The green indicates the papers I mentioned at the presentation

Grand challenges in evolutionary developmental biology
Alessandro Minelli
Front. Ecol. Evol., 12 January 2015 | doi: 10.3389/fevo.2014.00085
http://journal.frontiersin.org/article/10.3389/fevo.2014.00085/full
.

Making quantitative morphological variation from basic developmental processes: Where are we? The case of the Drosophila wing
Matamoro-Vidal Alexis, Salazar-Ciudad Isaac and Houle David

One of the aims of evolutionary developmental biology is to discover the developmental origins of morphological variation. The discipline has mainly focused on qualitative morphological differences (e.g., presence or absence of a structure) between species. Studies addressing subtle, quantitative variation are less common. The Drosophila wing is a model for the study of development and evolution, making it suitable to investigate the developmental mechanisms underlying the subtle quantitative morphological variation observed in nature. Previous reviews have focused on the processes involved in wing differentiation, patterning and growth. Here, we investigate what is known about how the wing achieves its final shape, and what variation in development is capable of generating the variation in wing shape observed in nature. Three major developmental stages need to be considered: larval development, pupariation, and pupal development. The major cellular processes involved in the determination of tissue size and shape are cell proliferation, cell death, oriented cell division and oriented cell intercalation. We review how variation in temporal and spatial distribution of growth and transcription factors affects these cellular mechanisms, which in turn affects wing shape. We then discuss which aspects of the wing morphological variation are predictable on the basis of these mechanisms. This article is protected by copyright. All rights reserved.

Dev Dyn. 2015 Jan 23. doi: 10.1002/dvdy.24255. [Epub ahead of print]
http://onlinelibrary.wiley.com/doi/10.1002/dvdy.24255/pdf

Enhancer–core-promoter specificity separates developmental and housekeeping gene regulation
Muhammad A. Zabidi, et al
The core promoters of developmental and housekeeping genes are shown to have distinct specificities for different enhancer sequences in Drosophila, and this specificity separates developmental and housekeeping gene regulatory programs across the genome.

Gene transcription in animals involves the assembly of RNA polymerase II at core promoters and its cell-type-specific activation by enhancers that can be located more distally. However, how ubiquitous expression of housekeeping genes is achieved has been less clear. In particular, it is unknown whether ubiquitously active enhancers exist and how developmental and housekeeping gene regulation is separated. An attractive hypothesis is that different core promoters might exhibit an intrinsic specificity to certain enhancers. This is conceivable, as various core promoter sequence elements are differentially distributed between genes of different functions, including elements that are predominantly found at either developmentally regulated or at housekeeping genes. Here we show that thousands of enhancers in Drosophila melanogaster S2 and ovarian somatic cells (OSCs) exhibit a marked specificity to one of two core promoters--one derived from a ubiquitously expressed ribosomal protein gene and another from a developmentally regulated transcription factor--and confirm the existence of these two classes for five additional core promoters from genes

with diverse functions. Housekeeping enhancers are active across the two cell types, while developmental enhancers exhibit strong cell-type specificity. Both enhancer classes differ in their genomic distribution, the functions of neighbouring genes, and the core promoter elements of these neighbouring genes. In addition, we identify two transcription factors--Dref and Trl--that bind and activate housekeeping versus developmental enhancers, respectively. Our results provide evidence for a sequence-encoded enhancer-core-promoter specificity that separates developmental and housekeeping gene regulatory programs for thousands of enhancers and their target genes across the entire genome.

Nature. 2015 Feb 26;518(7540):556-9. doi: 10.1038/nature13994. Epub 2014 Dec 15.

