GLOUCESTER MARINE
GENOMICS INSTITUTE

2018 GMGI SCIENCE FORUM

SPEAKER ABSTACTS AND BIOGRAPHIES

KEYNOTE SPEAKER:

DAVID GALLO, PhD
Director of Special Projects, Woods Hole Oceanographic Institution

BIOGRAPHY:

Dr. Gallo has been at the forefront of ocean exploration for more than 25 years, participating in and being witness to the development of new technologies and scientific discoveries that shape our view of planet earth. He has participated in expeditions to all of the world's oceans and was one of the first scientists to use a combination of robots and submarines to explore the deep seafloor. He co-led an expedition to create the first detailed and comprehensive map of the RMS *Titanic* and is involved in planning an international expedition to locate and document the wreckage of Ernest Shackleton's ship, HMS *Endurance*. He is one of a few humans to witness the tremendous variety of life and unique adaptations of deep ocean organisms and is committed to conveying the excitement and importance of ocean exploration to the public-at-large. He has given more than 10 TED and TEDx presentations, has appeared in numerous documentaries and television news programs and is the recipient of numerous awards for his role in exploration and communications.

ABSTRACT:

Beyond the Titanic: The Oceans and Humanity

Oceans cover more than 70% of our planet with an average depth of about 2 1/2 miles. In the past they were shrouded in myth and mystery. With new technology we can now observe the deepest parts of the ocean with unprecedented clarity. Today we understand that the oceans largely control the air we breath, the food we eat, and the water we drink. Despite these facts the oceans remain largely unexplored and poorly understood. The oceans are changing faster than we can understand them and the future of humanity is at risk.

ROSALIND M. ROLLAND, D.V.M
Senior Scientist and Director, Marine Stress Ocean Health, New England Aquarium

BIOGRAPHY:

Dr. Rosalind (Roz) Rolland is the Director of Ocean Health and a Senior Scientist at the Anderson-Cabot Center for Ocean Life at the New England Aquarium (NEAq). Dr. Rolland also holds a Research Faculty appointment at The School for the Environment, UMASS-Boston. Dr. Rolland received her Bachelor's degree in Natural Sciences from the University of Wisconsin-Madison, and her DVM degree from Tufts University Veterinary School. Prior to joining the NEAq, Dr. Rolland worked as a Conservation Scientist at the World Wildlife Fund and as Science Director of the Center for Conservation Medicine at Tufts Veterinary School.

Dr. Rolland's research is focused on development of non-invasive methods to study health, reproduction and stress responses in large whales. She pioneered methods to measure an array of hormones in large, free-swimming whales using samples of scat and respiratory vapor (blow), and her program discovered that hormones are deposited in baleen, yielding a retrospective record of physiologic data. She has led projects investigating diseases, marine biotoxins, and the effects of underwater noise on large whales, and led development of a method to monitor health of North Atlantic right whales using photographs. The objective of Dr. Rolland's research program is to better understand the risks posed to large whales by human impacts on their marine habitat.

Dr. Rolland's work has resulted in numerous scientific publications and she is the co-editor (with Dr. Scott Kraus) of the definitive book on right whales, *The Urban Whale: North Atlantic Right Whales at the Crossroads* published by Harvard University Press in 2007. Dr. Rolland's research program has received widespread international attention in the popular press including stories by Science Magazine, the New York Times, Boston Globe, National Wildlife, National Public Radio, CBC Radio, BBC World News, Globe and Mail, Greenwire, New Scientist, and Science Daily Science Monitor among others.

ABSTRACT:

Ocean industrialization and stress responses in North Atlantic right whales

The western North Atlantic right whale (*Eubalaena glacialis*) is one of the most critically endangered whale populations globally with fewer than 450 individuals surviving. If current population trajectories continue, functional species extinction could occur within 25 years. Because the right whale range is nearshore along the heavily industrialized coastline of eastern North America, right whales are exposed to multiple stressors resulting from human activities. Thus, this population has been severely impacted by mortalities from vessel collisions and fishing gear entanglements, and by impaired reproduction; not a single calf was born in 2018. Assessing the sub-lethal impacts of

different types of disturbance in large whales is particularly difficult, as data and samples on individual whales are hard to obtain, and linking disturbance events with changes in health, reproduction and survival is challenging. Over the past two decades, we developed an approach to assess and monitor health in right whales using photographs, and we validated immunoassays for a panel of hormones to study stress responses and reproduction using fecal samples collected from free-swimming right whales. Results of our research shows declining health in right whales over three decades likely contributing to low calving rates, extremely elevated glucocorticoid ("stress") hormones in whales chronically entangled in fishing gear, and significant stress responses in right whales exposed to high levels of underwater noise from ship traffic. Our more recent approaches to study right whale physiology include analysis of steroid and thyroid hormones in respiratory vapor, and developing a retrospective profile of stress levels and reproductive history using hormones measured in baleen. These measures of health and stress integrate the effects of multiple stressors, and can be used to assess the cumulative impacts of living in the "urban ocean" for right whales.

