Adaptive introgression enables evolutionary rescue from extreme environmental pollution

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Radical environmental change that provokes population decline can impose constraints on the sources of genetic variation that may enable evolutionary rescue. Adaptive toxicant resistance has rapidly evolved in Gulf killifish (*Fundulus grandis*) that occupy polluted habitats. We show that resistance scales with pollution level and negatively correlates with inducibility of aryl hydrocarbon receptor (AHR) signaling. Loci with the strongest signatures of recent selection harbor genes regulating AHR signaling. Two of these loci introgressed recently (18 to 34 generations ago) from Atlantic killifish (*F. heteroclitus*). One introgressed locus contains a deletion in AHR that confers a large adaptive advantage [selection coefficient ($s = 0.8$)]. Given the limited migration of killifish, recent adaptive introgression was likely mediated by human-assisted transport. We suggest that interspecies connectivity may be an important source of adaptive variation during extreme environmental change.

Human alterations of the environment can be swift and severe, and thereby result in population declines and increased selective pressures. Adaptation requires genetic variation from mutations, standing variation, migration, or interspecific hybridization (introgression). However, declining population size coupled with immediate threats to fitness may constrain the sources of genetic variation that enable evolutionary rescue (1, 2); new mutations arise slowly, standing variation may be insufficient, habitat fragmentation may limit migration, and hybridization may be rare and deleterious. Little is known of the relative importance of these sources of variation in the context of evolutionary rescue.

Gulf killifish (*Fundulus grandis*) are common in coastal estuaries along the northern Gulf of Mexico. They occupy the Houston Ship Channel, in coastal estuaries along the northern Gulf of Mexico. They occupy the Houston Ship Channel, which is heavily polluted with halogenated and polycyclic aromatic hydrocarbons (HAHs and PAHs, respectively) resulting from more than 60 years of industrial activity (3), forming a gradient of contamination through Galveston Bay (4) (Fig. 1A). Many HAHs cause cardiac deformities in developing vertebrates that directly impair fitness (5, 6). Nevertheless, *F. grandis* persist at these sites and are resistant to the normally lethal effects of these toxicants (7). We examine the molecular underpinnings of apparently evolved resistance to extreme pollution among populations densely sampled across the pollution gradient, using experimental and population genomic approaches. We integrate prior work on the sister taxon of *F. grandis*, the Atlantic killifish (*F. heteroclitus*), which has also adapted to similar chemicals (8), to uncover the evolutionary history of key adaptive variants.

We sampled fish from 12 sites spanning the pollution gradient (Fig. 1A and table S1), spawned them separately in the laboratory, and exposed their embryos to a range of concentrations of polychlorinated biphenyl 126 (PCB126, a model HAH). At the population level, resistance to toxicity, as measured by rates of cardiac teratogenesis, is correlated with pollution along this gradient, where fish from the most polluted sites are resistant to concentrations of HAHs 1000 times higher than normally teratogenic levels (Fig. 1, B and C). Resistance is retained through at least two generations in a clean environment (fig. S1) and is intermediate in hybrids from crosses between sensitive and resistant populations (7), indicating a genetic basis.

Aryl hydrocarbon receptor (AHR) signaling mediates HAH-induced cardiac teratogenesis (9). We compared AHR pathway function (CYP1A activity in response to PCB126 exposure) (10) (fig. S2) among populations across the pollution gradient. Similar to resistance, desensitization of the AHR pathway scales with levels of pollution (HAH). At the population level, resistance to toxicity, as measured by rates of cardiac teratogenesis, is correlated with pollution along this gradient, where fish from the most polluted sites are resistant to concentrations of HAHs 1000 times higher than normally teratogenic levels (Fig. 1, B and C). Resistance is retained through at least two generations in a clean environment (fig. S1) and is intermediate in hybrids from crosses between sensitive and resistant populations (7), indicating a genetic basis.

