Division of Pharmacology
Department of Oral Biology

Outline

Our specialty aria is "Ca^{2+}signaling". Ca^{2+} acts as an important intracellular messenger for the regulation of a wide range of biological processes, including secretions, neuronal activities, cell differentiation and migration. We are studying the mechanisms for generating intracellular Ca^{2+} signaling and its functions with a combination of molecular imaging techniques, molecular biology, and gene modification, and trying to elucidate roles of Ca^{2+} signaling in various biological events.

Bio-imaging is a topic of great interest in the bioscience community. Since the isolation of green fluorescent protein (GFP), researchers have reaped an art for creating a tool, which enables the direct visualization of biological functions. We are on the cutting edge of developing biosensors for visualizing inositol 1,4,5 trisphosphate (IP_3), the most important intracellular messenger for triggering Ca^{2+} responses in non-excitable cells. We use these techniques for studying the regulations of salivary secretions and tooth development.

Saliva secretion is vital for maintenance of oral health and functions. Stimulations of the M_3 muscarinic acetylcholine receptors (mAChRs) resulting in increased flow of salivary secretions through the Ca^{2+} signaling. Most of the studies in this field have been carried out in *in vitro* model systems. Recently, the virus vector-mediated gene delivery allowed us to visualize Ca^{2+} response of salivary glands in live animals with the real time monitoring of salivary secretions and blood flows.

It has been known that amelogenesis imperfecta is caused by the deficiency of store-operated calcium entry (SOCE), the main Ca^{2+} influx mechanisms in non-excitable cells. These findings suggest important roles of SOCE on amelogenesis. We visualized Ca^{2+} responses in rat dental epithelial cells (SF2) and human dental pulp stem cell (DPSP) using genetically encoded calcium indicators, G-GECO and R-GECO, and examined the role of SOCE on the cell migration and gene expression.

Faculty members (Left→Right)



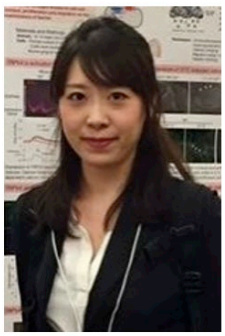
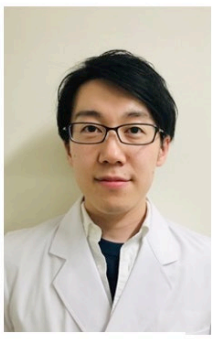
Professor;
Akihiko TANIMURA, Ph.D.
Associate professor;
Akihiro NEZU, Ph. D.
Assistant professor;
Shingo Senba, Ph. D.

Postgraduate students (Left→Right)


- **Div. of Pharmacology**
  Tahmina Akter, D.D.S
  Rezon Yanuar, D.D.S

- **Div. of Reconstructive Surgery for Oral and Maxillofacial Region**
  Mari SHIMATANI, D.D.S.,

Tenure Assistant (Left→Right)