DIANA BAETSCHER, PhD Candidate

BIOGRAPHY:

Diana is a PhD candidate who studies molecular ecology and population genetics/genomics at the University of California, Santa Cruz and NOAA's Southwest Fisheries Science Center. Her research focuses on larval dispersal in multiple species of Pacific rockfishes, and more recently, using genetic assignment to study seabird bycatch from Alaskan longline fisheries. Diana also studied population structure in Atlantic river herring.

ABSTRACT:

Close-kin mark-recapture identifies patterns of larval dispersal in a nearshore marine fish

Baetscher, D.S.[1,2*], Anderson, E.C.[2], Carr, M.H.[3], Malone, D.P.[3], Saarman, E.T.[3], Garza, J.C.[1,2]

1 – Department of Ocean Sciences, University of California, Santa Cruz
2 – Southwest Fisheries Science Center, NOAA Fisheries
3 – Department of Ecology and Evolutionary Biology, University of California, Santa Cruz

Nearshore marine species with pelagic larvae typically exhibit very little population structure in current-driven ecosystems, suggesting long distance dispersal and high gene flow. Because of this, quantifying dispersal is challenging, but remains a compelling goal, particularly for the design of marine protected areas (MPAs). Genetic analyses have revolutionized our ability to estimate demographic connectivity over small spatial scales.

When close-kin mark-recapture (CKMR) is applied to parent-offspring relationships, we obtain estimates of larval dispersal – the distance between a sedentary adult and its settled progeny. CKMR also reveals the variety of dispersal trajectories from a single parent when genetic markers have sufficient statistical power to identify full-sibling relationships. For species with large population sizes, intensive sampling is critical for increasing the likelihood of detecting parent-offspring or full-sibling matches. In this study, we genotyped over 14,000 rockfishes (genus *Sebastes*) sampled from Monterey and Carmel bays along roughly 25 km of coastline. As is sometimes the case in marine fishes, visual identification of juveniles is often unreliable. To address this challenge, we used a panel of 96 microhaplotype markers that were designed for pedigree inference in kelp rockfish (*S. atrovirens*), and in addition, can differentiate among 50 species of common eastern Pacific rockfishes. First, we distinguished kelp rockfish from other species sampled, and then identified eight parent-offspring pairs with high confidence. These matches indicate juveniles born inside of MPAs experience a variety of fates: dispersing to nearby MPAs, remaining within the same MPA as their parent, and settling outside of a reserve. Additionally, we identified 25 full-sibling pairs, which occurred throughout the sampling area, including two pairs of young-of-the-year siblings sampled in consecutive years. Our study provides direct evidence of patterns of dispersal for a nearshore fish along an open coastline in a temperate, current-driven ecosystem.

MARK STOECKLE, MD
Senior Research Scientist, The Rockefeller University, NY

BIOGRAPHY

Mark Stoeckle is Senior Research Associate in the Program for the Human Environment at The Rockefeller University. Dr. Stoeckle's interests include environmental genomics and DNA barcoding. His DNA barcoding work with high school students attracted wide attention including front-page articles in The New York Times and Washington Post. Dr. Stoeckle is a graduate of Harvard University and Harvard Medical School. Dr. Stoeckle published the first time-series environmental DNA study of the lower Hudson River estuary in 2017, and presented on eDNA at the United Nations in September 2018. He is helping organize the first national meeting on marine environmental DNA to be held at Rockefeller University in November 2018.

ABSTRACT

Fishing for DNA: environmental DNA tracks seasonal movements of fish and marine mammals

In 2008, researchers first demonstrated that small volumes of pond water contain enough environmental DNA (eDNA) to accurately determine whether or not an invasive frog species is present. Around this time, the DNA barcoding initiative firmly demonstrated that most animal species can be distinguished by a short stretch of mitochondrial DNA. This led to profiling aquatic animal communities by “metabarcoding”,

using high-throughput sequencing of pooled mitochondrial DNA segments amplified from environmental samples. Here we present results using this approach in coastal waters of New York and New Jersey. We discuss prospects for eDNA to improve monitoring of marine fish and mammals.

