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There is an increasing need to link genotypic, phenotypic and environmental information as means to explain and predict the adaptive response of organisms to the current and rapid rate change of environmental conditions. Despite the ease to gather more biological and environmental information, the explanatory relationship of cause and effect for adaptation in wild populations remains a difficult task, given the complex nature of interactions that take place in the natural world. In order to unequivocally prove a real case of adaptation in natural settings, we first need to identify phenotypes under selection, understand the underlying genetic basis of such phenotypes and identify potential drivers of selection whit their respective influences in populations’ fitness. On the one hand, some genomic studies have shed light on these issues by pinpointing genes that contribute to phenotypic variation but have lacked the ecological mechanisms driving the evolution of the trait. On the other hand, experimental studies have revealed the action of natural selection on traits but without actual knowledge of the molecular mechanisms behind them. To make matters worse, one thing is to detect signals of strong selection, normally associated to few and recent loci, and other far more cumbersome is to discover polygenic basis of adaptation in which the adaptive trait depends on multiple loci. However, the integrative approach of using genomics, phenotypic, developmental, ecological and experimental data has come to the rescue of the hitherto unsurmountable challenge of deciphering biological adaptation.

Nadeau et al. (2016) combined fine-scale genome mapping, population genomics, gene expression approaches to identify the *cortex* gene in butterflies of the genus *Heliconius*. These insects exhibit various color patterns on their wings under control of 1 Mb locus *Yb*. SNPs within this region strongly associated with specific colors in three species, in which a set of SNPs was fixed for one allele in a species with a yellow bar, while the alternate allele was fixed in other species lacking that bar. Complementary, authors investigated variants around *cortex* gene to search for regulation activity with a microarray composed of probes for all predicted genes in a *H. Melpomene.* Their findings corroborated that this gene was the only one to show significant differences in expression in two butterfly races and led them to suggest that it controls pigmentation patterning through scale cell developments. Although study thoroughly described genotypic-phenotypic variation, it only infers natural selection on the coloration gene because it is widely present in the order and some species have aposematic patterns.

Contrastingly, Bosse et al. (2017) relied exclusively on a genomic analysis to derive the phenotypic trait under selection, an even postulate a driver of selection, based on long-term population morphological observations of a species of bird in Europe. A wide-genome scan across three populations of the great tit (*Parus major*) was sufficient to identify candidate loci under divergent selection, by deeming the first eigenvector from a PCA as a putative phenotype. Some singled-out loci contained genes related to skeletal and beak development according to gene ontology databases, which in turn displayed marked population structure (*Fst*  ) between the United Kingdom and the Netherlands populations. A GWAS on beak length found large overlapping with the previous analysis suggesting that genes involved in beak size have experienced divergent selection in the UK. One allele at the SNP that was most significantly associated with increased bill length also had higher frequencies within the UK accompanied by an extended homozygous haplotype indicative of a hard selective sweep. A comparison of beak length and reproductive success between the two divergent populations found that longer beaks confer a fitness advantage and its size has increased over years as shown by museum´s specimens. The authors proposed that that increase in beak size may be related to a rise in food availability in that region where bird feeders are common.

Although the las two studies successfully stablished genotype-phenotypic relationships and, to some degree, the impact on fitness, they lacked the identification of the real selective pressure driving adaptation. Meanwhile, Barret et al. (2019) were able to connects all the dots, from the genomic to the phenotype, and the effect of predation upon the survival rate of divergently coat-colored mice. Recent geological changes introduced a new light-color soil to the sand Hills of Nebraska where the deer mice (*Peromyscus maniculatus*) inhabit. Mice pigmentation coat correlates with substrate color, leading to the hypothesis that this phenotypic change is due to selection for camouflage against bird predation. Variation in the locus *Agouti* mediates pigmentation in this species making it an ideal system to test the effect of genotype on phenotype and ultimately fitness. An experimental setting to estimate survival of light versus dark colored mice on similar or mismatching background soil, consisted on placing an equal proportion of animals in field enclosures devoid of native mice and land predators but open to birds of prey. Mice that matched habitat type had grater survival rates than foreign ones, suggesting adaptation to local environment where divergent natural selection acted on dorsal brightness between the two kind of soils. All mice were genotyped and SNPs in or near the *Agouti* locus were scored, finding greater allele frequencies at this locus in the light than in the dark enclosures, concordant with reduced survival in the former one. To find if those changes were best explained by selection or neutrality, the authors estimated the probability that the distribution of genotype frequencies was a random subsample from the original distribution. Interestingly, in the dark enclosures *Agouti* allele frequencies were consistent with selection. Overall, the coupling of a field experiment with genomic resources showed that genetic variation at a locus matched phenotypic changes that are in turn subjected to a predatory selective pressure.

**References**

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