Evolution of the new vertebrate head by co-option of an ancient chordate skeletal tissue

A defining feature of vertebrates (craniates) is a pronounced head that is supported and protected by a robust cellular endoskeleton. In the first vertebrates, this skeleton probably consisted of collagenous cellular cartilage, which forms the embryonic skeleton of all vertebrates and the adult skeleton of modern jawless and cartilaginous fish. In the head, most cellular cartilage is derived from a migratory cell population called the neural crest, which arises from the edges of the central nervous system. Because collagenous cellular cartilage and neural crest cells have not been described in invertebrates, the appearance of cellular cartilage derived from neural crest cells is considered a turning point in vertebrate evolution. Here we show that a tissue with many of the defining features of vertebrate cellular cartilage transiently forms in the larvae of the invertebrate chordate Branchiostoma floridae (Florida amphioxus). We also present evidence that during evolution, a key regulator of vertebrate cartilage development, SoxE, gained new cis-regulatory sequences that subsequently directed its novel expression in neural crest cells. Together, these results suggest that the origin of the vertebrate head skeleton did not depend on the evolution of a new skeletal tissue, as is commonly thought, but on the spread of this tissue throughout the head. We further propose that the evolution of cis-regulatory elements near an ancient regulator of cartilage differentiation was a major factor in the evolution of the vertebrate head skeleton.

David Jandzik, Aaron T. Garnett, Tyler A. Square, Maria V. Cattell, Jr-Kai Yu & Daniel M. Medeiros
Nature 518, 534–537 (26 February 2015) doi:10.1038/nature14000

Evolution of Darwin’s finches and their beaks revealed by genome sequencing

Sangeet Lamichhaney, Jonas Berglund, Markus Sällman Almén, Khurram Maqbool, Manfred Grabherr, Alvaro Martinez-Barrio, Marta Promerová, Carl-Johan Rubin, Chao Wang, Neda Zamani, B. Rosemary Grant, Peter R. Grant, Matthew T. Webster & Leif Andersson

Darwin's finches, inhabiting the Galápagos archipelago and Cocos Island, constitute an iconic model for studies of speciation and adaptive evolution. Here we report the results of whole-genome re-sequencing of 120 individuals representing all of the Darwin's finch species and two close relatives. Phylogenetic analysis reveals important discrepancies with the phenotype-based taxonomy. We find extensive evidence for interspecific gene flow throughout the radiation. Hybridization has given rise to species of mixed ancestry. A 240 kilobase haplotype encompassing the ALX1 gene that encodes a transcription factor affecting craniofacial development is strongly associated with beak shape diversity across Darwin's finch species as well as within the medium ground finch (Geospiza fortis), a species that has undergone rapid evolution of beak shape in response to environmental

changes. The ALX1 haplotype has contributed to diversification of beak shapes among the Darwin's finches and, thereby, to an expanded utilization of food resources.

Nature 518, 371–375 (19 February 2015) doi:10.1038/nature14181

R/qtlcharts: Interactive Graphics for Quantitative Trait Locus Mapping
Karl W. Broman

Every data visualization can be improved with some level of interactivity. Interactive graphics hold particular promise for the exploration of high-dimensional data. R/qtlcharts is an R package to create interactive graphics for experiments to map quantitative trait loci (QTL) (genetic loci that influence quantitative traits). R/qtlcharts serves as a companion to the R/qtl package, providing interactive versions of R/qtl's static graphs, as well as additional interactive graphs for the exploration of high-dimensional genotype and phenotype data.

Genetics February 2015 199:359-361; Early online December 18, 2014,doi:10.1534/genetics.114.172742

An Estimate of the Average Number of Recessive Lethal Mutations Carried by Humans
Ziyue Gao, Darrel Waggoner, Matthew Stephens, Carole Ober, and Molly Przeworski

The effects of inbreeding on human health depend critically on the number and severity of recessive, deleterious mutations carried by individuals. In humans, existing estimates of these quantities are based on comparisons between consanguineous and non-consanguineous couples, an approach that confounds socioeconomic and genetic effects of inbreeding. To overcome this limitation, we focused on a founder population that practices a communal lifestyle, for which there is almost complete Mendelian disease ascertainment and a known pedigree. Focusing on recessive lethal diseases and simulating allele transmissions, we estimated that each haploid set of human autosomes carries on average 0.29 (95% credible interval [0.10, 0.84]) recessive alleles that lead to complete sterility or death by reproductive age when homozygous. Comparison to existing estimates in humans suggests that a substantial fraction of the total burden imposed by recessive deleterious variants is due to single mutations that lead to sterility or death between birth and reproductive age. In turn, comparison to estimates from other eukaryotes points to a surprising constancy of the average number of recessive lethal mutations across organisms with markedly different genome sizes.