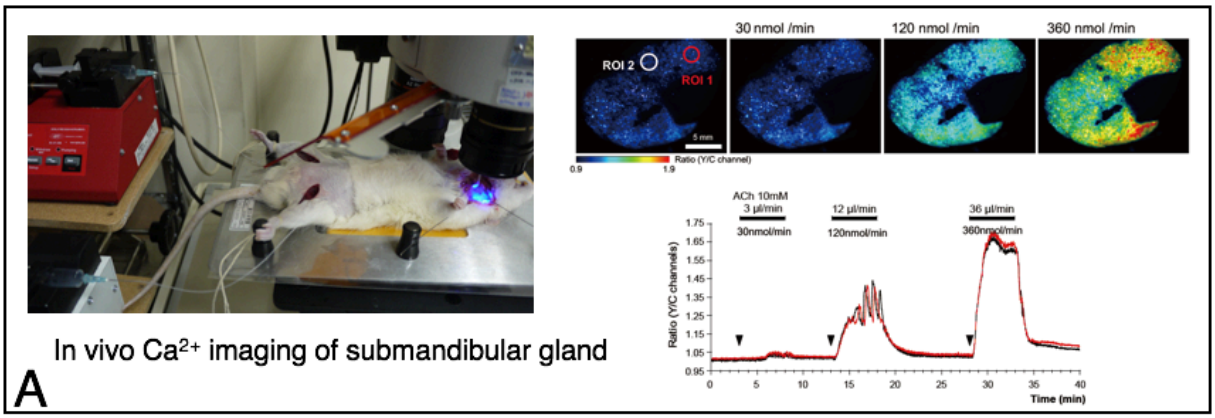



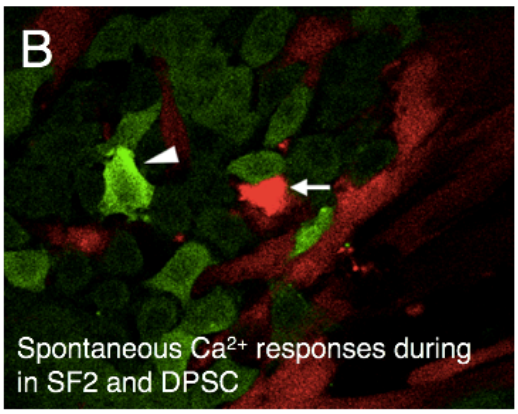
- **Div. of Pediatric Dentistry**
  Erika MINOWA, Ph. D.

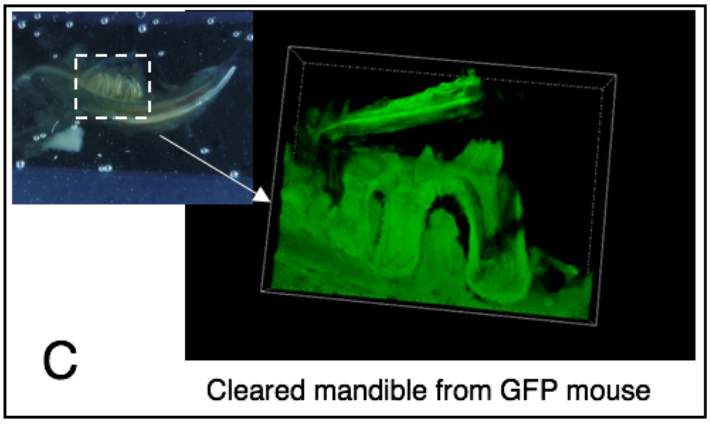
- **Div. of Dental Anesthesiology**
  Kenji GOH, D.D.S.,

Main research in progress

1) Development of fluorescent biosensors
2) In vivo Ca^{2+} imaging of salivary glands for improving salivary functions (A)
3) Role of Ca^{2+} responses for the control of tooth development (B)
4) Bone and Cancer imaging using Tissue Clearing Technology (C)







Selected publications

* Ishida N, Murata K, Morita T, Semba S, Nezu A & Tanimura A. Spontaneous calcium responses of SF2 rat dental epithelial cells stably expressing the calcium sensor G-GECO. Biomed Res, 42(5), 193-201, 2021.

* Tanimura A & Shuto S. Competitive Fluorescent Ligand Assay for Inositol 1,4,5-Trisphosphate. Methods in molecular biology (Clifton, NJ), 2091, 137-144, 2020.

* Ishikawa S, Kobayashi M, Hashimoto N, Mikami H, Tanimura A, Narumi K, Furugen A, Kusumi I & Iseki K. Association Between N-Desmethylclozapine and Clozapine-Induced Sialorrhea: Involvement of Increased Nocturnal Salivary Secretion via Muscarinic Receptors by N-Desmethylclozapine. J Pharmacol Exp Ther, 375(2), 376-384, 2020.

*Takahashi A, Morita T, Murata K, Minowa E, Jahan A, Saito M, Tanimura T. Effects of full-length human amelogenin on the differentiation of dental epithelial cells and osteoblastic cells. Arch Oral Biol 107, 104479, 2019.

* Nezu A, Morita T, Nagai T, Tanimura A. Simultaneous monitoring of Ca^{2+} responses and salivary secretion in live animals reveals a threshold intracellular Ca^{2+} concentration for salivation. Exp Physiol 104: 61-69, 2019.

* Sneyd J, Han JM, Wang L, Chen J, Yang X, Tanimura A, Sanderson MJ, Kirk V, Yule DI. On the dynamical structure of calcium oscillations. Proc Natl Acad Sci U S A 114: 1456-1461, 2017.

* Oura T, Murata K, Morita T, Nezu A, Arisawa M, Shuto S, Tanimura A. Highly Sensitive Measurement of Inositol 1,4,5-Trisphosphate by Using a New Fluorescent Ligand and Ligand Binding Domain Combination. Chembiochem 17: 1509-1512, 2016.

* Nezu A et al., Partial agonistic effects of pilocarpine on Ca^{2+} responses and salivary secretion in the submandibular glands of live animals. Experimental Physiology, 100: 610-651, 2015.

* Tanimura A et al., A fluorescence-based method for evaluating inositol 1,4,5-trisphosphate receptor ligands: Determination of subtype selectivity and partial agonist effects. J Biotechnol, 167: 248-54, 2013.