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Bioinformatics of corals: Investigating heterogeneous omics data from coral holobionts for insight into reef health and resilience

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Coral reefs are home to over 2 million species and provide habitat for roughly 25% of all marine animals, but they are being severely threatened by pollution and climate change. A large amount of genomic, transcriptomic and other -omics data from different species of reef building corals, the uni-cellular dinoflagellates, plus the coral microbiome (where corals have possibly the most complex microbiome yet discovered, consisting of over 20,000 different species), is becoming increasingly available for corals. This new data present an opportunity for bioinformatics researchers and computational biologists to contribute to a timely, compelling, and urgent investigation of critical factors that influence reef health and resilience. This paper summarizes the content of the Bioinformatics of Corals workshop, that is being held as part of PSB 2021. It is particularly relevant for this workshop to occur at PSB, given the abundance of and reliance on coral reefs in Hawai'i and the conference's traditional association with the region.

Keywords: coral reefs, coral holobiont, non-model organisms, functional genomics, genotype to phenotype, genome and environment, workshop.

1. Introduction, Background and Motivation

Corals are important natural resources that are key to the oceans' vast biodiversity and provide economic, cultural, and scientific benefits. Coral colonies are comprised of clonal cnidarian polyps that depend on a symbiotic relationship with algae in the family Symbiodiniaceae.¹ The dinoflagellate algae harvest light and synthesize nutrients in exchange for shelter and nitrogen sources.² Coral reefs cover only 0.1% of the ocean floor, but are home to the largest density

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of animals on earth, rivaling rain forest habitats in species diversity.³ The symbiosis, which was originally thought to primarily include endosymbiotic algae, is now known to extend to a much more complex community than anticipated with thousands of bacteria, bacteriophages, viruses and fungi, in addition to Symbiodiniaceae.^{4,5} Thus, corals are more like cities than individual animals, as they provide factories, housing, restaurants, nurseries, and more for an entire ecosystem, both at the micro and macro levels. The entirety of the organism community in a coral is referred to as a *holobiont*.

The environmental sensitivity and symbiotic biological complexity of corals makes understanding the genomic variability that influences vulnerability and resilience of local coral reef systems very challenging.² However, improving this understanding has taken on increasing urgency, as coral reefs are declining rapidly due to the consequences of climate change. For example, mass coral bleaching, or the expulsion of the symbiotic algae due primarily to thermal stress driven by marine heatwaves, is resulting in substantial coral mortality.⁶ Fortunately, a large amount of genomic, transcriptomic and other omics data from different species of reefbuilding corals (e.g.,⁷), the uni-cellular dinoflagellates,⁸ and the highly diverse coral microbiome,⁹ is becoming increasingly available for corals.¹⁰⁻¹⁴ This is a terrific opportunity for bioinformatics researchers and computational biologists to contribute to a timely, compelling and urgent investigation of critical factors that influence reef health and resilience.¹⁵

We have recruited some of the premier experts who are working on bioinformatics of coral reefs to participate in our workshop already. We will introduce this exciting topic to the PSB community, with the goal of energizing collaborations and approaches to address the compelling problems in this captivating and complex system. It is particularly relevant for this session to occur in Hawai'i given the abundance of and reliance on coral reefs in the region. Coral genomes from this location show some of the highest complexity to date,¹⁶ exemplifying the bioinformatic challenges faced by the field in the study of the coral metaorganism. This convergence of complex multi-organism data and critical need to address this globally declining ecosystem provides a timely and impactful topic for a Workshop at PSB 2021.

2. Workshop Presenters

The workshop consists of four invited presentations, and then short contributed talks. The invited speakers are:

- Christian Voolstra, Ph.D. (Professor of Genetics of Adaptation in Aquatic Systems, Department of Biology, University of Konstanz, Germany)
- Ross Cunning, Ph.D. (Research Scientist, John G. Shedd Aquarium, Chicago, USA)
- Zachary Fuller, Ph.D. (Postdoctoral Fellow, Dept. of Biological Sciences, Columbia University, USA)
- Cheong Xin (CX) Chan, Ph.D. (Senior Research Fellow, Australian Centre for Ecogenomics, School of Chemistry and Molecular Biosciences, The University of Queensland, Australia)

3. Invited Presenters' Abstracts

The abstracts of the invited presentations appear below.

