Press report – Aug-Sept 2016 – Virginie Courtier

Evolutionary Genetics

Gibert, J. M., Mouchel-Vielh, E., De Castro, S., & Peronnet, F. (2016). Phenotypic Plasticity through Transcriptional Regulation of the Evolutionary Hotspot Gene tan in Drosophila melanogaster. *PLoS Genet, 12*(8), e1006218.
Same cis-regulatory element of tan involved in:
- temperature plasticity in *D. melanogaster*
- intraspecific variation in *D. melanogaster*
- intraspecific dimorphism in *D. erecta*
- interspecific variation between *D. santomea* and *D. yakuba* (3 independent loss-of-function mutations)

It is suggested that environmental conditions might give more substrate for selection, explaining why this gene has frequently been involved in evolution of pigmentation.

Yassin, A., Delaney, E. K., Reddiex, A. J., Seher, T. D., Bastide, H., Appleton, N. C., ... & Kopp, A. (2016). The pdm3 locus is a hotspot for recurrent evolution of female-limited color dimorphism in Drosophila. *Current Biology*, *26*(18), 2412-2422.
Female-limited color dimorphism exists in >20 *Drosophila montium* subgroup species. In four species, this trait maps near the same transcription factor gene, *pdm3.* The trait appears to have originated three independent times via the same locus. Repeated gene use indicates a bias in the evolution of female-specific dimorphism. Surprisingly, pdm3 has not been implicated in the evolution of sex-specific pigmentation outside the montium subgroup, suggesting that the genetic paths to sexual dimorphism may be constrained within a clade but variable across clades.

Signor, S. A., Liu, Y., Rebeiz, M., & Kopp, A. (2016). Genetic convergence in the evolution of male-specific color patterns in Drosophila. *Current Biology*, *26*(18), 2423-2433.
Male-specific pigmentation has been gained and lost multiple times. In four species pairs, changes in pigmentation involve cis-regulatory changes in the gene *ebony. T*his functional convergence has a different molecular basis in different species, reflecting both parallel fixation of ancestral alleles and independent origin of distinct mutations with similar functional consequences. Our results show that a strong evolutionary constraint at the gene level is compatible with a dominant role of chance at the molecular level.

Fisher, H. S., Jacobs-Palmer, E., Lassance, J. M., & Hoekstra, H. E. (2016). The genetic basis and fitness consequences of sperm midpiece size in deer mice. *bioRxiv*, 077826.
Here we examine two sister-species of Peromyscus mice with divergent mating systems. We find that the promiscuous species produces sperm with longer midpiece than the monogamous species, and midpiece size correlates positively with competitive ability and swimming performance. Using forward genetics, we identify a gene associated with midpiece length: Prkar1a, which encodes the R1α regulatory subunit of PKA. R1α localizes to midpiece in Peromyscus and is differentially expressed in mature sperm of the two species yet is similarly abundant in the testis. We also show that genetic

variation at this locus accurately predicts male reproductive success. Our findings suggest that rapid evolution of reproductive traits can occur through cell type-specific changes to ubiquitously expressed genes and have an important effect on fitness.

Merenciano, M., Ullastres, A., de Cara, M. A. R., Barrón, M. G., & González, J. (2016). Multiple Independent Retroelement Insertions in the Promoter of a Stress Response Gene Have Variable Molecular and Functional Effects in Drosophila. *PLoS Genet*, *12*(8), e1006249.

Population Genetics

Sung, W., Ackerman, M. S., Dillon, M. M., Platt, T. G., Fuqua, C., Cooper, V. S., & Lynch, M. (2016). Evolution of the Insertion-Deletion Mutation Rate Across the Tree of Life. *G3: Genes| Genomes| Genetics*, *6*(8), 2583-2591.
Using direct estimates of indel rates from 14 phylogenetically diverse eukaryotic and bacterial species, along with measures of standing variation in such species, we obtain results that imply an inverse relationship of mutation rate and effective population size. These results, which corroborate earlier observations on the base-substitution mutation rate, appear most compatible with the hypothesis that natural selection reduces mutation rates per effective genome to the point at which the power of random genetic drift (approximated by the inverse of effective population size) becomes overwhelming. Given the substantial differences in DNA metabolism pathways that give rise to these two types of mutations, this consistency of results raises the possibility that refinement of other molecular and cellular traits may be inversely related to species-specific levels of random genetic drift.

O Tenaillon, JE Barrick, N Ribeck, DE Deatherage, JL Blanchard, ...Tempo and mode of genome evolution in a 50,000-generation experiment Nature 536 (7615), 165-70
Here we analysed 264 complete genomes from 12 Escherichia coli populations to characterize their dynamics over 50,000 generations. The populations that retained the ancestral mutation rate support a model in which most fixed mutations are beneficial, the fraction of beneficial mutations declines as fitness rises, and neutral mutations accumulate at a constant rate. We also compared these populations to mutation-accumulation lines evolved under a bottlenecking regime that minimizes selection. Nonsynonymous mutations, intergenic mutations, insertions and deletions are overrepresented in the long-term populations, further supporting the inference that most mutations that reached high frequency were favoured by selection. These results illuminate the shifting balance of forces that govern genome evolution in populations adapting to a new environment.

