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Unexpected role for dosage compensation in the control of dauer arrest, insulin-like signaling, and FoxO transcription factor activity in *Caenorhabditis elegans,* pp. 619–629

Kathleen J. Dumas, Colin E. Delaney, Stephane Flibotte, Donald G. Moerman, Gyorgyi Csankovszki, and Patrick J. Hu

The results of this study suggest that the dosage compensation machinery responsible for equalizing gene expression from sex chromosomes might respond to external cues. The authors show that dauer arrest in *C. elegans* is controlled by dosage compensation through its regulation of expression of components of a conserved insulin-like signaling pathway that inhibits FoxO transcription factor activity.

Pigment pattern formation in the guppy, *Poecilia reticulata,* involves the *Kita* and *Csf1ra* receptor tyrosine kinases, pp. 631–646

Verena A. Kottler, Andrey Fadeev, Detlef Weigel, and Christine Dreyer

Male guppies (*Poecilia reticulata*) are exceptionally beautiful, while females are inconspicuously colored. Male coloration is shaped by a complex interplay between sexual and natural selection in wild populations, but little is known about the genes involved. This article reveals that the receptor tyrosine kinases *Kita* and *Csf1ra* are essential for guppy pigmentation, providing the first molecular insight into guppy pigment pattern formation.

Computational inference methods for selective sweeps arising in acute HIV infection, pp. 737–752

Sivan Leviyang

During an HIV infection, cytotoxic T lymphocytes (CTLs) kill HIV infected cells. HIV can escape CTL killing through mutations that often quickly sweep through the infecting HIV population. Such selective sweeps are complex, combining multiple mutation pathways through which HIV can escape. Further, in early infection when CTL killing is thought to be strongest, both the CTL and HIV populations expand and contract in size. In this work, the author develops both Bayesian and hypothesis-based inference methods to analyze HIV selective sweeps. The methods are applied to HIV patient datasets to infer and analyze the rate at which HIV escapes from CTL response.

Rare variant association testing under low-coverage sequencing, pp. 769–779

Oron Navon, Jae Sul, Buhm Han, Lucia Conde, Paige Bracci, Jacques Riby, Christine F. Skibola, Eleazar Eskin, and Eran Halperin

It is still costly to sequence the thousands of individuals necessary for detecting associations of rare variants with phenotypes, so low coverage sequencing is widely used. This article describes two novel methods for identifying associations of rare variants that take into account the uncertainty and genotyping errors resulting from low sequence coverage. These methods outperform others with both low and high sequence coverage, and under different scenarios of disease architecture.

Dissecting high-dimensional phenotypes with Bayesian sparse factor analysis of genetic covariance matrices, pp. 753–767

Daniel E. Runcie, and Sayan Mukherjee

High-dimensional phenotyping is key to the genomics era, but making sense of hundreds of traits at a time is a challenge. Genetic covariances described by a G-matrix reveal developmental modules and evolutionary constraints. Existing methods for fitting G-matrices are either overwhelmed by the computational challenges of high-dimensional traits, or fail to capture the underlying biology, so these authors derived a novel Bayesian model that efficiently estimates G-matrices for very high-dimensional traits such as gene expression.

Estimating variable effective population sizes from multiple genomes: a sequentially Markov conditional sampling distribution approach, pp. 647–662

Sara Sheehan, Kelley Harris, and Yun S. Song

Accurate estimates of effective population sizes are needed to provide a clear picture of human colonization history. Here, the authors present a new coalescent-based method that can efficiently infer changes in effective population size from multiple genomes, providing access to a new store of information about the recent past. They apply their method to the genomes of multiple human individuals of European and African ancestry to obtain a detailed population size change history during recent times.

Is structural squation modeling advantageous for the genetic improvement of multiple traits?, pp. 561–572

Bruno D. Valente, Guilherme J. Rosa, Daniel Gianola, Xiao-Lin Wu, and Kent A. Weigel

Priors in whole-genome regression: the Bayesian alphabet returns, pp. 573–596

Daniel Gianola

Genomic-BLUP decoded: a look into the black box of genomic prediction, pp. 597–607

David Habier, Rohan L. Fernando, and Dorian J. Garrick

This issue of *GENETICS* features three articles that tackle genomic prediction of traits. Valente *et al.* (and see Commentary by Rousset) assess whether use of structural equation models, which can convey causal relationships among traits, improves predictions. Gianola explores the role of prior assumptions about the distribution of marker effects in Bayesian whole-genome regression models, finding that claims made about genetic architecture using these methods must be taken with caution. And Habier *et al.* look into the black box of Genomic-BLUP, a statistical method that uses relationships between individuals calculated from single nucleotide polymorphisms (SNPs) to capture relationships at quantitative trait loci (QTL).

This Month's Perspectives

Robert Heath Lock and his text-book of genetics, 1906, pp. 529–537

A. W. F. Edwards

This month's Perspectives article chronicles one of the first genetics textbooks, published only 6 years after the rediscovery of Mendel's work, and tells of the influence it had on several future luminaries of the field.

This Month in the American Journal of Human Genetics

Dissecting disease inheritance modes in a 3D protein network challenges the "guilt-by-association" principle, Am. J. Hum. Genet. 93(1)

Yu Guo, Xiaomu Wei, Jishnu Das, Andrew Grimson, Steven M. Lipkin, Andrew G. Clark, and Haiyuan Yu

Network-based approaches have suggested that mutations in genes encoding interacting proteins can lead to the same disease phenotype, otherwise known as the "guilt-by-association" principle. Questions remain about how the mode of inheritance fits into this principle. By examining where recessive and dominant mutations are located when mapped onto a 3D protein interaction network, Guo *et al*. determine that dominant mutations do not necessarily follow this "guilt-by-association" principle. Unlike recessive mutations, dominant point mutations are not more likely to be located on protein interaction interfaces. Furthermore, dominant truncating mutations are enriched between interfaces, suggesting that these mutants might encode functional protein fragments in which some, but not all, of the protein interactions are preserved.