TIM SULLIVAN, PhD
Fisheries Research Scientist, Gloucester Marine Genomics Institute

BIOGRAPHY:

Tim Sullivan is GMGI's fishery research scientist. He has a background in population genetics, fishery science, and molecular and disease ecology. Before joining GMGI, Tim was a postdoctoral fellow in behavioral genomics at the University of Arkansas. He completed his Doctoral studies at the University of Louisiana at Lafayette where he researched genomics, larval, and disease ecology of blue crabs *Callinectes sapidus* in the Gulf of Mexico and his M.S. research at the University of Toledo where he studied spatial and temporal population structure of Great Lakes yellow perch *Perca flavescen.*

ABSTRACT:

Molecular ecology of crustacean disease: Candidate genes for pathogen resistance

Infectious diseases are a pervasive threat to marine populations and ecosystems. Identification of genes that contribute to variation in disease resistance is critical for management of marine animals. Here we use case-control comparisons to screen variants of candidate disease-resistance genes of the blue crab, *Callinectes sapidus* for association with infection by pathogenic *Vibrio* spp. bacteria and the parasitic dinoflagellate *Hematodinium perezi*. Transcripts of candidate genes were identified by functional annotation of blue crab transcriptomes. Single nucleotide polymorphisms (SNPs) in ~200 of these candidate resistance genes were identified in alignments of transcripts from multiple individuals. Blue crabs from the coast of Louisiana were genotyped for these SNPs and tested for infection by pathogenic bacteria in the genus *Vibrio* and the dinoflagellate *Hematodinium perezi* with PCR-based assays. We then used latent factor mixed models to test for associations between SNPs and pathogens. Two SNPs were associated with infection by *H. perezi*, while 10 SNPs and 1 multi-SNP haplotype were associated with infection by *Vibrio* spp.. Annotated biochemical functions for these candidate resistance genes include: ubiquitination, wound healing, signaling, lysosome function, and phagocytosis. Lastly, we identified correlations between resistant allele frequency and stressful environmental conditions in marshes throughout Louisiana and changes in resistant allele frequency among life stages (Larvae, juvenile, and adult) that suggest the potential for strong selection at these candidate gene regions.

LONE GRAM, PhD
Professor, Technical University of Denmark, Department of Biotechnology and Biomedicine

BIOGRAPHY:

Lone Gram received her MSc in 1985 and her PhD in 1989 from the Royal Veterinary and Agricultural University in Copenhagen. She has worked on fish technology projects in African and spent research visits at University of New South Wales and at Harvard Medical School. She has since 2000 been a professor in bacteriology, currently at the Technical University of Denmark. She received the Villum Annual Award in 2016 and has since January 2018 been leading a center of excellence on microbial secondary metabolites.

ABSTRACT:

Roseobacter group bacteria as probiotics in marine larviculture

Aquaculture has for decades been one of the fastest growing protein producing sectors and an important source of high quality protein for the growing world population. One of the constraints is bacterial diseases. Tremendous progress in disease control has been made using vaccination programs, however, antibiotics are being used against some agents and at some life stages, such as the larval stages where the immune system is not matured. Use of antibiotics is to be limited due to the alarming development and spread of antibiotic resistance in pathogenic bacteria and one alternative is the use of beneficial bacteria, so-called probiotics. Several species of marine bacteria belonging to the *Roseobacter* clade produce antibacterial compounds that antagonize fish pathogenic bacteria. The primary compound, tropodithietic acid, acts as a so-called antiporter, and target bacteria do not develop resistance against the compound. The roseobacters are part of the normal microbiota of marine systems and here we describe how roseobacters can inhibit fish pathogenic vibrios in several live feed systems (algae, Artemia, rotifers, copepods) used in marine larvi-culture. Also, roseobacters can reduce mortality in cod and turbot larvae challenged with pathogenic Vibrio, and they are thus promising disease control alternatives to antibiotics in marine larviculture.

