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Correlation between Phenotype and Genotype Summary

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Understanding how genetic signatures of selection translate into variation in fitness and phenotypes is key for predicting adaptive evolution in new or changing environments. Barrett et al. (2018), Bosse et al. (2016), and Nadeau et al. (2016) are three studies that worked to identify connections between genotype, phenotype, and fitness, using different molecular techniques. Barrett investigated wild mice populations from different environments to identify drivers of allele frequency change to understand how natural selection influences the evolution of these populations. Bosse investigated how genetic signatures of selection translate into variation in fitness and phenotypes using different populations of the great tit (*Parus major*). Nadeau used fine-scale mapping techniques along with population genomics and gene expression analyses to identify a gene called *cortex*, which regulates pattern switches on the wings in multiple species of *Heliconius* butterflies. From their analyses, they found that the *cortex* genehas become a major target for natural selection acting on color and pattern variation in these butterflies.

Each study focused on different questions within the broad topic of phenotype/genotype correlations, which is reflected in the vast differences of techniques used among studies.

*Methodology*

To examine the link between genotype and phenotype, Barrett focused on the ecological factor that drives natural selection. They combined a field experiment with laboratory-based genomics to identify the ecological and molecular mechanisms underlying adaptation in recently evolved, cryptically colored populations of deer mice (*Peromyscus maniculatus*). To test for selection that favors locally adapted pigment phenotypes, they collected wild mice from dark and light environments. These mice were introduced to field enclosures that were open to avian predators to assess selection favoring locally adapted pigment phenotypes. They found selection on pigmentation, demonstrated through the higher survival of mice with locally cryptic dorsal pigmentation. To determine whether the changes in allele frequency are best explained by selection or neutrality, they used a model based on random mortality, from which they found allele frequency changes consistent with selection. They conducted additional analyses to test the functional link between a variant associated with survival and pigmentation as well as to uncover the causal molecular mechanism. From these analyses, they found further evidence suggesting selection as the key factor in dorsal pigmentation variation. What is the molecular mechanism?

Compared to Barrett, Bosse examined the phenotype-genotype relationship by analyzing selection on polygenic traits. They used data from a long-term study of great tits in the United Kingdom and Netherlands. To identify loci under divergent selection between populations, they ran a genome-wide association study (GWAS), which identified outlier regions of the genome likely to be under divergent selection. This was further supported by FST analyses. To examine the genetic architecture of bill length in the UK population, they again performed a GWAS to test for associations between SNP genotypes and the trait, fitting one SNP at a time. They then ran analyses that fitted all SNPs in one model. To further examine how natural selection has shaped bill length variation, they tested how variation at the COL4A5 locus was related to annual reproductive success using generalized linear mixed model. To further understand the selection for longer bills in the UK population, they examined both spatiotemporal variation and the effects of supplementary feeding.

Nadeau identified a region of the genome that contains genes that regulate the color and pattern pigmentation in butterflies. They used a population genomics approach to identify SNPs associated with phenotypic variation within this region. They also used patterns of divergence at wing pattern loci to identify SNPs associated with color pattern elements across many individuals with various color pattern phenotypes. They designed a microarray with probes to determine whether sequence variants around the *cortex* gene were regulating its expression. From this, they found that *cortex* was the only gene across the entire region to show significant differences in expression. Their final analysis involved *in situ* hybridization of *cortex* in final instar larval hindwing discs, which showed expression in wing regions that would become black in the adult wing.

*Conclusions*

From their study, Barrett found that when standing variation is available, natural selection can cause shifts in allele frequencies, which results in evolutionary change. They were able to predict changes in both the trait (dorsal brightness) and the underlying mechanisms as well as patterns of existing phenotypic and genotypic variation across habitat types. These results helped increase understanding about the functional connections between genotype, phenotype, and fitness.

Bosse demonstrated polygenic adaptation by identifying associations between loci that have responded to selection, fitness variation, and phenotypic variation. Their use of genomic and ecological data in natural populations increased understanding of both the underlying mechanisms and evolutionary consequences of natural selection.

Nadeau found *cortex* to be the only gene to be differentially expressed between differently patterned wing regions in the candidate region of the genome. They identified *cortex* as the major regulator of color and pattern based on genotype-by-phenotype associations.

**Literature Cited**

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