Genetics genetics.114.173351; Early online February 18, 2015,doi:10.1534/genetics.114.173351

Dramatic Enhancement of Genome Editing by CRISPR/Cas9 Through Improved Guide RNA Design
Behnom Farboud and Barbara J. Meyer

Success with genome editing by the RNA-programmed nuclease Cas9 has been limited by the inability to predict effective guide RNAs and DNA target sites. Not all guide RNAs have been successful, and even those that were varied widely in their efficacy. Here we describe and validate a strategy for Caenorhabditis elegans that reliably achieved a high frequency of genome editing for all targets tested in vivo. The key innovation was to design guide RNAs with a GG motif at the 3' end of their target-specific sequences. All guides designed using this simple principle induced a high frequency of targeted mutagenesis via nonhomologous end joining (NHEJ) and a high frequency of precise DNA integration from exogenous DNA

templates via homology-directed repair (HDR). Related guide RNAs having the GG motif shifted by only three nucleotides showed severely reduced or no genome editing. We also combined the 3' GG guide improvement with the co-CRISPR / co-conversion approach for increasing mutant recovery. By this co-conversion scheme, animals were only screened for genome editing at designated targets if they exhibited a dominant phenotype caused by Cas9-dependent editing of an unrelated target. Combining the two strategies further enhanced the ease of mutant recovery, thereby providing a powerful means to obtain desired genetic changes in an otherwise unaltered genome.

Genetics genetics.115.175166; Early online February 18, 2015,doi:10.1534/genetics.115.175166

Causes of natural variation in fitness: Evidence from studies of Drosophila populations
Brian Charlesworth

DNA sequencing has revealed high levels of variability within most species. Statistical methods based on population genetics theory have been applied to the resulting data and suggest that most mutations affecting functionally important sequences are deleterious but subject to very weak selection. Quantitative genetic studies have provided information on the extent of genetic variation within populations in traits related to fitness and the rate at which variability in these traits arises by mutation. This paper attempts to combine the available information from applications of the two approaches to populations of the fruitfly Drosophila in order to estimate some important parameters of genetic variation, using a simple population genetics model of mutational effects on fitness components. Analyses based on this model suggest the existence of a class of mutations with much larger fitness effects than those inferred from sequence variability and that contribute most of the standing variation in fitness within a population caused by the input of mildly deleterious mutations. However, deleterious mutations explain only part of this standing variation, and other processes such as balancing selection appear to make a large contribution to genetic variation in fitness components in Drosophila.

PNAS 2015 112 (6) 1662-1669; published ahead of print January 8, 2015,doi:10.1073/pnas.1423275112

Decoupling of evolutionary changes in transcription factor binding and gene expression in mammals
Emily S. Wong, David Thybert, Bianca M. Schmitt, Klara Stefflova, Duncan T. Odom, and Paul Flicek

To understand the evolutionary dynamics between transcription factor (TF) binding and gene expression in mammals, we compared transcriptional output and the binding intensities for three tissue-specific TFs in livers from four closely related mouse species. For each transcription factor, TF-dependent genes and the TF binding sites most likely to influence mRNA expression were identified by comparing mRNA expression levels between wild-type and TF knockout mice. Independent evolution was observed genome-wide between the rate of change in TF binding and the rate of change in mRNA expression across taxa, with the exception of a small number of TF-dependent genes. We also found that binding intensities are preferentially conserved near genes whose expression is dependent on the TF, and the conservation is shared among binding peaks in close proximity to each other near the TSS. Expression of TF-dependent genes typically showed an increased sensitivity to changes in binding levels as measured by mRNA abundance. Taken together, these results highlight a significant tolerance to evolutionary changes in TF binding intensity in mammalian

transcriptional networks and suggest that some TF-dependent genes may be largely regulated by a single TF across evolution.