![Fig. 1](http://science.sciencemag.org) Variation in sensitivity to pollution among *F. grandis* populations distributed along a steep pollution gradient in Galveston Bay (USA). (A) Pollution gradient is scaled by color, from low (blue) to high (black). Populations include resistant (black, R1 to R3), intermediate-high resistance (red, IH1 to IH3), intermediate-low resistance (gold, IL1 to IL3), and sensitive (blue, S1 to S3). Genomics data were collected for populations denoted with circles. (B) Population variation in cardiac deformities in embryos exposed to PCB126 (error bars indicate standard error of the mean). Population variation in sensitivity to PCB-induced cardiac deformities [log median effective concentration (EC50)] correlates with (C) habitat pollution and (D) AHR pathway inducibility (CYP1A activation by PCB126). (E) PCB-induced CYP1A activity varies among individuals and populations.
that intermediate populations are distinguished from resistant populations, not by selection on different loci, but rather by weaker selection at the same loci. Genomic regions showing the strongest signatures of selection harbor genes encoding key regulators of the AHR signaling pathway. AHR1a and AHR2a are centered in the most highly ranked shared outlier region (chromosome 1; Fig. 2C and fig. S8). Two paralogs of aryl hydrocarbon receptor nuclear translocator (ARNT), which dimerize with AHR to activate transcription (fig. S2), are within the second- and third-ranked shared outlier regions on chromosomes 8 and 10, respectively (Fig. 2C and figs. S9 to S11). Aryl hydrocarbon receptor interacting protein (AIP) regulates nuclear translocation of pollutant-activated AHR and is within the R1–R2 shared outlier region on chromosome 2 (Fig. 2C and fig. S12). Signatures of selection in multiple AHR pathway elements, coupled with additional selection signatures throughout the genome, indicate that AHR pathway modification is an important component of polygenic adaptation to the fitness challenges present in this urban estuary.

The top-ranked outlier region spans ~2 Mb and encompasses the tandem paralogs AHR1a and AHR2a (Fig. 2E). We detected a 77-kb deletion spanning these genes at high frequency in resistant populations (85, 83, and 68% in R1, R2, and R3, respectively), at moderate frequency in intermediate populations (25% and 5% in IH1 and IH2, respectively), and in only one heterozygous individual from a sensitive population (Fig. 2E and figs. S13 and S14). Given that the AHR pathway is profoundly desensitized in resistant populations (Fig. 1, D and E, and fig. S3) and moderately desensitized in intermediate populations and that its experimental knockdown is protective of toxicity (9), we propose that this mutation is important for the adaptive phenotype. Five different deletions in AHR genes have now been associated with rapidly evolved resistance to HAHs across three species of wild fish (8, 12). Consistent with the “less-is-more” hypothesis (13), this suggests that rapid adaptation by disabling mutations may be common. We speculate that sweeps of such large-effect loci may quickly recover fitness after extreme environmental change, whereas smaller-effect loci, perhaps with reduced negative pleiotropy, advance more slowly.

We analyzed whole-genome sequences from F. grandis and F. heteroclitus to contrast variants associated with resistance. In resistant F. grandis, the region containing the AHR deletion on chromosome 1, as well as the region from chromosome 10 encompassing ARNT, was more similar to F. heteroclitus haplotypes than to other F. grandis haplotypes (Fig. 3, A and B, and fig. S10), which could result from incomplete lineage sorting or admixture. The species divergence time estimated from elsewhere in the genome predated the divergence of the selected haplotypes (Fig. 3C), suggesting admixture as the source.

