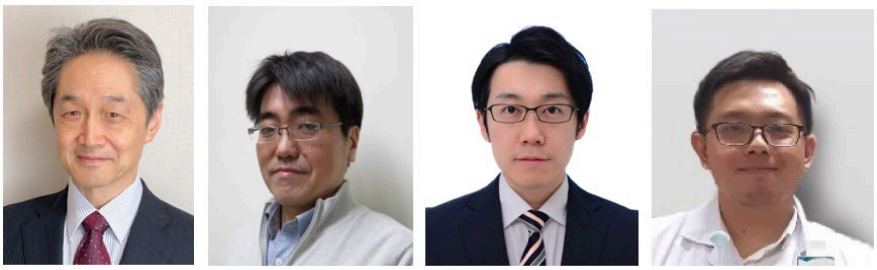
Division of Pharmacology
Department of Oral Biology

Outline

The Department of Pharmacology aims to understand various biological phenomena using live imaging technology to visualise reactions in cells and animals, tissue transparency technology to visualise three-dimensional tissue without sectioning, and molecular biological and genetic analysis technology to understand various biological phenomena from morphological, functional and molecular perspectives, and to link these to treatment and diagnosis. Our major focus of research is on 'saliva and salivary glands', but we also collaborate with clinical departments on bone invasion of cancer, tooth development, drug-induced gingival hyperplasia, and astrocyte function.

We also provide research support for undergraduate students who are interested in research. The results of these studies have been presented at conferences and in academic papers. Many of these students are also active as faculty members or postgraduate students in our university and in other universities.

Faculty members (Left→Right)

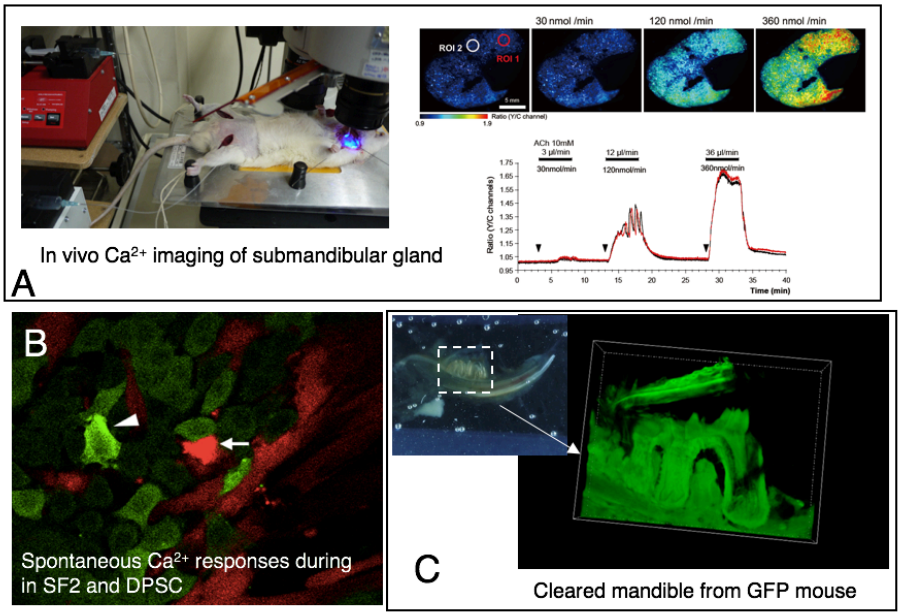


Professor;
Akihiko TANIMURA, Ph.D.
Associate professor;
Akihiro NEZU, Ph. D.
Assistant professor;
Kenji GOH
Postdoctoral Researcher
Rezon YANUAR

Postgraduate students
Nisrina Ekayani NASRUN (Division of Reconstructive Surgery for Oral and Maxillofacial Region)
Chiaki KANAKUBO (Division of Paediatric Dentistry)

Undergraduate student
Shiori KATOH（Fifth-year dental student）、Saizo ITOH（Fourth-year dental student）

Specific research topics.



Salivation and xerostomia: Stimulation of muscarinic receptors in salivary cells causes salivation by increasing intracellular Ca^{2+} concentration. Our laboratory has conducted advanced research to visualize the Ca^{2+} response in live animals and to monitor salivary secretions and blood flow in real time using rats expressing a Ca^{2+} sensor protein (YC-Nano50) in the salivary glands using viral vector-based gene transfer (A). This study has highlighted the importance of blood flow in salivary secretion. The importance of mastication in maintaining salivary gland function and its molecular mechanisms are also being investigated by genetic analysis.

