PERSPECTIVES

Thermal intolerance led to coral bleaching on a reef in American Samoa during a 2015 marine heatwave.

PHOTO: RACHAEL BAY

GENOMICS

Can genomes predict coral bleaching?

Expansion of the coral genomic tool kit could facilitate more informed conservation

By **Rachael A. Bay** *and* **Leslie Guerrero**

Coral reefs provide more than 1 billion people with food and income, yet these vital ecosystems are at risk because of rising ocean temperatures. Warming can induce coral bleaching, the breakdown of symbiosis between the coral animal and the photosynthetic algae that live within their cells, which can ultimately lead to coral death. Predicting which coral individuals are most tolerant to warming temperatures is essential to effective conservation plans. On page 268 of this issue, Fuller *et al.* (*1*) use genomic tools to predict bleaching outcomes for *Acropora millepora* corals. In doing so, they provide an integrative framework to advance predictions of climate change resilience on coral reefs, leading to more informed conservation and restoration efforts.

The frequency and severity of global coral bleaching episodes has been steadily increasing in recent decades (*2*, *3*), leading to mass mortality of corals and transformation of coral reef ecosystems (*4*). But not all corals are the same. In the 1970s, it was observed that corals from different oceanic regions had different upper thermal limits (*5*), leading to the general observation that warmer waters—for example, equatorial regions—harbor more heat-tolerant corals (*6*). Later observations of bleached corals immediately adjacent to unbleached corals opened the door to a role for intrinsic mechanisms of thermal tolerance variation. It is now known that thermal tolerance in corals is a function of the genetics of the coral, the algal symbiont and microbial community, and the environment that the coral has experienced (*7*–*10*).

Despite advancements in the use of genomic technology in corals over the past decade, the understanding of the genes responsible for determining thermal tolerance remains incomplete. This is partially due to the lack of high-quality genomic resources. To solve this problem, Fuller *et al.* produced a chromosome-level genome assembly from a single *A. millepora* coral. Genome assemblies serve as a "backbone" for genomic comparisons of individuals and populations, but assembling genomes in corals has proven difficult, in part because sequencing technology has been insufficient to resolve large repetitive regions. The genome Fuller *et al.* created using long-read

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technology to cope with repetitive regions will be an enormous resource for future studies of coral ecology, evolution, cell biology, and development, facilitating previously untenable investigations in this ecologically important system.

With the aid of the new genome assembly, Fuller *et al.* endeavored to uncover the genetic variants associated with coral bleaching and test whether these variants could be used to predict individual bleaching susceptibility. One challenge is that bleaching is a complex trait. It is highly polygenic, encoded by many genes across the genome rather than a few key genes. This makes identifying the causative genetic variants difficult. Fuller *et al.* borrowed tools first used in human disease and agricultural applications to calculate "polygenic scores," combining the effects of many variants across the genome. In humans, this method was first used to predict the risk for schizophrenia and bipolar disease (*11*). Since, it has been used to predict traits as diverse as milk fat in dairy cows (*12*) and cancer risk in humans (*13*).

Fuller *et al.* sequenced genomes for 213 colonies of the coral *A. millepora* on the Great Barrier Reef. The colonies were collected during a bleaching event in 2017, so the authors also recorded the bleaching status for each colony. They found that although no individual genetic variants are significantly associated with bleaching, the combined polygenic score provides some predictive power. Furthermore, integrating this information with environmental variables (such as temperature and salinity) and symbiont species information, the authors were able to explain the majority (62%) of variation in bleaching among individuals.

The authors also scanned the genome for evidence of natural selection more generally. They found an unusually high amount of genetic diversity in a gene called *sacsin*. This gene encodes a co-chaperone that modulates heat shock protein 70 (Hsp70), which is involved in heat stress responses and is highly conserved throughout the tree of life. Hsp70 and associated proteins maintain proper protein folding during cellular stress before aggregations of misfolded proteins become toxic. Primarily studied within the context of human neurodegenerative disease, *sacsin* is important for the degradation of damaged mitochondria (*14*). These findings offer clues about coral cellular health mechanisms, especially considering that mitochondria play a role in response to thermal stress. Selection has maintained high genetic diversity of this locus for tens of millions of years, a time that long predates the split between *A. millepora* and other closely related species (*1*). This raises questions about the historical drivers of the genetic diversity of *sacsin* in *A. millepora* and the coral-specific role of *sacsin*.