MICHAEL BROSNAHAN, PhD
Assistant Scientist, Biology Department, Woods Hole Oceanographic Institution

BIOGRAPHY:

Michael Brosnahan is an Assistant Scientist in the Biology Department at the Woods Hole Oceanographic Institution. His overarching interest is in how microbial life cycles control the ecology and biogeography of toxic algal blooms in the ocean. Through this research he has led or contributed to several initiatives to develop and deploy Internet-connected in situ sensor technologies that provide remarkably rich descriptions of natural blooms in real time. These initiatives are revealing new aspects of the ecology and behavior of

these organisms while also pointing to new ways to manage and mitigate their negative impacts.

ABSTRACT:

Toxin production by an inshore bloom of the harmful dinoflagellate Alexandrium catenella

Michael L. Brosnahan[1], Juliette L. Smith[2], Gregory J. Doucette[3], Alexis D. Fischer[4], David M. Kulis[1], Stephanie Lim[5], David K. Ralston[1], Rob Olson[1], Heidi M. Sosik[1], and Donald M. Anderson[1]

[1]Woods Hole Oceanographic Institution, Woods Hole, MA 02543
[2]Virginia Institute of Marine Science, Gloucester Point, VA
[3]NOAA National Ocean Service, Charleston, SC
[4]University of California – Santa Cruz, Santa Cruz, CA
[5]Scripps College, Claremont, CA

Paralytic shellfish poisoning (PSP) is among the most severe toxin syndromes caused by harmful algal blooms yet there are still many unknowns about the transfer of PSP toxins into coastal ecosystems and the food supply. The dinoflagellate *Alexandrium catenella*, the most widespread PSP-causing species globally, has been studied intensively within the Nauset Marsh estuary (Cape Cod, MA USA) through deployments of new phytoplankton sensor technologies. Observations of *A. catenella* are enabled in part by the retentive nature of Nauset's terminal kettle ponds, which facilitates effective monitoring from fixed observatory sites. Selective retention also often results in near monospecific blooms. Our sensor installations are producing unprecedented insights into this species' behavior and physiology in situ. Among several noteworthy results are that naturally occurring *A. catenella* blooms develop more quickly, are more readily converted to cysts, and produce more toxins than had previously been known or thought possible. With high-frequency profiling through the full depth of one of these kettle ponds, the overall size of the *A. catenella* population in total cell number and biovolume has been characterized through several cycles of bloom development and decline. In combination with cell toxin measurement and cell imaging-derived estimates of division rate, it's possible to characterize the dynamics and scale of toxin production at a population level. Such whole population estimates provide a foundation for quantitative exploration of the supply and fate of PSP toxins in the environment.

RAMUNAS STEPANAUSKAS, PhD
Senior Research Scientist and Director of the Single Cell Genomics Center, Bigelow Laboratory for Ocean Sciences

BIOGRAPHY:

Dr Ramunas Stepanauskas obtained his PhD in ecology from Lund University, Sweden. He was a postdoctoral associate at the University of Georgia in 2000-2004. He then went on to become an assistant research scientist at Savannah River Ecology Laboratory at the University of Georgia. In 2005, Ramunas became a senior research scientist at the Bigelow Laboratory for Ocean Sciences. In 2009, he became a founding director of Bigelow Laboratory Single Cell Genomics Center, having established the first high throughput, shared user facility for microbial single cell genomics. He has also held a research faculty appointment at Colby College since 2009.

ABSTRACT:

Ocean Microbiome Datafication

Data-rich, molecular analyses are becoming important sources of knowledge about the composition and activities of microorganisms in the oceans and other environments. Yet, today only a small fraction of these meta-'omics data (short DNA, RNA and peptide sequences) can be accurately interpreted and assigned to specific microbial lineages and metabolisms. This is largely due to the lack of adequate reference genome databases, compounded by the vast microbial diversity and resistance to cultivation. To address this challenge, we sequenced 20,000 individual bacteria, archaea and virus particles from a global set of epipelagic environments in tropical and subtropical ocean using an unbiased, Big Data approach. This database, which we call GORG-Tropics, provides some of the first insights into the global pangenomes, infections, biogeography and sizes of many of the bacterial and archaeal lineages that dominate tropical and subtropical, surface ocean. We show that GORG-Tropics enables accurate taxonomic and functional assignments of the majority of meta-omics data from this environment. Intriguingly, we found that every microbial cell in this large data set was genomically unique, and that a large fraction of the global bacterioplankton coding potential was present in a single drop of seawater. GORG-Tropics expands the capacity of oceanography's cyber-infrastructure and enhances the interpretation of diverse marine omics studies. It also demonstrates that relevant representation of complex microbiomes in genome databases is an achievable goal and may be applicable in other environments.