Genome Res. February 2015 25: 167-178; Published in Advance November 13, 2014, doi:10.1101/gr.177840.114

Loss of *Drosophila* pheromone reverses its role in sexual communication in *Drosophila suzukii*

Teun Dekker, Santosh Revadi, Suzan Mansourian, Sukanya Ramasamy, Sebastien Lebreton, Paul G.Becher, Sergio Angeli, Omar Rota-Stabelli, Gianfranco Anfora

The Drosophila pheromone cis-11-octadecenyl acetate (cVA) is used as pheromone throughout the melanogaster group and fulfils a primary role in sexual and social behaviours. Here, we found that Drosophila suzukii, an invasive pest that oviposits in undamaged ripe fruit, does not produce cVA. In fact, its production site, the ejaculatory bulb, is atrophied. Despite loss of cVA production, its receptor, Or67d, and cognate sensillum, T1, which are essential in cVA-mediated behaviours, were fully functional. However, T1 expression was dramatically reduced in D. suzukii, and the corresponding antennal lobe glomerulus, DA1, minute. Behavioural responses to cVA depend on the input balance of Or67d neurons (driving cVA-mediated behaviours) and Or65a neurons (inhibiting cVA-mediated behaviours). Accordingly, the shifted input balance in D. suzukii has reversed cVA's role in sexual behaviour: perfuming D. suzukii males with Drosophila melanogaster equivalents of cVA strongly reduced mating rates. cVA has thus evolved from a generic sex pheromone to a heterospecific signal that disrupts mating in D. suzukii, a saltational shift, mediated through offsetting the input balance that is highly conserved in congeneric species. This study underlines that dramatic changes in a species' sensory preference can result from rather 'simple' numerical shifts in underlying neural circuits.

Proc. R. Soc. B: 2015 282 20143018; DOI: 10.1098/rspb.2014.3018. Published 25 February 2015

Parental age influences developmental stability of the progeny in Drosophila

Betina Colines, Nahuel Cabrera Rodríguez, Esteban R. Hasson, Valeria Carreira, Nicolás Frankel

The stochastic nature of biochemical processes is a source of variability that influences developmental stability. Developmental instability (DI) is often estimated through fluctuating asymmetry (FA), a parameter that deals with within-individual variation in bilateral structures. A relevant goal is to shed light on how environment, physiology and genotype relate to DI, thus providing a more comprehensive view of organismal development. Using Drosophila melanogaster isogenic lines, we investigated the effect of parental age, parental diet and offspring heterozygosity on DI. In this work, we have uncovered a clear relationship between parental age and offspring asymmetry. We show that asymmetry of the progeny increases concomitantly with parental age. Moreover, we demonstrate that enriching the diet of parents mitigates the effect of age on offspring symmetry. We show as well that increasing the heterozygosity of the progeny eliminates the effect of parental age on offspring symmetry. Taken together, our results suggest that diet, genotype and age of the parents interact to determine offspring DI in wild populations. These findings provide us with an avenue to understand the mechanisms underlying DI.

Proc. R. Soc. B: 2015 282 20142437; DOI: 10.1098/rspb.2014.2437. Published 11 February 2015

Altered retinoic acid signalling underpins dentition evolution

Yann Gibert, Eric Samarut, Emmanuel Pasco-Viel, Laure Bernard, Véronique Borday-Birraux, AlexaSadier, Catherine Labbé, Laurent Viriot, Vincent Laudet

Small variations in signalling pathways have been linked to phenotypic diversity and speciation. In vertebrates, teeth represent a reservoir of adaptive morphological structures that are prone to evolutionary change. Cyprinid fish display an impressive diversity in tooth number, but the signals that generate such diversity are unknown. Here, we show that retinoic acid (RA) availability influences tooth number size in Cyprinids. Heterozygous adult zebrafish heterozygous for the cyp26b1 mutant that encodes an enzyme able to degrade RA possess an extra tooth in the ventral row. Expression analysis of pharyngeal mesenchyme markers such as dlx2a and lhx6 shows lateral, anterior and dorsal expansion of these markers in RA-treated embryos, whereas the expression of the dental epithelium markers dlx2b and dlx3b is unchanged. Our analysis suggests that changes in RA signalling play an important role in the diversification of teeth in Cyprinids. Our work illustrates that through subtle changes in the expression of rate-limiting enzymes, the RA pathway is an active player of tooth evolution in fish.