Identifying genes under selection is useful for understanding coral biology, but this study's predictive framework could also advance current conservation and management efforts—for example, by identifying tolerant individuals for prioritization of protected areas, outplanting efforts, or selective breeding. Equally important to consider, however, are the potential consequences of limiting the future coral gene pool on the basis of a single trait. Trade-offs are common in nature, and although more thermally tolerant corals might survive the next heat wave, those same individuals might also carry undesirable traits such as disease susceptibility or low reproductive success. Experimentally testing for these trade-offs will increase the probability of success for conservation efforts. Ultimately, however, the only way to curb coral mortality and ensure future reef health is through climate change mitigation to reduce the incidence and intensity of heat wave events.

There is still much to learn about the genetic and environmental underpinnings of coral bleaching, and each step forward will enhance our predictive capacity. Fuller *et al.* show that genomic information improves the ability to explain individual variation in coral bleaching outcomes. It remains to be seen whether this polygenic score is reliable across independent samples and distant geographies. However, the authors provide a framework for integration of environmental and genomic data that could be used to predict the bleaching susceptibility of a coral even before a heat wave occurs and could be applied to any species of conservation concern. Such tools could enhance conservation and restoration practices by identifying individuals likely to be tolerant to future warming. ■

REFERENCES AND NOTES

1. Z. L. Fuller *et al.*, *Science* **369**, eaba4674 (2020).
2. J. M. Lough, K. D. Anderson, T. P. Hughes, *Sci. Rep.* **8**, 6079 (2018).
3. T. P. Hughes *et al.*, *Science* **359**, 80 (2018).
4. T. P. Hughes *et al.*, *Nature* **556**, 492 (2018).
5. S. L. Coles, P. L. Jokiel, C. R. Lewis, *Pac. Sci.* **30**, 159 (1976).
6. P. L. Jokiel, in *Coral Health and Disease*, E. Rosenberg, Y. Loya, Eds. (Springer, 2004), pp. 401–425.
7. S. R. Palumbi, D. J. Barshis, N. Traylor-Knowles, R. A. Bay, *Science* **344**, 895 (2014).
8. R. A. Bay, S. R. Palumbi, *Curr. Biol.* **24**, 2952 (2014).
9. G. B. Dixon *et al.*, *Science* **348**, 1460 (2015).
10. A. C. Baker, C. J. Starger, T. R. McClanahan, P. W. Glynn, *Nature* **430**, 741 (2004).
11. International Schizophrenia Consortium, *Nature* **460**, 748 (2009).
12. M. K. Hayr, T. Druet, D. J. Garrick, *J. Anim. Sci.* **94** (suppl_2), 13 (2016).
13. M. J. Machiela *et al.*, *Genet. Epidemiol.* **35**, 506 (2011).
14. F. Morani *et al.*, *Sci. Rep.* **9**, 11878 (2019).

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CANCER

Nailing a Fe-rocious form of cancer

Disseminated cancer cells in brain fluids hijack iron from macrophages for metastatic survival

By **Livia Garzia**[1] *and* **Michael D. Taylor**[2]

Numerous cancer types can metastasize to a remote and inhospitable part of the human central nervous system (CNS): the subarachnoid or leptomeningeal space. This covers the surface of the nervous system and contains the cerebrospinal fluid (CSF). The CSF is largely hypocellular in healthy humans and has limited metabolic resources. It provides protective buoyancy for the brain and permits circulation of micronutrients and growth factors in the ventricular system. The CSF constitutes a relatively accessible proxy of the health of the CNS, and it is routinely sampled by physicians through a lumbar puncture. On page 276 of this issue, Chi *et al.* (*1*) reveal how human cancer cells thrive in this specialized anatomical location by hijacking a high-affinity iron transport system. This work highlights how studying tumor cell properties in the context of the challenges posed by the microenvironment can reveal unknown biology and possible approaches to therapy.

Lung and breast cancers can develop metastases in several organs, most commonly the bones, liver, and lungs. On rare occasions, disseminated cancer cells can reach the brain microvasculature, cross the blood-CSF barrier, and attach to the meninges, membranous layers that surround the CNS and form the subarachnoid space. Cancer cells then somehow thrive in the CSF-filled subarachnoid space and spread to the surface of the pia mater (a meningeal membrane). This leptomeningeal metastasis is an incurable condition; most patients succumb within months, and survival for 1 year is extremely rare (*2*). The CSF is a chal-

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