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750-1000 Summary 2

Correlation between phenotype and genotype

Words: 985

*The gene cortex controls mimicry and crypsis in butterflies and and moths*

Nadeau et al. 2016

*Linking a mutation to survival in wild mice*

Barrett et al. 2018

*Recent natural selection causes adaptive evolution of an avian polygenic trait*

Bosse et al. 2016

*Summary*

The Nadeau et al. paper focuses on identifying what gene (*cortex*) regulates pattern switches on the wings of several different species of *Heliconius* butterflies. To do this, their research team used population genomics, specifically fine-scale mapping, and gene expression analysis. Their results suggest the *cortex* gene is responsible for the pigmentation pattern variation in several species and is a target for natural selection that is acting on color and pattern variation.

The Barrett paper investigated wild mice in varying environments to focus on using an estimate of natural selection on pigmentation traits and identifying the underlying pigment locus to assess how a mutation causes phenotypic change. Altogether, the main goal of this paper was to address the drivers of allele frequency change to shed light on natural selection influencing the evolution of these wild mice.

The Bosse paper focused on explaining variation in fitness and phenotype with genetic signatures of selection on various advantageous traits in great tits (*Parus major*). The research team found that bill length variation was associated with the collagen gene, *COL4A5*.

All three papers aimed to further explain the relationship between genotype and phenotype, but used various molecular techniques. Nadeau specifically addressed function, compared to Barrett focusing on a strong ecological force driving natural selection, and compared to Bosse specifically analyzing selection on polygenic traits.

*Methods*

The Nadeau paper identified, based on previous literature, a region of the genome that contains multiple genes that are regulators of color and pattern pigmentation. The research team identified SNPs in this region that were strongly associated with phenotypic variation as well as information about divergence patterns at these loci to assess a wide variety of phenotypes. These data were presented by genotype-by-phenotype association figures, presenting the association of the SNP identified to the phenotype of wing pattern seen. The research team designed microarrays to determine if the variation around *cortex* was regulating gene expression. They found that correlation was more related to variation in introns of the *cortex* gene. Further, the team tested the possibility of background transcription and splice variants with RT-PCR. Finally, in-situ hybridization was used to investigate if expression influenced a particular phenotype, the black color variant.

The Barrett paper focused more on pairing the ecological mechanisms driving these changes, specifically change in soil color by environment, with the molecular mechanisms that underlie this change in pigmentation. The research team used a field experimental approach and then laboratory-based genomic tests to reach their conclusions. Mice from dark and light sites were sampled and transplanted to varying field enclosures to assess selection favoring locally adapted pigment phenotypes. The team found that survival was much higher in dark enclosures, and mice in a habitat that matched their origin, suggesting mice are locally adapted. The results of the transplant experiment suggest divergent natural selection. The research team created a model based on random mortality in order to compare their results and conclude that the changes in allele frequency was due to selection instead of random chance. They used several other models to test if the variants could account for observations of SNPs and genotype bias in survivors. The results from all models used suggests selection to be the biggest factor in changes of dorsal pigmentation.

The Bosse paper used fine-scale ecological and genomic data to investigate polygenic selection on this model system bird. The team identified genomic variation with SNPs, suggesting high genetic diversity and low linkage disequilibrium with sample sites. They used PCA to show low genetic structure, large effective population size, and high levels of gene flow. Genome-wide association studies (GWAS) were used with the first eigenvector from the PCA as the “phenotype” in order to identify loci under selection. Outlier regions found suggest divergent selection, supported with FST values. Genes identified were associated with bill length, and used in mixture model analysis to assess percentage variation explained by the gene. The locus focused on, *COL4A5*, was compared to reproductive success with generalized linear mixed model (GLMM) and found to be significant.

Although these papers had similar broad end goals, they differed in the specific questions they were addressing, which led to differences in methods used. The Bosse paper methods were more similar to the other papers we read regarding population structure and landscape genomics, where as the Barrett paper focused on manipulating ecological systems. The Nadeau paper used methods that were focused on finding an association and then testing that association to identify function. Reading these three papers gave insight into different ways to answer complicated, and often tough to experimentally show, direct relationship between genotype and phenotype.

*Larger picture*

The Nadeau paper identified *cortex* as the only gene that was differentially expressed and correlated to variations of wing pattern phenotypes. Although it is possible to have other genes influencing this phenotype, based on strong genotype-by-phenotype associations, the research team suggests *cortex* to be the main regulator.

The Barrett paper showed that when standing genetic variation occurs, natural selection influences allele frequency and thus drives evolution. The results indicated changes in phenotype and the molecular mechanisms (▵Ser mutation) underlying this trait. This paper properly identified the connection of phenotype to genotype by function.

The Bosse paper used analysis of genomic data to identify association between loci and fitness variables, suggesting polygenic selection. The research team used extensive ecological and genomic data to connect underlying genotypic mechanisms to phenotypic changes.   
 All three papers were investigating how genomic mechanisms that underlie phenotypic variation could be evolving via natural selection. And how that natural selection was influencing changes in both molecular mechanisms and phenotypic variation. These papers focused on using different methods to associate a particular gene or locus with variation in phenotype and attempted to provide more information about why that molecular mechanism may be connected to the phenotype.