LEONID MOROZ, PhD
Distinguished Professor, Department of Neuroscience, The Whitney Laboratory for Marine Bioscience, University of Florida

BIOGRAPHY:

Leonid L. Moroz is Distinguished Professor of Neuroscience, Genetics, Chemistry and Biology at the University of Florida. He earned his Ph.D. in physiology and developmental biology in 1989; then performed his postdoctoral research at the University of Leeds (UK) and at the University of Illinois. Dr. Moroz was an HHMI International Scholar and, in 1998, was recruited to the University of Florida.

Prof. Moroz takes advantages of marine biodiversity (>20 phyla) to understand how neurons operate, learn and remember; and how this complexity formed. He reveals that neurons and centralized brains independently evolved from ancestral cell lineages. Using massive single-cell genomics, he is reconstructing how the descendants of these cell lineages “come together” to form nervous systems of ctenophores and cnidarians or brains of octopuses or humans. Unique floating labs have been developed to sequence marine organisms directly aboard (Ship-Seq) to reconstruct the genealogy of neurons and make “better brains”. This real-time oceanic genomics implements cutting-edge technologies (e.g. single-cell RNA-seq, epigenomics, RNA editing & RNA modifications) to decipher genomic mechanisms underlying the origins of animal innovations, and use this knowledge to repair, design and construct novel neural circuits; enhance memory and regeneration capabilities.

Prof Moroz’ research was covered by more than one hundred media outlets both internationally (from Australia to Europe, translated to Japanese, Chinese, Arabic, Spanish, German, Russian and French, etc.) and nationally including *Associated Press*, *Reuters*, *BBC* (UK), *ABC News* and *MSNBC*, *Fox News*, *National Geographic*, *Spiegel*, *New York Times*, *Washington Post*, *Chicago Tribune*, *Scientific American*, *the Scientist*, *New Scientist*, *History Channel*, etc.

ABSTRACT:

Origins of cell types, neurons and brains through the lens of single-cell genomics: Insights from the first one million cells sequenced across phyla

Leonid L. Moroz[1,2]

1. Dept. of Neuroscience, Brain Institute, Whitney Lab., University of Florida, FL 32611
2. Whitney Lab for Marine Bioscience, University of Florida, FL 32080

The genomic mechanisms underlying the tremendous diversity of cell phenotypes, and neurons in particular, are largely unknown. This diversity reflects complex evolutionary histories of ancestral cell lineages, where cell types can be defined as units of evolution with distinct gene regulatory programs. Our task is to identify such programs. Here, by

sequencing >2.5 millions of cells (scRNA-seq) from representatives of 15 phyla (about 1/2 of the extant animal body-plans), my laboratory, with interdisciplinary collaborations across the globe, attempted (1) to decipher the genealogy of cell types; and (2) to identify genomic toolkits controlling cell phenotypes. Unique floating labs have been developed to sequence marine organisms directly aboard (Ship-Seq). Comprehensive cell atlases were constructed from 20+ species, highlighting major transitions in the formation of tissues, organs and neuro-muscular organization. In key reference species (i.e. ctenophores, known as the sister group to Metazoa; *Xenoturbella* - the sister to bilaterians; *Aplysia* and *Drosophila*), we sequenced virtually all neurons (Brain-seq) with approximately 20x coverage. Amazingly, we can identify single-neuron homologies at the scale of about 400 million years! Our model suggests that neurons evolved at least 2-3 times from ancestral secretory cells (in ctenophores, cnidarians and bilaterians). There were 9-12 parallel centralization events, which lead to independent formations of "chimeric" brains, ~500+ million years ago from genetically distinct cell populations. Using machine learning, cell-specific ncRNAs and RNA modifications, we began to predict neural subtypes and even recognize neuronal and glial identities with 90-99% probability.

The proposed synthesis of single-cell "omic"/machine-learning approaches and phylogeny leads to the concept of "Periodic System of Neurons/Cell Types" with predictive power for cellular phenotypes. Such unbiassed Evolutionary Cell Systematics is the conceptual analog of the Periodic System of Chemical Elements. Arguably, marine animals are the most suitable for the proposed tasks of NeuroSystematics because the world oceans represent the greatest taxonomic and body-plan diversity.