Proc. R. Soc. B: 2015 282 20142764; DOI: 10.1098/rspb.2014.2764. Published 4 February 2015

From *shavenbaby* to the naked valley: trichome formation as a model for evolutionary developmental biology

Saad Arif, Sebastian Kittelmann and Alistair P. McGregor

Microtrichia or trichomes are non-sensory actin protrusions produced by the epidermal cells of many insects. Studies of trichome formation in Drosophila have over the last 30 years provided key insights towards our understanding of gene regulation, gene regulatory networks (GRNs), development, the genotype to phenotype map, and the evolution of these processes. Here we review classic studies that have used trichomeformation as a model to shed light on Drosophila development as well as recent research on the architecture of the GRN underlying trichomeformation. This includes the findings that both small peptides and microRNAs play important roles in the regulation and evolution of this network. In addition, we review research on the evolution of trichome patterns that has provided novel insights into the function and architecture of cis-regulatory modules, and into the genetic basis of morphological change. We conclude that further research on these apparently simple and often functionally enigmatic structures will continue to provide new and important knowledge about development and evolution.

Evol Dev. 2015 Jan;17(1):120-6. doi: 10.1111/ede.12113.

Quantitative evolutionary dynamics using high-resolution lineage tracking

Sasha F. Levy1,2,3*, Jamie R. Blundell4,5*, Sandeep Venkataram5 , Dmitri A. Petrov5 , Daniel S. Fisher4,5 & Gavin Sherlock1

Evolution of large asexual cell populations underlies ~30% of deaths worldwide, including those caused by bacteria, fungi, parasites, and cancer. However, the dynamics underlying these evolutionary processes remain poorly understood because they involve many competing beneficial lineages, most of which never rise above extremely low frequencies in the population. To observe these normally hidden evolutionary dynamics, we constructed a

sequencing-based ultra high-resolution lineage tracking system in Saccharomyces cerevisiae that allowed us to monitor the relative frequencies of ~500,000 lineages simultaneously. In contrast to some expectations, we found that the spectrum of fitness effects of beneficial mutations is neither exponential nor monotonic. Early adaptation is a predictable consequence of this spectrum and is strikingly reproducible, but the initial small-effect mutations are soon outcompeted by rarer large-effect mutations that result in variability between replicates. These results suggest that early evolutionary dynamics may be deterministic for a period of time before stochastic effects become important.

Nature (2015) doi:10.1038/nature14279

Evolution of sexual traits influencing vectorial capacity in anopheline mosquitoes
Sara N. Mitchell, Evdoxia G. Kakani, Adam South, Paul I. Howell, Robert M. Waterhouse, and Flaminia Catteruccia
Mating plugs transferred to female mosquitoes prevent multiple male partners, change physiology, and favor parasite development.
The availability of genome sequences from 16 anopheline species provides unprecedented opportunities to study the evolution of reproductive traits relevant for malaria transmission. In Anopheles gambiae, a likely candidate for sexual selection is male 20-hydroxyecdysone (20E). Sexual transfer of this steroid hormone as part of a mating plug dramatically changes female physiological processes intimately tied to vectorial capacity. By combining phenotypic studies with ancestral state reconstructions and phylogenetic analyses, we show that mating plug transfer and male 20E synthesis are both derived characters that have coevolved in anophelines, driving the adaptation of a female 20E-interacting protein that promotes oogenesis via mechanisms also favoring Plasmodium survival. Our data reveal coevolutionary dynamics of reproductive traits between the sexes likely to have shaped the ability of anophelines to transmit malaria.

Science 27 February 2015: 985-988.

Perspective: **An unexpected cost of sex**
Suzanne H. Alonzo
Science 27 February 2015: 948-949.
Coevolution of male and female mosquitoes influences whether mosquitoes transmit human malaria

Class I Myosins Have Overlapping and Specialized Functions in Left-Right Asymmetric Development inDrosophila.
Okumura T, Sasamura T, Inatomi M, Hozumi S, Nakamura M, Hatori R, Taniguchi K, Nakazawa N, Suzuki E, Maeda R, Yamakawa T, Matsuno K.

