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Views and Commentaries

Epigenetics Is Back!

Hsp90 and Phenotypic Variation

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Back in 1942, C.H. Waddington proposed a new mechanism of evolutionary change, which he termed "genetic assimilation".[1,2] The idea was that certain environmental or genetic factors can disrupt the normally canalized (i.e., stable) course of development of living organisms. This disruption may then generate phenotypic variation that could allow a population to persist in a novel or stressful environment until new mutations would eventually let natural selection fix ("assimilate") the advantageous phenotypic variants.

In recent years, the molecular bases of the widespread heat shock response[3-6] have been suggested to play a role in phenotypic evolution by acting as "capacitors" of morphological change, providing a molecular basis for Waddington's genetic assimilation.[7,8] The idea is that heat shock proteins (Hsp) normally buffer the organism against a variety of sources of disruption of its developmental system. This may yield as a side effect the accumulation of genetic variation that can be expressed once the "capacitor" is inactivated. While most of the novel phenotypes will likely be maladaptive, their frequency and variety may boost the chances of natural selection to find a new route through the current adaptive landscape.

Now new work by Sollars et al.[9] augments the scope of the potential role of HSP proteins in evolution with the suggestion that the same role of capacitor can be catalyzed not only by genetic, but also by faster (and less stable) epigenetic changes. These authors used a sensitized isogenic strain of *Drosophila melanogaster* to show that reduced activity of Hsp90 is linked to an alteration in the state of the chromatin, itself related to the increased phenotypic variation expressed by this strain. The resulting anomalous phenotypes (affecting the development of the eye, in this case) remain epigenetically heritable even after the normal function of Hsp90 has been restored. The authors correctly conclude that genetic variation is not in fact required for the selection and fixation of the sort of ectopic growth they have studied.

This is one of the most convincing pieces of evidence that epigenetic variation is far from being a curious nuisance to evolutionary biologists, but may play a fundamental role in adaptation to rapidly changing environmental conditions, side by side with standard genetic variation. While something along these lines has been proposed several times before,[10-13] strong theoretical arguments in favor of the importance of epigenetic mechanisms have been advanced more frequently in the recent literature.[14-16] It seems that empirically oriented biologists are finally finding a way to respond to the call and make some progress more than 60 years after Waddington's seminal paper.

In particular, Sollars et al. propose a scenario in which stress causes a breakdown in the Hsp90 system, for example by lowering its activity. This indirectly causes what they refer to as a "chromatin effect" (mediated by an interaction with TrxG proteins). In evolutionary terms, this means that a potentially adaptive phenotype could be fixed very rapidly via epigenetic mechanisms, without having to wait for the proper genetic variation to arise (as in Waddington's original proposal). The resulting evolutionary change is both more rapid and less stable (which means that it can easily be reversed, should the environmental conditions call for it) than either classical evolution by allelic substitution or Waddington's version of genetic assimilation.

Of course, all of this need to be taken with a large grain of salt: we are far from a satisfactory understanding of the genetic and epigenetic bases of the capacitor phenomenon, we have only observed the production of macroscopic phenotypic changes that are unlikely to be of adaptive value, and we have few ideas on how to go about demonstrating the relevance of all of this to naturally evolving populations outside of the laboratory. Nonetheless, it seems that genetic assimilation and epigenetics, after decades of neglect, are finally back on the center stage of evolutionary research. Perhaps this time they will remain in the spotlight long enough to be incorporated in mainstream evolutionary theory.

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