Bioinformatics Center
– Chemical Life Science –

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Scope of Research

We are interested in understanding the functioning and evolution of biological systems at varying scales from tiny microbes up to the Earth's environment, by leveraging rapidly accumulating big data in life science and bioinformatics approaches. We currently focus on 1) the evolution of viruses and their links to the origin of life, 2) microbial ecology in different ecosystems, and 3) the development of bioinformatics methods and biological knowledge resources for biomedical and industrial applications. To fuel these research activities, we take part in environmental sampling campaigns such as *Tara* Oceans. Our resources and developed tools are accessible through GenomeNet (www.genome.jp) to scientific communities and the public.

KEYWORDS
GenomeNet
Bioinformatics
Environmental Genomics
Virology
Molecular Evolution

Selected Publications

Li, Y.; Hingamp, P.; Watai, H.; Endo, H.; Yoshida, T.; Ogata, H., Degenerate PCR Primers to Reveal the Diversity of Giant Viruses in Coastal Waters, *Viruses*, **10,** 496 (2018).

Endo, H.; Ogata, H.; Suzuki, K., Contrasting Biogeography and Diversity Patterns between Diatoms and Haptophytes in the Central Pacific Ocean, *Sci. Rep.*, **8,** 10916 (2018).

Mihara, T.; Koyano, H.; Hingamp, P.; Grimsley, N.; Goto, S.; Ogata, H., Taxon Richness of "Megaviridae" Exceeds Those of Bacteria and Archaea in the Ocean, *Microbes Environ.*, **33,** 162-171 (2018).

Yoshida, T.; Nishimura, Y.; Watai, H.; Haruki, N.; Morimoto, D.; Kaneko, H.; Honda, T.; Yamamoto, K.; Hingamp, P.; Sako, Y.; Goto, S.; Ogata, H., Locality and Diel Cycling of Viral Production Revealed by a 24 h Time Course Cross-omics Analysis in a Coastal Region of Japan, *ISME J.*, **12,** 1287-1295 (2018).

Yoshikawa, G.; Askora, A.; Blanc-Mathieu, R.; Kawasaki, T.; Li, Y.; Nakano, M.; Ogata, H.; Yamada, T., Xanthomonas Citri Jumbo Phage XacN1 Exhibits a Wide Host Range and High Complement of tRNA Genes, *Sci. Rep.*, **8,** 4486 (2018).

Nishiyama, H.; Nagai, T.; Kudo, M.; Okazaki, Y.; Azuma, Y.; Watanabe, T.; Goto, S.; Ogata, H.; Sakurai, T., Supplementation of Pancreatic Digestive Enzymes Alters the Composition of Intestinal Microbiota in Mice, *Biochem. Biophys. Res. Commun.*, **495,** 273-279 (2018).

Unraveling the Diversity and Ecological Role of Eukaryotic Viruses in the Sunlit Ocean

Viruses are abundant, diverse and essential component of marine ecosystems. They killed a large fraction of cells daily, thereby having a consequent impact on the ocean biogeochemistry and evolution of their host. While most efforts to characterize their diversity and ecology have been focused on bacterial viruses, current molecular sequence data derived from marine samples indicate that the diversity of eukaryotic viruses is vast and largely unexplored; with virtually no knowledge on the role that the various lineages fulfill in the environment.

We use omics data and associated metadata generated during the *Tara Ocean* expedition to explore the diversity and ecological role of eukaryotic viruses in the marine realm. Samples were collected in the sunlit layer of worldwide-distributed oceanic stations (Figure 1.A) and processed to generate metagenomes of bacterial-sized organisms (0.2 to 3 micron). This captures sequences of dsDNA viruses with large virion or dsDNA viruses replicated within their host cell. Samples were also processed to generate meta-transcriptomes of eukaryotic organisms (0.8 to 2000 micron). This captures transcripts of viruses actively infecting their hosts and RNA genomes. We use state of the art bioinformatics techniques to query viral genes out the several terabytes of molecular sequences generated. Next, we use marker genes to depict the diversity of eukaryotic viruses (Figure 1.B) and we compute their abundance across samples. This serves as the baseline to explore association between eukaryotic viral abundance and environmental parameters. For example, we test for association between viral abundance and export of carbon in the water column. We also look for co-abundance patterns between viral marker genes and host marker genes to detect virus-cell interactions. Results will serve as guidelines for further targeted studies aiming at characterizing viral-host systems and their role in oceans.

