GMGI
CELEBRATING 10 YEARS

GMGI Science Forum
Thursday, October 26, 2023
Speaker Biographies and Abstracts

Mak Saito, Ph.D.

Senior Scientist, Department of Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution.

Dr. Saito's research interests include bioinorganic chemistry of novel marine metalloenzymes, environmental proteomics, trace metal biogeochemistry and chemical speciation, and the use of trace metals as micronutrients by marine phytoplankton and impacts on carbon cycling. He has a B.A. in Biology and Environmental Studies from Oberlin College and a Ph.D. in Chemical Oceanography from MIT/WHOI Joint Program. He was the Harry Hess Postdoctoral Fellow at Princeton University.
https://www.whoi.edu/profile/msaito/

Exploring metal uses within marine organisms using advanced proteomic techniques

The availability of metals in the oceans differs from terrestrial environments, where low solubility in seawater results in metal nutrition sufficiency being a significant challenge to the marine microbial life. In the Saito laboratory, we have developed proteomic techniques that deeply survey proteins use in the microbial populations in the oceans. Moreover, we have developed a metalloproteomic capability that can identify the major reservoirs of metals within cells using a dual mass spectrometry approach that couples plasma and orbitrap mass spectrometers. Using these two approaches, key metal enzymes have been identified as major uses of iron, zinc, copper and nickel in marine microbial populations. In this talk the diversity of marine microbial metalloproteins in the Pacific Ocean and Southern Oceans will be discussed and their implications for improving climate models will be discussed.

Katie Lotterhos, Ph.D.

Associate Professor, Marine and Environmental Sciences, Marine Science Center, Northeastern University

Dr. Lotterhos research uses eco-evolutionary genomics to understand how climate has shaped biodiversity and how a now rapidly changing climate will affect biodiversity in the future. Her research uses theory and experiment to inform each other and develops novel statistical methodology to integrate data across biological, spatial, and temporal scales. Current research projects include responses of marine invertebrates to ocean acidification and pollution, the population dynamics of fisheries with applications to management and marine reserve design, and methods development in statistical genomics. She is the leading investigator for the Research Coordination Network for Evolution in Changing Seas. She has a B.S. in Physics from Binghamton University and a Ph.D. in Biology from Florida State University.
https://cos.northeastern.edu/people/katie-lotterhos/

Promises and pitfalls of genomic forecasting

Predicting organisms' vulnerabilities to rapid and multivariate climate change is a major scientific challenge. Genomic forecasting is a promising new field that integrates genomics with projecting populations responses to environmental change. This talk will highlight how adaptation in multivariate environments can lead to unexpected patterns at the alleles under selection, which has implications for the inference of the genetic basis of adaptation and for predicting vulnerability to environmental change.

Emma Strand, Ph.D.

Postdoctoral Research Scientist, Gloucester Marine Genomics Institute

Dr. Emma Strand is a Postdoctoral Scientist with the Fisheries & Aquaculture team at Gloucester Marine Genomics Institute. Emma is a marine molecular biologist whose research focuses on using genomic techniques to understand drivers of physiological tolerance in response to environmental conditions, and to improve sustainable conservation practices and management for marine invertebrates and fisheries. Her current work investigates the physiological and epigenetic mechanisms underlying phenotypic differences in corals as well as the application of epigenetics to predict age in fish. Emma has a B.S. in Biology from Loyola Marymount University, where she held research positions at Bermuda Institute of Ocean Sciences and Roatán Institute for Marine Sciences in Roatán, Honduras. Additionally, Emma has a Ph.D. in Biological and Environmental Sciences from the University of Rhode Island, with active research at Hawai'i Institute of Marine Biology and GUMP Research Station in Mo'orea, French Polynesia.

Genomic and physiological drivers of thermal tolerance in marine invertebrates

Marine heatwaves are increasing in frequency and intensity, with potentially catastrophic consequences for marine taxa and ecosystems such as coral reefs. Elucidating the physiological and genomic, specifically epigenetic, mechanisms underlying acclimatization and thermal stress response have become crucial for understanding phenotypic variation in the face of climate change. During this talk, Emma will discuss how marine environmental epigenetics, in concert with other genomic mechanisms, may play a key role in phenotypic variation in corals, and how epigenetics research can be integrated into environmental management.

Kim Parsons, Ph.D.