To formally test for introgression and to estimate the timing and strength of selection, we extended a coalescent theory–based inference method that distinguishes among modes of adaptation (14). Introggression of the deletion-bearing haplotype was much more likely than incomplete lineage sorting (Fig. 3E and figs. S15 to S17), consistent with divergence-time estimates (Fig. 3C). We inferred a large fitness advantage for individuals carrying the AHR deletion haplotype (s = 0.8), and very recent gene flow (16 generations before onset of selection; Fig. 3E), with the sweep occurring over 18 generations. This model estimates that introgression happened ~34 generations before the sampling event in 2014–2015. As we are unlikely to have sampled the true F. heteroclitus source population (resistance is widespread in this species), this time may be even shorter (15). For the adaptive ARNT region, we infer similar timing of gene flow (36 to 37
generations before sampling) and strong selective advantage ($s = 0.55$) (figs. S18 and S19). These alleles clearly have a large effect on fitness and so likely explain a large proportion of the genetic variance in pollution tolerance. We conclude that recent introgression from a few successful $F. heteroclitus$ migrants (figs. S17D and S19D) provided crucial genetic variation to rescue $F. grandis$ populations from rapid environmental change.

We evaluated the footprint of introgression in $F. grandis$ genomes by scanning for genomic segments (>400 kb) showing evidence of $F. heteroclitus$ ancestry. These ancestry blocks collapsed into 15 discrete regions totaling 70 Mb on nine chromosomes (Fig. 3A and figs. S20 and S21). Most large introgressed blocks are rare (11 of the 15 regions are found in fewer than five individuals) and are found exclusively in polluted populations (Fig. 3D). More than 30 Mb of the 40 Mb comprising chromosome 1 showed evidence of introgression in at least one individual, representing $F. heteroclitus$ ancestry that “hitchhiked” with the deletion sweep. Mean haplotype block size also suggests that the introgression event was recent (<65 to 155 generations before sampling; fig. S21). A recent discrete hybridization event occurred in the Houston Ship Channel, introducing highly advantageous adaptive haplotypes from $F. heteroclitus$ and leaving behind evidence of $F. heteroclitus$ ancestry scattered across the genome. Because $F. heteroclitus$ have small home ranges (16) and the nearest populations are in Florida, >2500 km away, human-mediated transport is the likely mechanism of introduction (17), possibly through ballast water transfer (18) or baitfish transport (19).

The importance of hybridization in conservation biology is contentious (20, 21). Recipient populations are at risk for negative ecological interactions with invaders, introduction of locally maladaptive or deleterious alleles, or genetic incompatibilities (22, 23). We propose that $F. heteroclitus$ introgression into Galveston Bay was sufficiently rare to preclude extensive accumulation of deleterious variation in $F. grandis$, and that the adaptive advantage afforded by introgressed loci was sufficient to overcome maladaptation imposed by linked loci. Although a growing body of work shows that ancient hybridization can contribute adaptive genetic variation [e.g., (24, 25)], our work shows that hybridization can provide variation crucial for adaptation following swift and extreme environmental change.

REFERENCES AND NOTES
15. See supplementary materials.

ACKNOWLEDGMENTS

Competing interests: The authors declare no competing interests.

Data and materials availability: Sequence data are archived at the National Center for Biotechnology Information (PRJNA437462); physiology and chemistry data and code (https://github.com/eoziolor/grandis_introgression) are on GitHub.

SUPPLEMENTARY MATERIALS
science.sciencemag.org/content/364/6439/455/suppl/DC1
Materials and Methods
Figs. S1 to S21
Tables S1 to S5
References (26–41)
4 October 2018; accepted 25 March 2019
10.1126/science.aav4155
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Science 364 (6439), 455-457.
DOI: 10.1126/science.aav4155

An unexpected advantage
Human activities are altering Earth’s environment in many ways. Will other species be able to adapt in the face of rapid change? Adaptation requires genomic variability, but declining populations lose diversity, which casts doubt on adaptation as a survival mechanism in today’s world. Oziolor et al. report a case of rapid adaptation to pollution in killifish, apparently enabled by introduction of a non-native congener within the last 30 generations (see the Perspective by Pfennig). This related species, possibly carried in ship ballast water, appears to have provided advantageous genetic variability that has allowed the native fish to adapt to its increasingly polluted environment.

Science, this issue p. 455; see also p. 433

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