GENOMICS

Genomic signatures of disease resistance in endangered staghorn corals

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White band disease (WBD) has caused unprecedented declines in the Caribbean *Acropora* corals, which are now listed as critically endangered species. Highly disease-resistant *Acropora cervicornis* genotypes exist, but the genetic underpinnings of disease resistance are not understood. Using transmission experiments, a newly assembled genome, and whole-genome resequencing of 76 *A. cervicornis* genotypes from Florida and Panama, we identified 10 genomic regions and 73 single-nucleotide polymorphisms that are associated with disease resistance and that include functional protein-coding changes in four genes involved in coral immunity and pathogen detection. Polygenic scores calculated from 10 genomic loci indicate that genetic screens can detect disease resistance in wild and nursery stocks of *A. cervicornis* across the Caribbean.

Increased global CO_2 emissions and the resulting ocean warming have devastated tropical reef corals by increasing the frequency and severity of thermal bleaching events (*1*–*3*) and disease outbreaks (*4*, *5*). Emergent infectious diseases in Caribbean corals cause high levels of coral mortality (*6*–*8*), with white band disease (WBD) killing up to 95% of the critically endangered Caribbean *Acropora* corals (*8*), and stony coral tissue loss disease (SCTLD) is, at present, decimating more than 20 key reef-building coral species (*6*, *7*). The rising toll of thermal bleaching and diseases on coral reefs globally has focused scientific efforts on identifying thermally resilient and disease-resistant coral species, individuals, genes, and symbionts that allow reef corals to adapt to future climate scenarios (*9*–*11*), including through human intervention (*9*). Adaptive polygenic variation for thermal tolerance with relatively high heritability exists in corals (*11*), although the identification of genetic markers that strongly influence thermal tolerance is more elusive (*12*). Less is known about the genetics of coral disease resistance. Phenotypic variation in disease resistance to WBD has been documented in the staghorn coral, *Acropora cervicornis* (*13*, *14*), and may be heritable and adaptive.

WBD is a highly transmissible, host-specific disease that infects the two sister species of Caribbean *Acropora* (*8*, *15*–*17*): the staghorn coral, *A. cervicornis*, and the elkhorn coral, *Acropora palmata*, as well as their hybrid species, *Acropora prolifera* (*18*, *19*). Since it was first observed in 1979 (*15*), WBD has killed up to 95% of Caribbean *Acropora* and is found throughout the greater Caribbean (*8*). WBD is caused by a bacterial pathogen or pathogens that can be arrested with antibiotics (*16*, *20*) and quorum-sensing inhibitors (*21*, *22*). Multiple putative bacterial pathogens have been associated with WBD (*20*, *23*), including *Vibrio* spp. (*24*, *25*), *Aquarickettsia* (*26*, *27*), and other bacteria (*23*). *A. cervicornis* genotypes display strong phenotypic variation in disease resistance (*13*, *14*) and mount a vigorous immune response to WBD infection (*28*, *29*), with highly resistant genotypes up-regulating genes involved in microRNA-induced posttranscriptional gene regulation (*29*).

We conducted a genome-wide association study (GWAS) to identify genetic variants associated with disease resistance to WBD in *A. cervicornis* from two geographically distant populations: Florida and Panama. Disease resistance was assayed in tank-based transmission experiments that were conducted separately in Florida and Panama with 50 coral genotypes from each location (Fig. 1A). Florida *A. cervicornis* were sourced from Coral Restoration Foundation nursery stocks, and the Panama *A. cervicornis* were sampled from wild populations in Bocas del Toro. A Cox proportional hazards model was used to calculate normalized disease-resistance scores across all 100 genotypes (Fig. 1B) while accounting for experimental and/or population effects of the two independent transmission experiments. Coral genotype explained 6.1% of the variation in disease resistance [χ^2(effective df = 65, reference df = 99) = 2392, $p < 0.0001$; df, degrees of freedom], experimental tank explained 8.4% of the variance [χ^2(7.8, 9) = 4779, $p = 0.00008$], and experiment location and/or population explained 28.8% of the variance [χ^2(0.99, 1) = 23,127, $p < 0.00001$]. The experiment location and population variation in the transmission experiments could result from a variety of factors (*30*), including differences in microbial exposure doses and host microbiomes as well as spatiotemporal environmental variation between the two study sites.

We randomly selected 48 genotypes from each population for whole-genome sequencing (WGS) and assembled and annotated a high-quality, de novo genome using adult tissue from the K2 genotype from Coral Restoration Foundation, Florida, with high-quality nanopore sequencing and short-read polishing. The 308-Mb scaffolded *A. cervicornis* K2 genome had an N50 of 2.8 Mb (where N50 is the minimum scaffold length needed to cover 50% of the

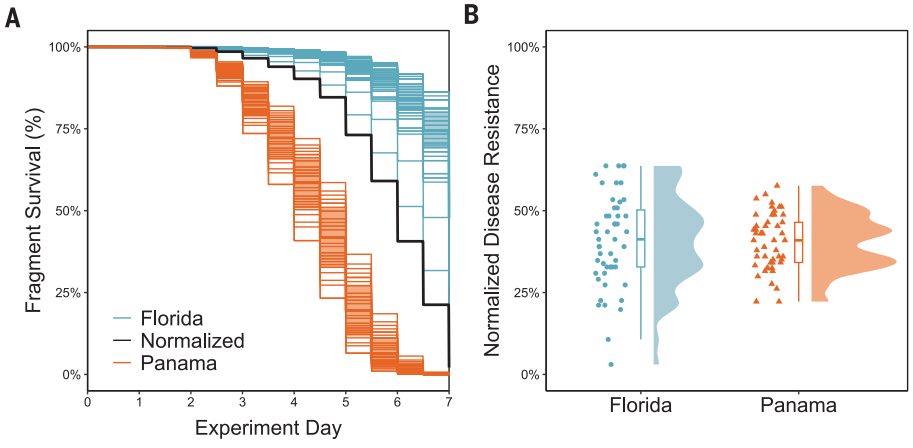

Fig. 1. Tank-based infection, survival, and disease resistance. (**A**) Fragment survival rates (%) from the two independent tank-based transmission experiments conducted in Florida (blue) and Panama (orange). A Cox proportional hazard model detected significant effects of genotype [χ^2(effective df = 65, reference df = 99) = 2392, $p < 0.0001$], experimental tank [χ^2(7.8, 9) = 4779, $p = 0.00008$], and experiment location and/or population [χ^2(0.99, 1) = 23,127, $p < 0.00001$] on fragment survival. Genotype explained 6.1% of the variation in survival, whereas experiment location and/or population (i.e., Florida versus Panama) explained 28.8% of the variation. (**B**) Normalized disease resistance (one minus the probability of infection; see methods for details) at day 6 of exposure for the 50 Florida and 50 Panama *A. cervicornis* genotypes that were surveyed. The center line represents the median, box limits are upper and lower quartiles, and whiskers are minimum and maximum values.

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