The class I myosin genes are conserved in diverse organisms, and their gene products are involved in actin dynamics, endocytosis, and signal transduction. Drosophila melanogaster has three class I myosin genes, Myosin 31DF (Myo31DF), Myosin 61F (Myo61F), and Myosin 95E (Myo95E). Myo31DF, Myo61F, and Myo95E belong to the Myosin ID, Myosin IC, and Myosin IB families, respectively. Previous loss-of-function analyses of Myo31DF and Myo61F revealed important roles in left-right (LR) asymmetric development and enterocyte maintenance, respectively. However, it was difficult to elucidate their roles in vivo, because of potential redundant activities. Here we generated class I myosin double and triple mutants to address this issue. We found that the triple mutant was viable and fertile, indicating that all three class I myosins were dispensable for survival. A loss-of-function analysis revealed

further that Myo31DF and Myo61F, but not Myo95E had redundant functions in promoting the dextral LR asymmetric development of the male genitalia. Myo61F overexpression is known to antagonize the dextral activity of Myo31DF in various Drosophilaorgans. Thus, the LR-reversing activity of overexpressed Myo61F may not reflect its physiological function. The endogenous activity of Myo61F in promoting dextral LR asymmetric development was observed in the male genitalia, but not the embryonic gut, another LR asymmetric organ. Thus, Myo61F and Myo31DF, but not Myo95E, play tissue-specific, redundant roles in LR asymmetric development. Our studies also revealed differential co-localization of the class I myosins with F-actin in the brush border of intestinal enterocytes.

Genetics. 2015 Feb 6. pii: genetics.115.174698.

Preprints (From Haldane's Sieve http://biorxiv.org/ and http://arxiv.org/):

Pervasive adaptation of gene expression in Drosophila
Posted on **February 24, 2015** by **Joe Pickrell**
Pervasive adaptation of gene expression in Drosophila
Armita Nourmohammad, Joachim Rambeau, Torsten Held, Johannes Berg, Michael Lassig
(Submitted on 23 Feb 2015)
http://arxiv.org/abs/1502.06406
Gene expression levels are important molecular quantitative traits that link genotypes to molecular functions and fitness. In Drosophila, population-genetic studies in recent years have revealed substantial adaptive evolution at the genomic level. However, the evolutionary modes of gene expression have remained controversial. Here we present evidence that adaptation dominates the evolution of gene expression levels in flies. We show that 64% of the observed expression divergence across seven Drosophila species are adaptive changes driven by directional selection. Our results are derived from the variation of expression within species and the time-resolved divergence across a family of related species, using a new inference method for selection. We identify functional classes of adaptively regulated genes, as well as sex-specific adaptation occurring predominantly in males. Our analysis opens a new avenue to map system-wide selection on molecular quantitative traits independently of their genetic basis.

Natural Selection Shapes the Mosaic Ancestry of the Drosophila Genetic Reference Panel and the D. melanogaster Reference Genome
Posted on **February 5, 2015** by **Joe Pickrell**
Natural Selection Shapes the Mosaic Ancestry of the Drosophila Genetic Reference Panel and the D. melanogaster Reference Genome
John E Pool
doi: http://dx.doi.org/10.1101/014837
North American populations of Drosophila melanogaster are thought to derive from both European and African source populations, but despite their importance for genetic research, patterns of admixture along their genomes are essentially undocumented. Here, I infer geographic ancestry along genomes of the Drosophila Genetic Reference Panel (DGRP) and the D. melanogaster reference genome. Overall, the proportion of African ancestry was estimated to be 20% for the DGRP and 9% for the reference genome. Based on the size of admixture tracts and the approximate timing of admixture, I estimate that the DGRP population underwent roughly 13.9 generations per year. Notably, ancestry levels varied

strikingly among genomic regions, with significantly less African introgression on the X chromosome, in regions of high recombination, and at genes involved in specific processes such as circadian rhythm. An important role for natural selection during the admixture process was further supported by a genome-wide signal of ancestry disequilibrium, in that many between-chromosome pairs of loci showed a deficiency of Africa-Europe allele combinations. These results support the hypothesis that admixture between partially genetically isolated Drosophila populations led to natural selection against incompatible genetic variants, and that this process is ongoing. The ancestry blocks inferred here may be relevant for the performance of reference alignment in this species, and may bolster the design and interpretation of many population genetic and association mapping studies.

