**Relating Genotype to Phenotype**

*Background*

A major scientific problem in evolutionary biology is identifying which genes control which phenotypic traits in different organisms. It seems obvious that a specific genotype would relate to a specific phenotype, but in practice, this exact relationship is difficult to determine. Many phenotypes are polygenic, making the issue even more complicated. It is easy to fall into the trap of assuming that correlation implies causation, so various strategies are used to identify specific genes and their effects on fitness. Often, genomic techniques are coupled with field observations or hybridization experiments to draw stronger conclusions.

*Summaries*

Bosse et al. studied birds in the UK and the Netherlands, and investigated the genetic factors influencing bill length and how those factors influenced fitness. They found that birds in the UK seemed to be experiencing selection for longer beaks, and that this trait largely controlled by the COL4A5 region. Researchers found overlap between outliers from EigenGWAS and FST analysis, implying divergent selection. They matched outliers with Geneontology terms to discover function. COL4A5 was one of the top three regions under divergent selection and was also associated with bill length. They found that the C allele variant was more common in the UK, in addition to finding long, homogeneous haplotypes. Bosse and their team coupled their genetic analysis with a long-term population study. They found that the number of chicks fledged in the UK was positively correlated with the presence of the C allele of COL4A5 and concluded that it provided a fitness advantage to UK populations. They did not find a significant relationship in the Netherlands.

Barrett et al. performed field and lab experiments on wild mice to identify the genotype affecting their fur color, and to link that with fitness. In the field, they set up multiple enclosures and switched some light and dark colored mice into enclosures of the opposite substrate color. Birds of prey, the mice’s main predators, could still eat them from above, but other ground predation was excluded. This meant that predators identifying the mice from above was the main selection pressure. They sequenced all individuals at multiple time points and found that mice showed non-random genotype frequencies after three months, and that SNPs associated with dorsal brightness showed evidence of selection. In lab mice, they found that the ΔSer mutation can alone affect dorsal brightness. By tracking changes in the *Agouti* ΔSer allele over time in different locations, they found significant decreases in the dark enclosure and were able to document selection pressure. Combining their results into a larger picture, Barrett et al. showed that a change in the ΔSer allele changed dorsal brightness, and that a change in dorsal brightness changed survival rate. Therefore, the ΔSer allele impacted survival, and could be an example of adaptive evolution.

Nadeau et al. studied different wing patterns in butterflies. They used population genetics to identify likely SNPs and hypothesized that the *cortex* gene was associated with a yellow forewing band in multiple species. They further tested naturally hybridizing populations and found that cortex was the only gene to show significant differences in expression. However, they found different results when they tried *in situ* hybridization. They inferred that *cortex* may be upregulated at different times throughout development. While their results were not as clear as in other studies, *cortex* was the only gene in the candidate region that was significantly differentially expressed. While other genes could also have an impact, *cortex* has been found to be important in other taxa as well, supporting Nadeau’s conclusion of its importance in wing pattern.

*Comparisons*

The goals of both Bosse and Barrett’s experiments were to link specific genotypes with fitness. This impacted their experimental design. They both used lab and field data to demonstrate associations between genotype and phenotype. However, they identified likely genes in different ways. Bosse performed EigenGWAS and FST analysis to identify outliers, while Barrett sequenced SNPs and found significant changes over time. To determine which phenotypic traits different genes were likely to control, the researchers used multiple different strategies. Bosse et al. made use of the Geneontology database, and matched terms to the sequence in question. Barrett et al., on the other hand, performed their own biochemical analysis to show that ΔSer affects hair pigmentation. They were able to lay out the exact steps by which that mutation would change dorsal brightness.

While both Bosse and Barrett used time-scale field data, only Barrett performed an actual field experiment, lending more credence to their claim of selection pressure. While the number of successfully fledging chicks is an important indicator of fitness, Bosse did not control for other factors, running the risk of implying that correlation implied causation.

Nadeau’s study had less of a focus on fitness, and more a focus on purely determining a specific gene’s impact on a specific trait. *In situ* hybridization is a good strategy here, and indeed it shed some light on possible different levels of gene expression throughout larval butterfly development. They did not, however, provide strong evidence for any kind of evolutionary implications of the *cortex* gene.

*Conclusions*

While there are multiple methods to analyze the connections between genotypes and phenotypes, it seems clear that field experiments are a necessary component to claim effects on fitness. When attempting to draw conclusions about adaptive evolution, multiple levels of analysis are needed, from genotype analysis, to phenotypic expression, to adaptive evolution.

**Sources**

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