Genetic Insights Emerge From the Shattered Remains of Lost Species

August 20, 2012

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At the close of the last ice age, towering continental glaciers slowly retreated northward, while populations of marine threespine stickleback fish (*Gasterosteus aculeatus*) began adapting to countless new bodies of fresh water in low-lying coastal areas. Some of these populations became trapped in small lakes and eventually split into pairs of species adapted to different lake habitats. The deep-bodied "benthic" species within these pairs became specialized for feeding on invertebrates in weedy inshore habitats, whereas the streamlined "limnetic" species became better adapted to foraging for plankton in open water. Remarkably, duos of species exactly like these were formed independently in five different lakes of British Columbia, a pattern that can only arise when parallel selection pressures drive evolutionary divergence along repeated environmental gradients.

The benthic and limnetic species are no older than 12,000 generations, which is extremely young by evolutionary standards. Viable and fertile hybrids are occasionally formed when benthics and limnetics interbreed, but the hybrids are ecologically unfit under the pristine conditions in which the species pairs evolved. In Enos Lake on Vancouver Island, however, the environmental gradient was recently disturbed, probably owing to the introduction of a non-native crayfish. The ensuing environmental damage increased the ecological success of hybrids relative to pure limnetics and benthics. As a consequence, the Enos species pair collapsed into a hybrid swarm. Principal investigator Dr. Catherine Peichel of the Human Biology Division, and her collaborators, recently turned this unfortunate environmental accident into an opportunity to genetically map complex traits in the threespine stickleback system, which promises to offer new insights into how genes underlie variation in our own complex traits.

Human evolution is mirrored by stickleback evolution in a few general ways, which motivates the Peichel Lab to use threespine sticklebacks to investigate the genetic basis of vertebrate traits. Unlike the classic inbred laboratory mouse, sticklebacks and humans are highly outbred and genetically diverse. Modern humans (*Homo sapiens*) migrated away from their place of origin in East Africa and adapted to new environments over the past 10,000 generations, which is very similar to the timeframe of stickleback evolution. Some geneticists also believe that occasional hybridization (with *Homo neanderthalensis*) impacted the evolution of modern humans, much like hybridization

has influenced stickleback adaptation to freshwater environments. Given these similarities, insights gained through sticklebacks in Enos Lake or elsewhere will promote a better understanding of how genes in other outbred vertebrates are linked to complex traits, including behaviors, morphological traits and many diseases.

Dr. Peichel investigated the Enos Lake hybrid swarm together with her former graduate student, Dr. Tiffany Malek, as well as with two collaborators from Michigan State University, Drs. Janette Boughman and Ian Dworkin. The researchers used a technique known as admixture mapping to investigate the association between hybrid male traits and blocks of the stickleback genome, which had been broken up and reshuffled by 10-20 generations of hybridization and recombination. The statistical basis of this technique is essentially the same as that used in a genome-wide association study, which has become a powerful approach for dissecting the genetic basis of human diseases. However, far fewer genetic markers are needed for admixture mapping in hybrids swarms of recent origin, because there has been less time for recombination to break up genomic blocks inherited from the parental species.

Malek *et al.* collected 508 male hybrids from Enos Lake. For each individual, they measured a number of traits related to body coloration and shape. Previously, Dr. Boughman and other stickleback researchers showed that these traits once differed between Enos Lake benthics and limnetics, and that the differences were a central part of their adaptation to distinct habitats prior to the introduction of crayfish. In the current genetic study, each hybrid male was genotyped using a panel of 576 microsatellite markers distributed across the genome. Malek *et al.* focused their efforts on seven markers that showed the strongest genetic differences between pools of individuals exhibiting the most extreme color patterns (e.g., see marker *Stn43* in the figure). In this way, the authors revealed that genomic regions on three different chromosomes were each statistically associated with both male color and body shape at the same time. Thus, by taking advantage of admixture mapping in a stickleback hybrid swarm, the findings of Malek *et al.* suggest that genomic clustering of adaptive traits, such as shape and color, may tend to characterize species that have colonized and adapted to novel environments.

Malek TB, Boughman JW, Dworkin I, Peichel CL. 2012. Admixture mapping of male nuptial colour and body shape in a recently formed hybrid population of threespine stickleback. *Mol. Ecol.*, published online ahead of print, 10 June 2012, doi: 10.1111/j.1365-294X.2012.05660.x.

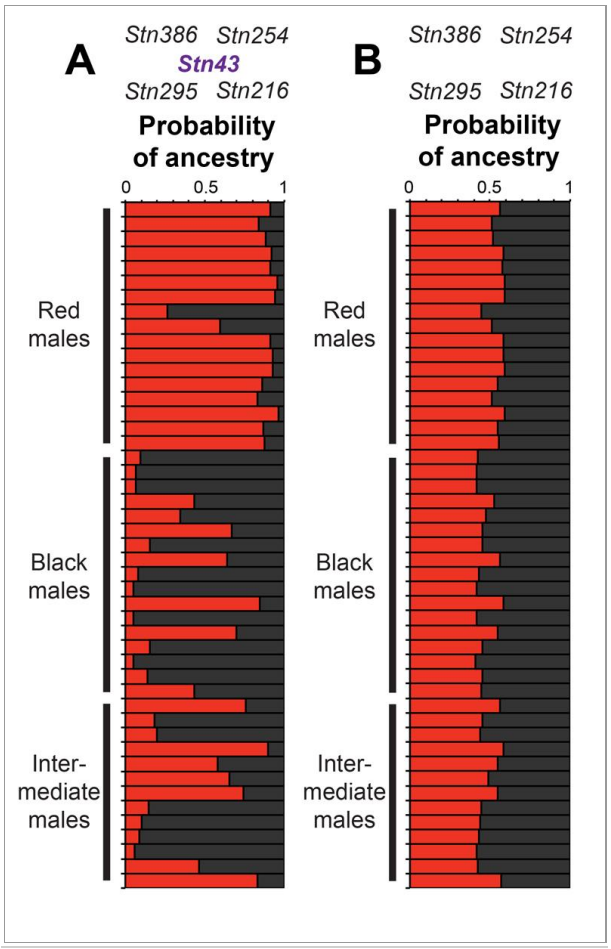

Image courtesy of Katie Peichel

The authors' population structure analysis of stickleback fish from Enos Lake demonstrated that a microsatellite marker (Stn43, purple font) resides in a genomic region influencing color variation. Microsatellites, which are listed above the results obtained using either five (A) or four (B) loci, are identified by 'Stn' plus unique number codes. Within each set of results, horizontal bars show estimated proportion of genetic ancestry in either of two most likely genotypic clusters (schematically coded red vs. black) for 47 male hybrids. Bars are grouped by phenotypic category based on male coloration. Note that significant genetic structure is apparent when Stn43 is included in the structure analysis (A). In this case, phenotypically red males exhibit genetic ancestry in the genotypic cluster coded red, while phenotypically black and intermediate males exhibit genetic ancestry in the genotypic cluster coded black. This evident structure apparently breaks downs into complete admixture (all males have equal 'red' and 'black' genetic ancestry) when Stn43 is excluded from the analysis (B), demonstrating the linkage of Stn43 to a nearby but unidentified gene affecting color variation.