A Single Gene Causes an Interspecific Difference in Pigmentation in Drosophila
Posted on **January 28, 2015** by **Joe Pickrell**
A Single Gene Causes an Interspecific Difference in Pigmentation in Drosophila
Yasir H. Ahmed-Braimah, Andrea L. Sweigart
doi: http://dx.doi.org/10.1101/014464
The genetic basis of species differences remains understudied. Studies in insects have contributed significantly to our understanding of morphological evolution. Pigmentation traits in particular have received a great deal of attention and several genes in the insect pigmentation pathway have been implicated in inter- and intraspecific differences. Nonetheless, much remains unknown about many of the genes in this pathway and their potential role in understudied taxa. Here we genetically analyze the puparium color difference between members of the Virilis group of Drosophila. The puparium of Drosophila virilis is black, while those of D. americana, D. novamexicana, and D. lummei are brown. We used a series of backcross hybrid populations between D. americana and D. virilis to map the genomic interval responsible for the difference between this species pair. First, we show that the pupal case color difference is caused by a single Mendelizing factor, which we ultimately map to an ~11kb region on chromosome 5. The mapped interval includes only the first exon and regulatory region(s) of the dopamine N-acetyltransferase gene (Dat). This gene encodes an enzyme that is known to play a part in the insect pigmentation pathway. Second, we show that this gene is highly expressed at the onset of pupation in light-brown taxa (D. americana and D. novamexicana) relative to D. virilis, but not in the dark-brown D. lummei. Finally, we examine the role of Dat in adult pigmentation between D. americana (heavily melanized) and D. novamexicana (lightly melanized) and find no discernible effect of this gene in adults. Our results demonstrate that a single gene is entirely or almost entirely responsible for a morphological difference between species.

Evolution of Conditional Cooperativity Between HOXA11 and FOXO1 Through Allosteric Regulation
Posted on **January 27, 2015** by **Joe Pickrell**
Evolution of Conditional Cooperativity Between HOXA11 and FOXO1 Through Allosteric Regulation
Mauris C. Nnamani, Soumya Ganguly, Vincent J. Lynch, Laura S. Mizoue, Yingchun Tong, Heather Darling, Monika Fuxreiter, Jens Meiler, Gunter P. Wagner
doi: http://dx.doi.org/10.1101/014381
Transcription factors (TFs) play multiple roles in different cells and stages of development. Given this multitude of functional roles it has been assumed that TFs are evolutionarily highly constrained. Here we investigate the molecular mechanisms for the origin of a derived functional interaction between two TFs that play a key role in mammalian pregnancy, HOXA11 and FOXO1. We have previously shown that the regulatory role of HOXA11 in mammalian endometrial stromal cells requires an interaction with FOXO1, and that the physical interaction between these proteins evolved long before their functional cooperativity. Through a combination of functional, biochemical, and structural approaches, we demonstrate that the derived functional cooperativity between HOXA11 and FOXO1 is

due to derived allosteric regulation of HOXA11 by FOXO1. This study shows that TF function can evolve through changes affecting the functional output of a pre-existing protein complex.

The genetics of resistance to Morinda fruit toxin during the postembryonic stages in Drosophila sechellia
Posted on **January 21, 2015** by **Joe Pickrell**
The genetics of resistance to Morinda fruit toxin during the postembryonic stages in Drosophila sechellia
Yan Huang, Deniz Erezyilmaz
doi: http://dx.doi.org/10.1101/014027
Many phytophagous insect species are ecologic specialists that have adapted to utilize a single host plant. Drosophila sechellia is a specialist that utilizes the ripe fruit of Morinda citrifolia, which is toxic to its sibling species, D. simulans. Here we apply multiplexed shotgun genotyping and QTL analysis to examine the genetic basis of resistance to M. citrifolia fruit toxin in interspecific hybrids. We find that at least four dominant and four recessive loci interact additively to confer resistance to the M. citrifolia fruit toxin. These QTL include a dominant locus of large effect on the third chromosome (QTL-IIIsima) that was not detected in previous analyses. The small-effect loci that we identify overlap with regions that were identified in selection experiments with D. simulans on octanoic acid and in QTL analyses of adult resistance to octanoic acid. Our high-resolution analysis sheds new light upon the complexity of M. citrifolia resistance, and suggests that partial resistance to lower levels of M. citrifolia toxin could be passed through introgression from D. sechellia to D. simulans in nature. The identification of a locus of major effect, QTL-IIIsima, is an important step towards identifying the molecular basis of host plant specialization by D. sechellia.