The metaorganism frontier - we are not alone*Christian Voolstra (University of Konstanz, Germany)*

Recent years have brought a changing imperative in life sciences sparked by the revolution of genomic tools to study the molecular composition and functional organization of organisms. The development of next-generation sequencing changed our understanding of microbial diversity associated with organisms and environments. There are now a multitude of studies that support the notion that a host-specific microbiome associates with multicellular organisms and provides functions related to metabolism, immunity, and environmental adaptation, among others. Consequently, interactions and communication mechanisms of members in this metaorganism presumably play a major role in maintaining host health, organismal homeostasis, and resilience to environmental disturbance. The seminar will highlight and discuss recent efforts to investigate coral metaorganism function and evolution using a suite of ecological, physiological, and molecular approaches.

Genotype by genotype by environment interactions in the conservation of reef corals*Ross Cunning (Shedd Aquarium, Chicago, USA)*

Current conservation goals for reef-building corals under climate change involve boosting desirable traits like heat tolerance and fast growth in natural and restored coral populations. This may be accomplished through a number of interventions including symbiotic manipulation, selective propagation and breeding, and assisted gene flow. However, the success of these interventions depends on understanding how the desired traits are controlled by the genes of the coral host, its algal symbionts, and the environment (i.e., genotype by genotype by environment interactions). Here I will describe research aimed at characterizing these interactions in the growth and thermal tolerance phenotypes of several Caribbean coral species through both laboratory and field approaches. In experimental manipulations of algal symbionts in the coral *Montastraea cavernosa*, different symbiont taxa modulated host gene expression, contributing to differences in thermal tolerance. In the endangered staghorn coral *Acropora cervicornis*, variability in thermal tolerance was linked to specific alleles for coral genes associated with the heat stress response. In the field, large-scale reciprocal transplant experiments in partnership with reef restoration practitioners are also revealing genotype by environment interactions, which, along with new technologies to quantify thermal tolerance, are being used to identify high-performing and resilient individuals across whole managed coral populations. This phenotypic catalog, combined with whole genome sequencing and analysis, will help determine the genomic basis of key performance traits, and guide effective intervention strategies for coral conservation under climate change.

Genome-wide association study (GWAS) of bleaching tolerance in a Great Barrier Reef coral*Zachary Fuller (Columbia University)*

Although reef-building corals are rapidly declining worldwide, there is considerable variation in bleaching response and heat tolerance within populations, which is in part heritable. To map the genetic basis of this variation and develop individual predictors of bleaching in the wild,

we conducted a genome-wide association study (GWAS) of bleaching in *Acropora millepora* from the Great Barrier Reef. We first generated a chromosome-scale genome assembly and obtained whole genome sequences for over 200 phenotyped samples collected at 12 reefs, across which we found little population structure. We show that we can reliably impute genotypes in low-coverage sequencing data with a modestly sized reference haplotype panel to obtain millions of high confidence single nucleotide polymorphism (SNP) calls. Testing 6.8 million SNPs for association with bleaching, we show that no single variant reaches genome-wide significance. However, we show a polygenic score constructed from the GWAS estimates is a significant predictor of bleaching. We then demonstrate the feasibility of such an approach by scaling up our GWAS to an increased sample size of more than 1000 whole-genome sequenced and phenotyped individuals. These results thus set the stage for the use of genomic-based prediction in coral conservation strategies.

Understanding genome evolution of coral symbionts

Cheong Xin Chan (University of Queensland, Australia)

The ecological success of corals in nutrient-poor waters relies on photosynthetic algal symbionts (Symbiodiniaceae) for supply of fixed carbon as energy, and nutrients. The evolution of these algae and its implications on coral evolution remains little known. Genomes of Symbiodiniaceae present a bioinformatics challenge, because of their large sizes (1-5 Gbp) and highly idiosyncratic features. In this talk, I will present our recent effort to generate *de novo* genome assemblies from diverse Symbiodiniaceae species and their free-living relative, and to develop a customised computational workflow for predicting genes from these genomes. Comparative analysis reveals high sequence and structural divergence, and conserved lineage-specific gene families of unknown function. I will also present the use of an alignment-free approach to capture comprehensive phylogenetic signal from these whole-genome sequences. Our results highlight the rapid evolution of coral symbionts that comprise an extensive phylogenetic diversity, and elucidate how selection acts within the context of a complex genome structure to facilitate local adaptation. These outcomes provide an important reference for research of coral holobionts and their resilience in changing environments.

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