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Gene expression variation in *Drosophila melanogaster* due to rare transposable element insertion alleles of large effect, pp. 85–93

Julie M. Cridland, Kevin R. Thornton, and Anthony D. Long

Cridland *et al.* report the first genome-wide analysis of how transposable element insertions contribute to gene expression variation in a population. They examined thousands of genes with rare transposable element insertions in 37 lines from the *Drosophila* Genetic Reference Panel and found that presence of a transposable element within or near a gene was significantly associated with reduced gene expression. Large decreases in expression were more pronounced for insertions near genes.

A novel cholinergic action of alcohol and the development of tolerance to that effect in *Caenorhabditis elegans*, pp. 135–149

Edward G. Hawkins, Ian Martin, Lindsay M. Kondo, Meredith E. Judy, Victoria E. Brings, Chung-Lung Chan, GinaMari G. Blackwell, Jill C. Bettinger, and Andrew G. Davies

Better understanding the genes and mechanisms involved in acute alcohol responses might allow us to predict an individual's predisposition to developing an alcohol use disorder. Hawkins *et al.* identify a novel alcohol-induced excitatory effect in *C. elegans*. The effect requires an acetylcholine receptor that contains the UNC-63 alpha subunit. Tolerance to the excitatory effect occurs during exposure to the drug, and this tolerance is prevented by altered function of the Sodium/Potassium transporter.

Maintenance of nucleosomal balance in *cis* by conserved AAA-ATPase Yta7, pp. 105–116

Laura M. Lombardi, Matthew D. Davis, and Jasper Rine

How do cells regulate the density of nucleosomes within genes? Using the highest resolution genome-wide techniques, Lombardi *et al.* show that the highly conserved yeast AAA-ATPase Yta7 directly promotes the proper degree of nucleosome spacing. Importantly, comprehensive double-mutant analysis demonstrates that Yta7 limits nucleosome density largely by inhibiting the histone H3/H4 chaperone Rtt106. This work identifies an important cellular antagonism which helps to maintain nucleosomal balance within genes.

Contrasting modes and tempos of venom expression evolution in two snake species, pp. 165–176

Mark J. Margres, James J. McGivern, Margaret Seavy, Kenneth P. Wray, Jack Facente, and Darin R. Rokyta

Understanding the genetic basis of adaptation requires the mapping of genotype to phenotype. To identify the processes driving patterns of phenotypic diversity, Margres *et al.* constructed genotype-phenotype maps and compared range-wide toxin-protein expression variation for two snake species with nearly identical ranges. Contrary to expectations, significant expression variation was only detected for one of the species. The results not only link expression variation at specific loci to divergence in a complex trait, but also have extensive conservation and biomedical implications.

A novel cryptochrome-dependent oscillator in *Neurospora crassa*, pp. 233–245

Imade Y. Nsa, Nirmala Karunarathna, Xiaoguang Liu, Howard Huang, Brittni Boetteger, and Deborah Bell-Pedersen

The core molecular oscillators of the conserved eukaryotic circadian clock are made up of a transcription/translation feedback loop involving clock genes. However, evidence in several model organisms suggests that the clock uses multiple molecular oscillators. Nsa *et al.* identified a *Neurospora* mutant that is rhythmic with a circadian period independent of the core FRQ/WCC oscillator. The activity of this novel oscillator requires CRYPTOCHROME, a component of the mammalian core oscillator. This mutant provides tools to unravel the complexity of the oscillator system and circadian clock evolution.

Allelic variation, aneuploidy, and nongenetic mechanisms suppress a monogenic trait in yeast, pp. 247–262

Amy Sirr, Gareth A. Cromie, Eric W. Jeffery, Teresa L. Gilbert, Catherine L. Ludlow, Adrian C. Scott, and Aimée M. Dudley

Severity of symptoms and age of onset of monogenic diseases can vary widely not only in response to environmental differences, but also due to the presence of genetic modifiers. Sirr *et al.* investigated the modifier genetics of a monogenic trait in a well-characterized yeast model of the human disease galactosemia. The results revealed multiple mechanisms by which the trait could be suppressed, including polymorphisms, aneuploidy of a chromosome harboring a transcriptional repressor, and a nongenetic effect.

A general unified framework to assess the sampling variance of heritability estimates using pedigree or marker-based relationships, pp. 223–232

Peter M. Visscher and Michael E. Goddard

Heritability is traditionally estimated from pedigree data by modelling the observed resemblance between relatives, and more recently, using relationships estimated from markers. Visscher and Goddard provide a single theoretical framework to calculate the asymptotic sampling variance of the heritability across a wide range of designs. The authors show that previous results are special cases of the general framework and that the variance in relationships in the sample is a key parameter in all experimental designs.

Penalized multimarker *vs.* single-marker regression methods for genome-wide association studies of quantitative traits, pp. 205–222

Hui Yi, Patrick Breheny, Netsanet Imam, Yongmei Liu, and Ina Hoeschele

Human genome-wide association studies (GWAS) are predominantly analyzed using single marker methods that fit an incorrect model to the data. Alternatives to Single Marker Analysis (SMA) test all or subsets of markers simultaneously and require a form of Penalized Regression. Yi *et al.* review Penalized Regression methods, extend them to incorporate False Discovery Rate control, investigate fusion-type penalties, assess their performance in comparison with SMA, and provide practical recommendations for the use of these methods in GWAS.

This Month in the American Journal of Human Genetics

The genetic ancestry of African, Latino, and European Americans across the United States, Am. J. Hum. Genet. 96(1): 37–53

Katarzyna Bryc, Eric Y. Durand, J. Michael Macpherson, David Reich, and Joanna L. Mountain

Owing to its unique history, the United States is often viewed as being something of a melting pot. The influx of, and admixture between, multiple populations over the past several hundred years has created a population whose diversity continues to increase. In this study, Bryc *et al.* leverage the massive amount of population and genetics data present in the 23 and me database to explore the genetic ancestry of present-day Americans. The analyses highlight the ways in which historical events shaped current-day regional differences in ancestry. Moreover, this work sheds light on the complexities that influence perceptions of race and ethnicity.