The P-element strikes again: the recent invasion of natural Drosophila simulans populations
Posted on **January 14, 2015** by **Joe Pickrell**
The P-element strikes again: the recent invasion of natural Drosophila simulans populations
Robert Kofler, Tom Hill, Viola Nolte, Andrea Betancourt, Christian Schlötterer
doi: http://dx.doi.org/10.1101/013722
The P-element is one of the best understood eukaryotic transposable elements. It invaded Drosophila melanogaster populations within a few decades, but was thought to be absent from close relatives, including D. simulans. Five decades after the spread in D. melanogaster, we provide evidence that the P-element has also invaded D. simulans. P-elements in D. simulans appear to have been acquired recently from D. melanogaster probably via a single horizontal transfer event. Expression data indicate that the P-element is processed in the germline of D. simulans, and genomic data show an enrichment of P-element insertions in putative origins of replication, similar to that seen in D. melanogaster. This ongoing spread of the P-element in natural populations provides an unique opportunity to understand the dynamics of transposable element spreads and the associated piRNA defense mechanisms.

Behavioral individuality reveals genetic control of phenotypic variability
Julien F. Ayroles, Sean M. Buchanan, Chelsea Jenney, Kyobi Skutt-Kakaria, Jennifer Grenier, Andrew G. Clark, Daniel L. Hartl, Benjamin L. de Bivort
(Submitted on 10 Sep 2014)
Variability is ubiquitous in nature and a fundamental feature of complex systems. Few studies, however, have investigated variance itself as a trait under genetic control. By focusing primarily on trait means and ignoring the effect of alternative alleles on trait variability, we may be missing an important axis of genetic variation contributing to phenotypic differences among individuals. To study genetic effects on individual-to-individual phenotypic variability (or intragenotypic variability), we used a panel of Drosophila inbred lines and focused on locomotor handedness, in an assay optimized to measure variability. We discovered that some lines had consistently high levels of intragenotypic variability

among individuals while others had low levels. We demonstrate that the degree of variability is itself heritable. Using a genome-wide association study (GWAS) for the degree of intragenotypic variability as the phenotype across lines, we identified several genes expressed in the brain that affect variability in handedness without affecting the mean. One of these genes, Ten-a, implicated a neuropil in the central complex of the fly brain as influencing the magnitude of behavioral variability, a brain region involved in sensory integration and locomotor coordination. We have validated these results using genetic deficiencies, null alleles, and inducible RNAi transgenes. This study reveals the constellation of phenotypes that can arise from a single genotype and it shows that different genetic backgrounds differ dramatically in their propensity for phenotypic variability. Because traditional mean-focused GWASs ignore the contribution of variability to overall phenotypic variation, current methods may miss important links between genotype and phenotype.

Large-scale assessment of olfactory preferences and learning in *Drosophila melanogaster*: behavioral and genetic measures

Elisabetta Versace , Julia Katharina Reisenberger

doi: http://dx.doi.org/10.1101/014357

Abstract

In the Evolve and Resequence method (E&R), experimental evolution and genomics are combined to investigate evolutionary dynamics and the genotype-phenotype link. This approach requires many replicates with large population sizes, which imposes severe restrictions on the analysis of behavioral phenotypes. Aiming to use E&R for investigating the evolution of behavior in *Drosophila*, we have developed a simple and effective method to assess spontaneous olfactory preferences and learning in large samples of fruit flies using a T-maze. We tested this procedure on (a) a large wild-caught population and (b) 11 isofemale lines of *Drosophila melanogaster*. Compared to previous methods, this procedure reduces the environmental noise and allows for the analysis of large population samples. Consistent with previous results, we show that flies have a spontaneous preference for orange *vs.* apple odor. With our procedure wild-derived flies exhibit olfactory learning in the absence of previous laboratory selection. Furthermore, we find genetic differences in the olfactory learning with relatively high heritability. We propose this large-scale method as an effective tool for E&R and genome-wide association studies on olfactory preferences and learning.

http://www.biorxiv.org/content/biorxiv/early/2015/01/26/014357.full.pdf