Genetics, Vol. 191, AUGUST 2012, Copyright © 2012

New negative feedback regulators of Egfr signaling in *Drosophila*, pp. 1213–1226

Jonathan P. Butchar, Donna Cain, Sathiya N. Manivannan, Andrea D. McCue, Liana Bonanno, Sarah Halula, Sharon Truesdell, Christina L. Austin, Thomas L. Jacobsen, and Amanda Simcox

While much is known about the checks and balances necessary for the precise specification of fly wings, these authors show that we didn't know it all. They report the discovery of two new negative regulators in the Egfr pathway that are conserved in other animals. Because a perfect wing is of critical importance to flies, it is likely that more such controls will be discovered.

On the prospects of whole-genome association mapping in *Saccharomyces cerevisiae*, pp. 1345–1353

Caitlin F. Connelly and Joshua M. Akey

Genome-wide association (GWA) studies have not caught on for model organisms. One challenge is population structure, which can result in spurious associations. This article shows that indeed, GWA studies in yeast are complicated by complex patterns of population structure that are not easily corrected by existing approaches. The authors expound on how careful study design and empirical tests of the effects of population structure will be necessary for carrying out GWA studies in model organisms.

Suppressors, screens, and genes: An educational primer for use with "A network of genes antagonistic to the LIN-35 retinoblastoma protein of *Caenorhabditis elegans*", pp. 1031-1035

Elizabeth A. De Stasio

This is the first of a new series of articles in *GENETICS*—Educational Primers—designed to guide educators in the use of current scientific literature in the classroom (see editorial in this issue). In this Primer, Elizabeth De Stasio explains how Polley and Fay used RNA interference, suppressor screens, and synthetic phenotypes to elucidate the function of the retinoblastoma protein in *C. elegans* (see article in this issue). Each Primer provides necessary background for students and offers a sample approach to classroom use of the original article, including discussion questions.

A resolution of the mutation load paradox in humans, pp. 1321–1330

Yann Lesecque, Peter D. Keightley, and Adam Eyre-Walker

It has been estimated that each of us receives, on average, at least two new harmful mutations from our parents. Previous theoretical work suggested that this high rate of harmful mutation should result in 88% of individuals failing to have offspring, and each female having to have more than 16 offspring on average, to maintain population size. Fortunately, those calculations are incorrect, as these authors show. They show that humans could tolerate hundreds of new harmful mutations if natural selection acts via competition between individuals.

SNP-ratio mapping (SRM): Identifying lethal alleles and mutations in complex genetic backgrounds by next-generation sequencing, pp. 1381–1386

Heike Lindner, Michael T. Raissig, Christian Sailer, Hiroko Shimosato-Asano, Rémy Bruggmann, and Ueli Grossniklaus

Mutations in essential genes are difficult to identify. Here the authors present a method for quick identification of homozygous-lethal alleles by next-generation sequencing. The authors' method, which can also be used to map second-site modifiers in complex genetic/transgenic backgrounds, can be applied to any genetic organism.

The mRNA decay pathway regulates the expression of the Flo11 adhesin and biofilm formation in *Saccharomyces cerevisiae*, pp. 1387–1391

Tricia L. Lo, Yue Qu, Nathalie Uwamahoro, Tara Quenault, Traude H. Beilharz, and Ana Traven

The gene encoding the yeast cell-wall adhesin Flo11 offers an excellent platform for learning how gene expression is controlled by extracellular signals and developmental pathways. Regulated expression of the cell-wall adhesins is also relevant to virulence properties of pathogenic fungi and industrial applications with yeasts. These investigators discover a novel mechanism controlling *FLO11* expression: the mRNA decay pathway inhibits the expression of transcriptional repressors of *FLO11*.

Fluctuations of fitness distributions and the rate of Muller's ratchet, pp. 1283–1293

Richard A. Neher and Boris I. Shraiman

Muller's ratchet is relentless, but its quantitative characterization has remained a challenge. This article offers a systematic analysis of the stochastic properties of the deleterious mutation selection-balance, and provides an accurate formula for the rate of Muller's ratchet.

A network of genes antagonistic to the LIN-35 retinoblastoma protein of *Caenorhabditis elegans*, pp. 1367–1380

Stanley R. G. Polley and David S. Fay

The pRb tumor suppressor of *Caenorhabditis elegans* (LIN-35) regulates a diverse range of cellular and developmental processes. This article describes genes that were identified as genetic suppressors of phenotypes associated with LIN-35/pRb loss of function in the worm. Because the encoded proteins are highly conserved, these may represent candidate targets for anticancer therapies, as their inactivation alleviates defects associated with a commonly inactivated tumor suppressor in humans.

Transvection is common throughout the *Drosophila* genome, pp. 1129–1141

David J. Mellert and James W. Truman

We know that *cis*-regulatory sequence elements can regulate transcription in *trans*, but what is the prevalence of their action in *trans*? These investigators show that *trans* interactions between transgenes inserted into the *Drosophila* genome is common, and provide insight into possible molecular mechanisms. Because *trans* interactions between transgenes can confound experimental strategies, the authors propose guidelines for using transgenes inserted via site-specific integration.

and

Comparing enhancer action in *cis* and in *trans*, pp. 1143–1155

Jack R. Bateman, Justine E. Johnson, and Melissa N. Locke

Sometimes two chromosomes are close enough that an enhancer on one can communicate in *trans* with a promoter on its neighbor. How does this "transvection" work? This article describes a transgenic approach to the study of transvection that simplifies sequence manipulation and enables precise quantification of changes to gene expression when enhancers act in *cis or trans.*

This Month in the American Journal of Human Genetics

A haplotype at STAT2 introgressed from Neandertals and serves as a candidate of positive selection in Papua New Guinea, Am. J. Hum. Genet. 91(2)

Fernando L. Mendez, Joseph C. Watkins, and Michael F. Hammer

Genomic comparisons support the hypothesis that admixture occurred between early humans and Neandertals. Perhaps not surprisingly, given the overall small genetic contribution from this archaic species, evidence for adaptive introgression has remained elusive. Now, through a re-sequencing analysis, Mendez *et al.* identify a haplotype (N) present in modern humans that introgressed from Neandertals. Interestingly, the introgressed haplotype is present at a high frequency in Melanesia and displays signatures of having undergone positive selection. Although the actual target of selection is unknown, candidate genes include STAT2, ERBB3, and ESYT1 which encode proteins involved in innate immunity, cell signaling, and calcium sensing, respectively. Of note, this article points to the possibility that there will be many future insights into the contributions that now extinct species have made to modern humans.