Research Biologist, Northwest Fisheries Science Center, National Marine Fisheries Service, NOAA, Seattle, WA

Kim Parsons, Ph.D. https://www.fisheries.noaa.gov/contact/kim-parsons-phd leads the Molecular Genetics team in the Conservation Biology Division at NOAA's Northwest Fisheries Science Center in Seattle, WA. Kim is a molecular ecologist whose research focuses on the development and application of genetic and genomic tools to support the conservation and management of marine species. Her research emphasizes the value of generating genetic data from a wide range of biological samples to address gaps in knowledge of stock structure, diet, health and genetic fitness of marine mammal populations. Kim's work leverages affiliations and collaborations with partners in academia as well as other government and non-governmental organizations. Her research spans many species and many oceans. Kim received a B.Sc. in Biology from the University of Victoria (Canada) and her Ph.D. in Zoology from the University of Aberdeen (UK).

Genomic technologies to support the management & conservation of cetaceans large and small

Genetic and genomic data are key for supporting the conservation and management of marine mammals, providing novel insights into population structure, diet and health. Advances in technology from next-generation sequencing to environmental DNA approaches have dramatically increased both the scope and scale of molecular studies for protected species yielding new opportunities to address previously intractable questions. Using recent examples, Kim will describe some of the recent advances and advantages of studying cetaceans in the 'omics era and discuss new directions that are currently under development.

Shelly Wanamaker, Ph.D.

Research Scientist, Gloucester Marine Genomics Institute

Shelly Wanamaker, Ph.D. joined GMGI in 2021 after spending 10 years on the West Coast, where she developed her interests in marine science. Shelly did postdoctoral research at the University of Washington's School of Aquatic and Fishery Sciences on how shellfish and salmon are impacted by different environmental conditions using omics methods. Prior to her postdoctoral work, Shelly completed a year-long National Science Foundation (NSF) Graduate Research Internship at National Oceanic and Atmospheric Administration's (NOAA)'s Northwest Fisheries Science Center investigating how ocean acidification affects the physiology of Dungeness crabs and pteropods (sea snails). Shelly got her Ph.D. in Biological Sciences from the University of California San Diego, and her dissertation included her NOAA work as well as a sequencing technology she developed that tests millions of protein interactions at one time, which she used to map out different biological pathways in the mustard plant Arabidopsis thaliana (a model for plant research akin to the mouse model for human research). Shelly has a B.S. in Biochemistry from Simmons College in Boston and also worked as a Research Technician at the Center for Cancer Systems Biology (CCSB), Dana Farber Cancer Institute, in the lab of Dr. Marc Vidal (a GMGI founder and board member), where she contributed to large-scale mapping of protein interactions in human and disease genomes.

Rapid CRISPR-based diagnostics for detecting marine genomic signatures in animals and the environment

Timely detection of harmful microbes is critical to controlling disease spread in humans and marine animals. Standard molecular diagnostic tests (e.g. PCR) require laboratories and lag in time-to-result leading to delayed action. Alternative methods like isothermal amplification and CRISPR/Cas detection have high sensitivity and specificity with minimal, inexpensive equipment that can be converted to user-friendly, field-deployable formats. Different than antibody/ELISA based rapid tests, these detect genetic targets which makes them easily adaptable. Using these methods, we developed diagnostics for DNA and RNA viruses that impact shrimp farming worldwide (White Spot Syndrome Virus (WSSV) and Taura Syndrome Virus). We then adapted the diagnostics to target toxic *P.seudo-nitzschia* that cause amnesic shellfish poisoning in humans. The LAMP + CRISPR assays we developed show similar sensitivity, specificity, and quantification to real-time PCR. Ultimately, adapting these technologies for rapid, inexpensive, user-friendly monitoring of disease in aquaculture and the environment will support economic growth by reducing supply loss, increasing productivity and sustainability."

Michael Schmale, Ph.D.

Professor of Marine Biology and Ecology and Director of the National Resource for Aplysia, Rosenstiel School of Marine, Atmospheric, and Earth Science, University of Miami

Dr. Schmale's research interests are in the development and study of marine animal models of disease processes, with an emphasis on cancer and viral diseases. Ongoing research includes a combination of laboratory and field studies to investigate the causative agents, distribution and mechanisms of carcinogenesis of natural occurring, transmissible tumors in bicolor damselfish fish on South Florida reefs. Dr. Schmale is also the director of the National Resource for Aplysia, an NIH-funded facility for production and research on California sea hares, *Aplysia californica*. His research on Aplysia includes studies of virology and aging.