MANDË HOLFORD, PhD
Associate Professor in Chemistry, Hunter College and City University of New York

BIOGRAPHY:

Dr. Mandë Holford is as an Associate Professor in Chemistry at Hunter College and CUNY-Graduate Center, with scientific appointments at the American Museum of Natural History and Weill Cornell Medicine. Her joint appointments reflect her interdisciplinary research, which goes from *mollusks to medicine,* combining chemistry and biology to discover, characterize, and deliver novel peptides from venomous marine snails as tools for manipulating cellular physiology in pain and cancer. Her laboratory investigates the power of venom to transform organisms and to transform lives when it is adapted to create novel therapeutics for treating human diseases and disorders. She has received several awards including being recently named a New Champion Young Scientist by the World Economic Forum, the prestigious Camille Dreyfus Teacher-Scholar Award, an NSF CAREER Award, and honored as a Breakthrough Women in Science by the Howard Hughes Medical Institute (HHMI) and NPR's Science Friday. Dr. Holford is actively involved in science education, advancing the public understanding of science, and science diplomacy. She is cofounder of KillerSnails.com, an award-winning learning games company that uses

extreme creatures, like venomous marine snails, as a conduit to advance scientific learning in K-12 classrooms. Dr. Holford codeveloped a premier Science Diplomacy course at The Rockefeller University to encourage early career scientists to think globally about the impacts of their research as it pertains to international relations. Dr. Holford is a Life Member of the Council of Foreign Relations, and a AAAS Science &Technology Policy Fellow. Dr. Holford received her PhD in Synthetic Protein Chemistry from The Rockefeller University. Twitter: @Scimaven | Email: mholford@hunter.cuny.edu

ABSTRACT:

From mollusks to medicine: A venomics approach for the discovery and characterization of therapeutics peptides

Breakthrough technological advancements have enabled interdisciplinary studies using genomics, transcriptomics, and proteomics to expand venom investigation to animals that produce small amounts of venom or lack traditional venom producing organs. One group of non-traditional venomous organisms that have benefitted from the rise of -omic technologies is the Terebridae (auger snails). Neglected organisms, such as venomous terebrid sea snails, offer a unique perspective for investigating the evolution of venomous animals and for identifying novel compounds with therapeutic potential. This talk will highlight venom, a nonmodel system, to discover new theories about evolution and new compounds for treating diseases pertaining to pain and cancer. There are currently six venom-derived drugs available commercially and they are used to treat a variety of ailments from pain to diabetes. In my laboratory we are examining how venom evolved over time in the Terebridae, and we are using this evolutionary knowledge as a roadmap for discovering and characterizing novel compounds with therapeutic potential. Specifically, we apply inventive tools from chemistry and biology to: (1) discover disulfide-rich peptides from venomous marine snails, (2) develop high-throughput methods for characterizing structure-function peptide interactions, and (3) deliver novel peptides to their site of action for therapeutic application.

PAUL JENSEN, PhD
Professor, Scripps Institution of Oceanography, University of California San Diego

BIOGRAPHY:

Paul Jensen is a Professor at the Scripps Institution of Oceanography at the University of California San Diego. He earned an MSc degree in microbiology from San Diego State University and a PhD degree in marine biology from SIO. His research interests intersect the fields of marine microbiology and natural product chemistry and include chemical ecology, “omic” sciences, molecular evolution, and developing new methods for natural product discovery. Studies in these areas focus on specific groups of marine bacteria to gain a better understanding of who they are, where they live, why they make natural products, and how we can better exploit them for useful purposes.

ABSTRACT:

From Sea to Pharmacy: Sequence-based Approaches to Marine Natural Product Discovery

Microorganisms remain one of our most important sources of natural product derived medicines. The search for new natural products now includes marine bacteria, which are yielding promising new compounds and drug leads. These efforts have been advanced by sequence-based technologies that allow us to predict natural product biosynthetic potential based on genomic or transcriptomic analyses prior to chemical or biological screening. Sequencing large numbers of closely related strains of marine bacteria provides opportunities to assess the diversity and distributions of biosynthetic gene clusters, how they evolve to yield new compounds, and how subtle changes in gene content and organization can have a major impact on compound production. These concepts will be addressed using the obligate marine actinomycete genus *Salinispora*. This genus has proven to be an effective model for natural product discovery and the source of the proteasome inhibitor salinosporamide A, which is scheduled to enter phase III clinical trials for the treatment of cancer.