28-34,2022
- \* Giri S, <u>Takada A</u>, Paudel D, Yoshida K, Furukawa M, Kuramitsu Y, Matsushita K, Abiko Y, Furuichi Y. An in vitro senescence model of gingival epithelial cell induced by hydrogen peroxide treatment. *Odontology*. Jan;110(1):44-53, 2022
- \* Yokoyama R, Kojima H, <u>Takai R</u>, Ohta T, Maeda H, Miyashita K, Mutoh M, Terasaki M. Effects of CLIC4 on Fucoxanthinol-Induced Apoptosis in Human Colorectal Cancer Cells. *Nutr Cancer*.;73(5):889-898, 2021
- \* Uehara O, Hiraki D, Kuramitsu Y, Matsuoka H, <u>Takai R</u>, Fujita M, Harada F, Paudel D, Takahashi S, Yoshida K, Muthumala M, Nagayasu H, Chiba I, Abiko Y. Alteration of oral flora in betel quid chewers in Sri Lanka. *J Microbiol Immunol Infect*. Dec;54(6):1159-1166. Jun 27, 2021
- \* Yoshida K, Uehara O, Kurashige Y, Paudel D, Onishi A, Neopane P, Hiraki D, Morikawa T, Harada F, <u>Takai R</u>, Sato J, Saitoh M, Abiko Y. Direct reprogramming of epithelial cell rests of malassez into mesenchymal-like cells by epigenetic agents. *Sci Rep.* Jan 20;11(1):1852, 2021
- \* Osada K, Ohta T, <u>Takai R</u>, Miyazono S, Kashiwayanagi M, Hidema S, Nishimori K. Oxytocin receptor signaling contributes to olfactory avoidance behavior induced by an unpleasant odorant. *Biol Open* 26;7(9): 2018
- \* <u>Takada A</u>, Matsushita K, Horioka S, Furuichi Y, Sumi Y. Bactericidal effects of 310 nm ultraviolet light-emitting diode irradiation on oral bacteria. *BMC Oral Health* 17.96, 2017

- \* <u>Arakawa T</u>, Obara N, Okayama M, <u>Hosiriluck N</u>, Irie K, Mizoguchi I, Takuma T. Lysophosphatidic acid is involved in a cellular signaling of periodontal ligament and tooth development. *Dent J Health Sci Univ Hokkaido* 35(2): 23-32, 2016
- \* <u>Takai R</u>, Uehara O, Harada F, Utsunomiya M, Chujo T, Yoshida K, Sato J, Nishimura M, Chiba I, Abiko Y. DNA hypermethylation of extracellular matrix-related genes in human periodontal fibroblasts induced by stimulation for a prolonged period with lipopolysaccharide derived from *Porphyromonas gingivalis. J Periodontal Res* 51(4):508-17. 2016
- \* Nakao Y, Konno-Nagasaka M, Toriya N, <u>Arakawa T</u>, Kashio H, Takuma T, Mizoguchi I. Mechanical load influences proteoglycan expression in rat TMJ disc. *J Dent Res* 94(1): 93-100, 2015
- \* Ito M, <u>Arakawa T</u>, Okayama M, Shitara A, Mizoguchi I, Takuma T. Gravity loading induces adenosine triphosphate release and phosphorylation of extracellular signal-regulated kinases in human periodontal ligament cells. *J Investig Clin Dent* 5, 266–274, 2014
- \* <u>Arakawa T</u>, Ohta T, Abiko Y, Okayama M, Mizoguchi I, Takuma T. A polymerase chain reaction-based method for constructing a linear vector with site-specific DNA methylation. *Anal Biochem* 416: 211-217, 2011