Nature Reviews Genetics | AOP, published online 24 December 2013; doi:10.1038/nrg3660

Purestock/Punchstock

EVOLUTION

An eye for cryptic variation

> consistent with a role for cryptic variation in the evolution of the eyeless trait

Cryptic variation refers to standing genetic variation that has negligible phenotypic effects until it is 'unmasked' in the presence of particular environmental conditions or genetic backgrounds. One mechanism of unmasking is through relief of heat shock protein 90 (HSP90)-mediated buffering under conditions of environmental stress. However, the importance of cryptic variation as a driver of adaptive evolution — beyond model organisms studied under laboratory conditions — is a matter of debate. A new study now suggests a key role for HSP90-buffered cryptic variation in the evolution of eye loss in natural populations of cavefish.

Astyanax mexicanus is a species of fish in which the evolution of cave-dwelling strains from surface-dwelling stains has involved the loss of eyes as an adaptation to the dark environment in caves. Given the known ability of HSP90 to buffer morphological variation in various model species, Rohner *et al.* investigated whether this also occurred for eye morphology in *A. mexicanus* by treating embryos of sighted, surface-dwelling strains with the HSP90 inhibitor radicicol. This resulted in a wider variability in both eye and eye socket sizes in the resulting adult population, which implies that HSP90-buffered cryptic variation can contribute to variation in eye morphology when such buffering is overcome. By contrast, the same treatments in cave-adapted strains resulted in a reduction in the size of the empty eye sockets without a change to the variability in their sizes. This is consistent with a role for cryptic variation in the evolution of the eyeless trait, through which the subset of 'small-eye' cryptic alleles would have been selectively retained in the cave-adapted strains. Such a mechanism was recapitulated by the authors through selective intercrossing of those radicicol-treated individuals with the smallest eyes: the resulting offspring also had small-eye phenotypes, even when they were not exposed to radicicol themselves. Whether continuing such a selection scheme will ultimately result in the eyeless phenotype of cave-adapted strains is currently unclear.

The relevance of the experiments so far hinges on whether a switch to a cave environment can induce an HSP90-inhibitory stress response to unmask cryptic variation, which is analogous to the radicicol treatments discussed above. Sampling the abiotic environment at various surface and cave locations, the authors identified a reduced salinity of water in the cave environments and showed that surface-adapted strains that were raised under cave salinity conditions indeed had gene expression signatures of an HSP90-inhibited stress response and increased variability in eye sizes.

Notably, the authors found no evidence of cryptic variation underlying other morphological features such as body size. Hence, it will be interesting to further characterize the importance of cryptic variation relative to other mechanisms, such as *de novo* mutations, in a range of evolutionary scenarios in various species.

Darren J. Burgess

ORIGINAL RESEARCH PAPER Rohner, N. *et al.* Cryptic variation in morphological evolution: HSP90 as a capacitor for loss of eyes in cavefish. *Science* **342**, 1372–1375 (2013)