08 Accelerator Grants

Monitoring ATP synthase re-organization linked to LTP by Cryo-Tomography

Accelerator Grant

- Karin Busch, Dept. of Biology, University of Münster, Germany
- Elizabeth Jonas, Dept. of Internal Medicine, Yale University, New Haven, USA
- Nicholas Tomkinson, Dept. of Pure and Applied Chemistry, University of Strathclyde, Glasgow, UK
- **Yoshikazu Tanaka, Graduate School of Life Sciences, Tohoku University, Japan**

The goal of our research is to establish how mitochondria, the energy powerhouses of the cell, rapidly support learning processes at the molecular level, even before genes are activated. We are particularly interested in understanding how mitochondria efficiently provide energy in the form of ATP, during a process called long-term potentiation (LTP), which is crucial for learning and memory formation. The production of ATP utilizes mini-batteries generated by charge separation across the inner mitochondrial membrane. However, it appears that ions are constantly flowing across the membrane, discharging the battery. We believe that mitochondria can increase ATP production by making their internal membranes less permeable to ions, thereby increasing the energy available for ATP synthesis. We also think that the key enzyme in ATP production, ATP synthase, allows ions to pass through without synthesizing ATP. We hypothesize that ATP synthase reorganizes during LTP to work more efficiently, however, we currently lack the tools to directly observe this reorganization.

The Accelerator grant allows the integration of the structural biologist Yoshikazu Tanaka, who specializes in the study of proteins at the molecular level, into the team. Through his expertise, we will observe changes in ATP synthase and its interactions with other proteins in their natural environment before and after LTP. This will allow us to determine whether a different configuration of ATP synthase leads to improved energy production during learning and memory formation. If our research is successful, it could provide new insights into the fundamental processes that drive learning and memory formation in the brain.

Decoding invisibility: from genome evolution to tissue optical properties in transparent fish

Accelerator Grant

- Filippo Del Bene, Dept. of Developmental Biology, Institut de la Vision, Paris, France
- Sönke Johnsen, Dept. of Biology, Duke University, Durham, USA
- Mirana Ramialison, Stem Cell Medicine, Murdoch Children's Research Institute, Parkville, Australia
- **Vincent Laudet, Marine Eco-Evo-Devo Unit, Okinawa Institute of Science and Technology Graduate University, Japan**

The transparency observed in *Danionella* species, including *D. cerebrum*, is closely linked to their small size and paedomorphic traits, where adults retain juvenile characteristics. Transparency, an energy-costly and active phenomenon, is often found in small species and is prevalent among fish larvae, suggesting a connection between larval stage, reduced size, and transparency. In teleosts, metamorphosis plays a crucial role in transitioning larvae into juveniles. This process is particularly pronounced in marine species but also occurs in freshwater fish such as zebrafish, where adult pigmentation patterns emerge during metamorphosis. In all teleosts, thyroid hormones regulate metamorphosis, orchestrating the transformation of multiple organs and ensuring proper ecological functionality in the juvenile stage. In paedomorphic species like *Danionella*, metamorphosis is likely attenuated, as adults retain juvenile-like characteristics, including simplified pigmentation patterns—a condition necessary but not sufficient for transparency.

Our project aims to compare the metamorphic processes of *Danionella* and zebrafish to explore how transparency and pigmentation develop, with an emphasis on the molecular, cellular, and endocrinological mechanisms at play. Through bulk RNASeq analysis and comparative studies of thyroid hormone response, we hypothesize that *Danionella* undergoes a highly reduced metamorphosis with minimal gene regulation changes, particularly affecting pigmentation and growth-related genes.

The Accelerator team member Vincent Laudet, renowned for his research on metamorphosis, pigmentation, and thyroid hormone regulation in fish, will lead this comparative analysis. In collaboration with existing team members, the team will also contribute to work packages focused on tissue ultrastructure, genomic loci associated with transparency, and experimental validation of genetic and ultrastructural determinants of body transparency. We also plan to test the trade-off between energetic cost of transparency and predation benefits by conducting predation experiments to rigorously evaluate the evolutionary advantages of transparency in *Danionella*. By integrating genomic, molecular, and ecological perspectives, this project will clarify the complex interplay between metamorphosis, paedomorphosis, and transparency in this unique model.

Deciphering the evolution, cellular biology and biogeochemistry of symbioses in anaerobic eukaryotes

Accelerator Grant

- Filip Husnik, Okinawa Institute of Science and Technology Graduate University, Japan
- Roxanne Beinart, Graduate School of Oceanography, University of Rhode Island, USA
- Courtney Stairs, Dept. of Biology, Lund University, Sweden
- **Hidetaka Nomaki, X-star, Japan Agency for Marine-Earth Science and Technology (JAMSTEC), Yokosuka, Japan**

This HFSP Accelerator project aims to expand our original project on protist-prokaryote symbioses in low-oxygen environments by incorporating several advanced biogeochemistry methods and foraminifera as a new model system. Foraminifera are large single-celled eukaryotes prominent in low-oxygen environments. However, they differ from other eukaryotes that thrive in such environments by retaining classical mitochondria, suggesting distinct adaptations to oxygen-depleted habitats.

Hidetaka Nomaki's expertise with foraminifera, *in situ* experiments in challenging environments, and stable-isotope labeling coupled with Nanoscale Secondary Ion Mass Spectrometry (NanoSIMS) will significantly advance our research capabilities. The project will integrate NanoSIMS with genomic and transcriptomic analyses to quantify carbon, nitrogen, and sulfur exchanges between foraminifera, ciliates, jakobids, breviates, and their symbionts. NanoSIMS will allow us to test the predicted metabolic interactions and provide quantitative estimates of nutrient transfer between partners. The addition of Nomaki to the original project will enable us to address previously inaccessible questions, pushing the boundaries of the original project's scope.