Elyashiv, E., Sattath, S., Hu, T. T., Strustovsky, A., McVicker, G., Andolfatto, P., ... & Sella, G. (2014). A genomic map of the effects of linked selection in Drosophila. PloS Genetics. August 18, 2016. http://dx.doi.org/10.1371/journal.pgen.1006130
Using genome-wide resequencing data from 125 lines in *Drosophila melanogaster*, various indices of selection were estimated. Our results corroborate estimates of a high fraction of beneficial substitutions in proteins and untranslated regions (UTR). They allow us to distinguish between the contribution of sweeps and other modes of selection around amino acid substitutions and to uncover evidence for pervasive sweeps in untranslated regions (UTRs). Our inference further suggests a substantial effect of other modes of linked selection and of adaptation in particular. More generally, we demonstrate that linked selection has had a larger effect in reducing diversity levels and increasing their variance in *D*.

melanogaster than previously appreciated.

Cheng, C., & Kirkpatrick, M. (2016). Sex-Specific Selection and Sex-Biased Gene Expression in Humans and Flies. *PLoS Genet, 12*(9), e1006170.
While there is an intimate connection between sex-biased gene expression and sex-specific selection, few empirical studies have studied this relationship directly. Here we compare the two on a genome-wide scale in humans and flies. We find a distinctive "**Twin Peaks**" pattern in humans that relates the strength of sex-specific selection, quantified by genetic divergence between male and female adults at autosomal loci, to the degree of sex-biased expression. Genes with intermediate degrees of sex-biased expression show evidence of ongoing sex-specific selection, while genes with either little or completely sex-biased expression do not. This pattern apparently results from differential viability selection in males and females acting in the current generation. The Twin Peaks pattern is also found in *Drosophila* using a different measure of sex-specific selection acting on fertility. We develop a simple model that successfully recapitulates the **Twin Peaks**. Our results suggest that many genes with intermediate sex-biased expression experience ongoing sex-specific selection in humans and flies.

Developmental Biology

Olsson, A., Venkatasubramanian, M., Chaudhri, V. K., Aronow, B. J., Salomonis, N., Singh, H., & Grimes, H. L. (2016). Single-cell analysis of mixed-lineage states leading to a binary cell fate choice. *Nature*.
Shows that stem cells generate progenitors that transition through a series of dynamically unstable states with mixed-lineage gene expression, culminating in the specification of cell-fate.
Here we use single-cell RNA sequencing coupled with a new analytic tool, iterative clustering and guide-gene selection, and clonogenic assays to delineate hierarchical genomic and regulatory states that culminate in neutrophil or macrophage specification in mice. We show that this analysis captured prevalent mixed-lineage intermediates that manifested concurrent expression of haematopoietic stem cell/progenitor and myeloid progenitor cell genes. It also revealed rare metastable intermediates that had collapsed the haematopoietic stem cell/progenitor gene expression programme, instead expressing low levels of the myeloid determinants, Irf8 and Gfi1. Genetic perturbations and chromatin immunoprecipitation followed by sequencing revealed Irf8 and Gfi1 as key components of counteracting myeloid-gene-regulatory networks. Combined loss of these two determinants 'trapped' the metastable intermediate.We propose that mixed-lineage states are obligatory during cell-fate specification, manifest differing frequencies because of their dynamic instability and are dictated by counteracting gene-regulatory networks.

Drosophila biology

Faria, V. G., Martins, N. E., Magalhães, S., Paulo, T. F., Nolte, V., Schlötterer, C., ... & Teixeira, L. (2016). Drosophila Adaptation to Viral Infection through Defensive Symbiont Evolution. *PLoS Genet, 12*(9), e1006297.
Wolbachia protects Drosophila melanogaster against several viral infections and the strength of the protection varies between variants of this endosymbiont. Since Wolbachia is maternally transmitted, its fitness depends on the fitness of its host. Therefore, Wolbachia populations

may be under selection when Drosophila is subjected to viral infection. Here we show that in D. melanogaster populations selected for increased survival upon infection with Drosophila C virus there is a strong selection coefficient for specific Wolbachia variants, leading to their fixation. Flies carrying these selected Wolbachia variants have higher survival and fertility upon viral infection when compared to flies with the other variants. These findings demonstrate how the interaction of a host with pathogens shapes the genetic composition of symbiont populations. Furthermore, host adaptation can result from the evolution of its symbionts, with host and symbiont functioning as a single evolutionary unit.

Techniques

Lamb, A. M., Walker, E. A., & Wittkopp, P. J. (2016). Tools and strategies for scarless allele replacement in Drosophila using CRISPR/Cas9. *Fly*, 1-12.
We executed this 2-stage allele swap using a novel transformation marker that drives expression in the pupal wings, which can be screened for in the presence of common eye-expressing reporters. The tools we developed can be used to make a single change or a series of allelic substitutions in a region of interest in any *D. melanogaster* genetic background as well as in other *Drosophila* species.

Review

Debat, V. (2016). Symmetry is beauty-or is it? The rise and fall of fluctuating asymmetry.. *Médecine sciences: M/S*, *32*(8-9), 774. In French