Damselfish Neurofibromatosis: An animal model of the role of mitochondria in cancer

Damselfish Neurofibromatosis (DNF) is a naturally occurring, infectious disease affecting bicolor damselfish (*Stegastes partitus*) on Florida reefs. This disease consists of multiple chromatophoromas (pigmented skin tumors), neurofibromas and malignant peripheral nerve sheath tumors (MPNSTs). The etiologic agent of this disease, the damselfish virus-like agent (DVLA), has been shown to replicate in the mitochondria of infected cells. Cancer cells have long been known to exhibit altered metabolism, typically characterized by major alterations in mitochondrial function. These changes adapt cancer cells to the demands of increased cell replication, often in hypoxic environments. Recent studies have also shown that mitochondrial alterations may be critical to the process of neoplastic transformation. DNF is an ideal model for investigation of the mechanisms by which changes in mitochondria may actually trigger neoplastic changes in infected cells. Evaluation of differentially expressed genes in normal skin versus tumor skin and versus MPNSTs revealed many large changes in up and down regulated genes. Analysis of canonical signaling pathways indicated conspicuous mitochondrial dysfunction in tumor skin and MPNSTs that included widespread reductions in expression of genes involved in both oxidative phosphorylation and the TCA cycle. An additional finding was significant and profound down-regulation of all 13 mitochondrial protein coding transcripts in tumor skin. Another strongly inhibited pathway involved signaling by Sirtuins (ie, SIRT3 and SIRT5). The observed down-regulation of these mitochondrial proteins as well as of SIRT3, a regulatory protein localized to mitochondria, would be expected to suppress both OxPhos and TCA pathways. This was confirmed using metabolic assays that showed significant suppression of most Oxphos respiratory complexes in these tumors. Thus a recurring theme in these comparisons was an overall alteration of mitochondrial function in DNF tumor cells. We have developed several hypotheses as to how DVLA infection induces these changes and how this may drive neoplastic transformation.

Brandon Weissbourd, Ph.D.

Assistant Professor of Biology, Investigator, The Picower Institute for Learning and Memory, Massachusetts Institute of Technology

Dr. Weissbourd uses the tiny, transparent jellyfish, *Clytia hemisphaerica*, to ask questions at the interface of nervous systems evolution, development, regeneration, and function. His foundation is in systems neuroscience, where he uses genetic and optical techniques to examine how behavior arises from the activity of networks of neurons. Building from this work, he investigates how the *Clytia* nervous system is so robust, both to the constant integration of newborn neurons and following large-scale injury. Lastly, he uses *Clytia's* evolutionary position to study principles of nervous system evolution and makes inferences about the ultimate origins of nervous systems. He received a B.A. in Human Evolutionary Biology from

Harvard University and a Ph.D. from Stanford University. https://biology.mit.edu/profile/brandon-weissbourd/

A genetically tractable jellyfish model for systems and evolutionary neuroscience

Jellyfish have successfully hunted the oceans for ~600 million years, making them perhaps the first free swimming animal predators on earth. Over this long history, they have played critical roles in ocean ecosystems, including tremendous socioeconomic impacts in modern times. Most recently, they are also presenting exciting model organisms for basic biological research due to their experimental tractability, evolutionary position, and shocking regenerative abilities. Here, I will describe the development of the jellyfish, *Clytia hemisphaerica*, as a laboratory model for neuroscience research. Using a suite of newly established genetic tools, I will present preliminary findings on how the distributed jellyfish nervous system is organized to robustly control behavior. Looking forward, *Clytia* presents exciting opportunities to deeply study the biology of these remarkable animals, with implications for systems, evolutionary, and regenerative neuroscience.

Matthew Harris, Ph.D.

Associate Professor, Department of Genetics, Harvard Medical School, Orthopaedic Research Laboratories, Boston Children's Hospital

Dr. Harris is an Associate Professor in the Department of Genetics at Harvard Medical School and at the Department of Orthopedics at Boston Children's Hospital. Dr. Harris specializes in comparative genetics and genomics focusing on the regulation of skeletogenesis and form. His work uses experimental models of vertebrate development, centering on the zebrafish as a platform for discovery of novel gene functions in development. Similarly, through comparative genomic approaches, his group identifies genetic networks regulating unique properties of development exposed through natural selection. Dr. Harris trained in the lab of Dr. John Fallon at the University of Wisconsin-Madison and with Dr. Christiane Nuesslein-Volhard at the Max-Planck Institute for Developmental Biology in Tuebingen, Germany.

Mother Carey's Children - leveraging genomics and oceanic diversity for discovery

There is a growing sea of genomic data that now extends from the common to organisms on the periphery of the imagination. 'Here be monsters' used to be a warning for sailors but now is a source of discovery. I will discuss work from my lab to mine phylogenetic patterns of variation within clades to identify genetic pathways underlying trait change, evolutionary diversity, and provide unique insight into hidden potential within our tissues.