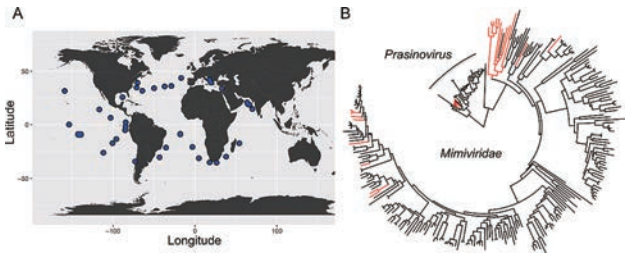

Figure 1. (A) Sampling sites of *Tara Oceans* expedition (2009-2012) used to analyze eukaryotic viruses. (B): Phylogeny of DNA polymerase B for large dsDNA viruses belonging to *Prasinovirus* and *Mimiviridae* unveils their large diversity in the sunlit ocean. Red: know viruses. Black: Viruses new to science.

Mice Intestinal Microbiota is Affected by the Administration of Pancreatic Enzymes

Pancreatic enzyme replacement therapy (PERT) is a treatment given to chronic pancreatitis patients to alleviate them of their pancreatic exocrine insufficiency (PEI) associated symptoms. Meanwhile, it has been recently inferred in a clinical study that the altered composition of intestinal microbiota is associated with the pathogenesis of the disease. Thus, in our study, we hypothesized that PERT exerts its effect not only through replenishing pancreatic digestive enzymes, but also by modifying the intestinal microbiota. To test this hypothesis, we conducted bacterial 16S rRNA gene targeted amplicon sequencing to investigate the intestinal microbiota of mice treated with either pancrelipase or tap water. The results have shown a difference in bacterial composition between these two groups of mice. Most interestingly two well-known beneficial bacteria have shown higher relative abundance in pancrelipase treated mice (Figure 2). One of them is *Akkermansia muciniphila*, which is known to benefit health through promoting intestinal barrier function. Another is *Lactobacillus reuteri*, which is a probiotic bacterium known to relieve intestinal inflammation. These results support our idea that PERT attenuates PEI-associated symptoms through the promotion of the colonization of beneficial bacteria, in addition to its already known mechanism. This project was done in collaboration with Dr. Sakurai's group in Kindai Univerisity Hospital.

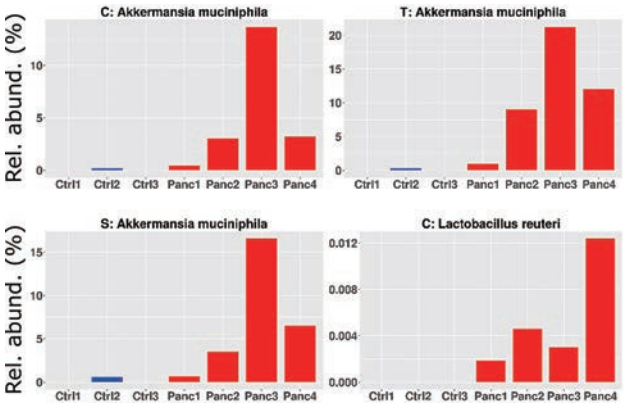

Figure 2. Relative abundance of two beneficial bacteria presenting significant difference in between pancrelipase-treated (shown in red) and tap water treated mice (shown in blue). The intestinal microbiota was observed at the cecum (C), transverse colon (T), and stool (S). Ctrl: control, Panc: Pancrelipase.