Molecular mechanisms of bone invasion in cancer: Bone destruction often occurs in oral squamous cell

carcinoma. We study the mechanisms of bone destruction in collaboration with the Division of Reconstructive Surgery for Oral and Maxillofacial Region. It is well known that cancer-induced bone destruction is caused by cancer-induced osteoclasts. We are investigating direct bone destruction by cancer cells and the possible involvement of osteocytes in bone destruction by three-dimensional analysis using tissue transparency methods.

Tooth development and Ca^{2+} signalling: In the process of tooth development, dentinal epithelial cells differentiate into ameloblasts through interaction with dental pulp stem cells. The importance of Ca2+ has been suggested by the lack of enamel formation in genetic disorders in which the Ca2+ influx mechanism called SOCE is dysfunctional. In collaboration with the Department of Paediatric Dentistry, we are investigating the relationship between Ca^{2+} and enamel dysplasia by live imaging (B) using cells expressing Ca^{2+} sensor proteins (G-GECO and R-GECO) and RNA-seq analysis.

Drug-induced gingival overgrowth and Ca^{2+} signalling: Gingival hyperplasia caused by phenytoin and Ca^{2+} antagonists is an important dental problem. We have been studying phenytoin-induced intracellular Ca^{2+} concentrations and gene expression in human gingival fibroblasts in collaboration with the Department of Paediatric Dentistry. We have shown that phenytoin increases the intracellular Ca2+ concentration of HGF by suppressing Na^{+}/Ca^{2+} exchange proteins and that this Ca2+ response alters collagen biosynthesis and metabolism (Research Achievement 3).

Functions of astrocytes and Ca^{2+} signaling: Astrocytes are now known to support neuronal cells and actively participate in functions such as neurotransmission. We have developed a method for isolating astrocytes from adult rats in high purity. Live imaging analysis of the expression of Ca^{2+} sensor protein (G-CaMP) in these astrocytes revealed that brain-derived neurotrophic factor increases the ATP sensitivity of astrocytes by approximately 10-fold. We plan to develop this experimental system to analyse the relationship between astrocyte hyperfunction and chronic pain.

Research by undergraduate students

A Shitara（1999-2003）: Differential Ca^{2+} responses induced by thrombin and thrombin-receptor agonist peptides in HSY-EA1 cells. Cell Biol Int 2003;27:1017-23.

M Shimatani and A. Iwata(2014-2017) : Inhibit muscarinic acetylcholine receptor-mediated calcium responses by local anesthetics **Research achievement 2**

N. Ishida and Y. Seki(2014-2017) : Three-dimensional structural analysis of hard tissue using novel tissue transparency techniques. **（C）**

C. Kanakubo and M. Yokoyama（2017-2019）: Ultrafast tissue transparency methods and their application to cancer diagnosis and the development of therapeutic agents.

S. Katoh（2022～present）:Effects of serotonin on salivary secretion.

S. Itoh（2024～present）: Structural and functional analysis of hard tissue using confocal laser microscopy.

Recent research achievements

1.Yanuar R, Semba S, Nezu A & Tanimura A. Muscarinic acetylcholine receptor-mediated phosphorylation of extracellular signal-regulated kinase in HSY salivary ductal cells involves distinct signaling pathways. J Oral Biosci, 66(2), 447-455, 2024.

2. Shimatani M, Morita T, Yanuar R, Nezu A & Tanimura A. Local anesthetics inhibit muscarinic acetylcholine receptor-mediated calcium responses and the recruitment of beta-arrestin in HSY human parotid cells. J Oral Biosci, 66(2), 465-472, 2024.

3. Minowa E, Hayashi Y, Goh K, Ishida N, Kurashige Y, Nezu A, Saitoh M & Tanimura A. Enhancement of receptor-mediated calcium responses by phenytoin through the suppression of calcium excretion in human gingival fibroblasts. J Periodontal Res, 58(2), 274-282, 2023.

4. Akter MT, Nezu A, Akamatsu T & Tanimura A. Role of aquaporin 5 and glandular blood flow in the acetylcholine-induced secretion of saliva in rats. Biomed Res, 44(2), 51-63, 2023.