Jeff Moffitt, Ph.D.
Assistant Professor, Department of Microbiology, Harvard Medical School
Investigator, Program in Cellular and Molecular Medicine, Boston Children's Hospital

Jeffrey Moffitt is an Assistant Professor in the Department of Microbiology at Harvard Medical School and the Program in Cellular Molecular Medicine at Boston Children's Hospital.

Jeff received his PhD from the University of California Berkeley in Physics working with Dr. Carlos Bustamante, where he developed novel methods to understand enzyme mechanism by measuring the Angstrom-scale movements of single molecules in real time. He then moved to Harvard University where he conducted postdoctoral research in the laboratory of Dr. Xiaowei Zhuang. In the Zhuang laboratory, Jeff co-developed multiplexed-error robust fluorescence in situ hybridization (MERFISH), a transcriptome-scale single-RNA-molecule imaging technique capable of imaging and identifying thousands of RNA molecules within single cells in intact tissue samples.

Jeff started his own laboratory in 2018, where he continues to develop new extensions of MERFISH and to apply these techniques to understand the spatial organization of commensal microbial communities, the role this organization plays on microbe-microbe and microbe-host interactions, and the role of the cellular organization of host tissues in the response to microbial perturbations. Jeff was named a Pew Biomedical Research Scholar in 2019.

Mapping the complexity of tissues with genomic microscopy

The behavior of tissues in health and disease arises from the complex interplay of the diversity of cell type and states found within those tissues. Different cell types and states, in turn, are defined by the genes they express. For this reason, techniques that can characterize the full diversity of genes expressed within single-cells have revolutionized our understanding of tissues by providing catalogs of the cell types within them. Unfortunately, most such single-cell transcriptomic techniques must first remove cells from tissues before characterizing thus, the spatial organization of the tissue is lost. I will discuss an exciting new suite of techniques known as spatial transcriptiomics—methods that can characterize gene expression within single cells without removing them from tissues, thus providing the ability to both define and discover cell types and map their spatial organization. Specifically, I will discuss one such method—MERFISH—which uses optical barcodes to image and identify thousands of different molecules simultaneously within individual cells. I will detail the development of this technique, highlight its performance, and share several recent applications of MERFISH for the construction of molecular and cellular maps of a range of tissues. The ability to not only build a list of the different types of cells in the mammalian body but also chart their intricate organization in all tissues promises both a deeper understanding of a wide range of biological questions and a powerful new window into the origin of a very wide range of disease.

KEYNOTE ADDRESS

Feng Zhang, Ph.D.

Investigator, Howard Hughes Medical Institute
Core Member, Broad Institute of MIT and Harvard
Investigator, McGovern Institute for Brain Research, MIT
James and Patricia Poitras Professor in Neuroscience, MIT
Departments of Brain and Cognitive Sciences and Biological Engineering, MIT

Feng Zhang is a molecular biologist focused on improving human health. He has developed multiple revolutionary technologies that are being used around the world to advance the study, diagnosis, and treatment of human diseases. He played an integral part in the development of optogenetics, pioneered the use of CRISPR systems for genome editing, and discovered a number of other natural systems, many of which he and his team have harnessed for therapeutic and diagnostic applications. This work is complemented by his work to develop novel delivery modalities for genetic therapeutics.

Zhang is a core member of the Broad Institute, an Investigator at the McGovern Institute for Brain Research, the James and Patricia Poitras Professor of Neuroscience at MIT, and a Howard Hughes Medical Investigator. He is also a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Medicine.

Exploration of Biological Diversity

Many powerful molecular biology tools have their origin in nature, and, often, microbial life. From restriction enzymes to CRISPR-Cas9, microbes utilize a diverse array of systems to get ahead evolutionarily. We are interested in exploring this natural diversity through bioinformatics, biochemical, and molecular work to better understand the fundamental ways in which living organisms sense and respond to their environment and ultimately to harness these systems to improve human health. Building on our demonstration that Cas9 can be repurposed for precision genome editing in mammalian cells, we began looking for novel CRISPR-Cas systems that may have other useful properties. This led to the discovery of several new CRISPR systems, including the CRISPR-Cas13 family that target RNA, rather than DNA. We developed a toolbox for RNA modulation based on Cas13, including methods for precision base editing. We are expanding our biodiscovery efforts to search for new microbial proteins that may be adapted for applications beyond genome and transcriptome modulation, capitalizing on the growing volume of microbial genomic sequences and building on our bioengineering expertise. We are particularly interested in identifying new therapeutic modalities and vehicles for delivering cellular and molecular cargo. We hope that this combination of tools and delivery modes will accelerate basic research into human disease and open up new therapeutic possibilities.