GENETICS, Vol. 199, MARCH 2015, Copyright © 2015

Locally epistatic genomic relationship matrices for genomic association and prediction, pp. 857–871

Deniz Akdemir and Jean-Luc Jannink

In breeding studies a distinction is made between the genetic value (additive + epistatic genetic effects) and the breeding value (additive genetic effects) of an individual, because some of the epistatic genetic effects will be lost due to recombination. Akdemir and Jannink argue that the breeder can take advantage of epistatic marker effects in regions of low recombination. To this end, they develop and illustrate the use of multiple kernel models for genomic prediction and association. The models provide good predictive performance along with useful explanatory information.

An enhanced gene targeting toolkit for *Drosophila*: Golic+, pp. 683–694

Hui-Min Chen, Yaling Huang, Barret D. Pfeiffer, Xiaohao Yao, and Tzumin Lee

Chen *et al.* report high-efficiency CRISPR-based gene targeting in *Drosophila* cystoblasts, which each develop into a single female germ cell and therefore guarantee independent targeting events per individual offspring. Compared to direct embryo injection, the new system allows efficient re-trials of large inserts or difficult loci. The system includes a repressor-based lethality selection to facilitate screening and can be readily scaled up for high-throughput genome editing.

The ABCs of eye color in *Tribolium castaneum*: orthologs of the *Drosophila white*, *scarlet*, and *brown* genes, pp. 749–759

Nathaniel Grubbs, Sue Haas, Richard W. Beeman, and Marcé D. Lorenzen

The ABC transporters White, Scarlet, and Brown are critical for proper eye pigmentation in *Drosophila*. Grubbs *et al.* cloned the three orthologous genes from the beetle *Tribolium castaneum*, characterized the promoters of all three genes, and analyzed eye-color mutants to identify lesions that will provide a new tool for analysis and genetic transformation. They also consider how these genes and eye pigmentation have changed during insect evolution.

Molecular proxies for climate maladaptation in a long-lived tree (*Pinus pinaster* Aiton, Pinaceae), pp. 793–807

Juan-Pablo Jaramillo-Correa, Isabel Rodríguez-Quilón, Delphine Grivet, Camille Lepoittevin, Federico Sebastiani, Myriam Heuertz, Pauline H. Garnier-Géré, Ricardo Alía, Christophe Plomion, Giovanni G. Vendramin, Santiago C. González-Martínez

Better understanding adaptive genetic responses to climate change will help predict range shifts and assist management of biological diversity. Jaramillo-Correa *et al.* identified 18 SNPs associated with climate in maritime pine (*Pinus pinaster* Aiton), an outcrossing, long-lived, keystone forest tree. Alleles at the candidate loci were successfully used to predict maladaptation to climate in a common garden under hot and dry climate conditions. Populations with low frequencies of locally advantageous alleles showed increased mortality, suggesting that distinct gene pools will decline to different degrees.

The mammalian cervical vertebrae blueprint depends on the *T* (*brachyury*) gene, pp. 873–883

Andreas Kromik, Reiner Ulrich, Marian Kusenda, Andrea Tipold, Veronika M. Stein, Maren Hellige, Peter Dziallas, Frieder Hadlich, Philipp Widmann, Tom Goldammer, Wolfgang Baumgärtner, Jürgen Rehage, Dierck Segelke, Rosemarie Weikard, and Christa Kühn

Although the vertebral column is highly diversified between vertebrates, the number of cervical vertebrae within mammals has been fixed for more than 200 million years. Kromik *et al.* report the first known mammalian spontaneous mutation that changes the fundamental seven-cervical-vertebrae blueprint. The mutation alters the *T/brachyury* gene, which plays a role in neuro-skeletal development. These data show the T protein is directly involved in the maintenance of the mammalian seven-cervical-vertebrae blueprint.

Unusual regulation of splicing of the cholinergic locus in *Caenorhabditis elegans*, pp. 729–737

Eleanor A. Mathews, Gregory P. Mullen, Jacob R. Manjarrez, and James B. Rand

The Cholinergic Gene Locus (CGL) encodes two genes required for release of acetylcholine; one gene is nested within the other, and the two gene products arise by alternative splicing. Mathews *et al.* report a novel form of splicing regulation in the *C. elegans* CGL mediated by two sets of complementary sequence elements. These sequence elements are able to form stem-loop structures in the pre-mRNA, which may favor specific alternative splice forms. The authors find comparable CGL elements in most animal phyla genomes, suggesting the mechanism is conserved.

Assessing gene-environment interactions for common and rare variants with binary traits using gene-trait similarity regression, pp. 695–710

Guolin Zhao, Rachel Marceau, Daowen Zhang, and Jung-Ying Tzeng

Accounting for *G×E* interactions can improve complex trait association studies and our understanding of genetic heterogeneity. However, *G×E* interactions can be difficult to find, as they require much larger samples and are sensitive to the misspecification of main effects model. These issues are exacerbated when working with binary phenotypes and rare variants. Zhao *et al.* present a powerful, robust method to evaluate *G×E* for common or rare variants with binary traits.

This Month's Perspectives

Fruit flies in biomedical research, pp. 639–653

Michael F. Wangler, Shinya Yamamoto, and Hugo J. Bellen

NIH and NSF funding for *Drosophila* research has declined in recent years, despite the model's numerous significant contributions to biomedical science. Wangler *et al.* highlight the strengths of *Drosophila* and argue the field will continue to reveal important biological insights that can be translated to human disease research. They argue that collaboration between *Drosophila* geneticists, human geneticists, bioinformaticians, and clinicians will improve the functional annotation of both genomes, providing important data for the diagnosis, study, and treatment of genetic disorders.

This Month in the American Journal of Human Genetics

Characterization of large structural genetic mosaicism in human autosomes, Am. J. Hum. Genet. 96(3)

Mitchell J. Machiela, Weiyin Zhou, Joshua N. Sampson, Michael C. Dean, Kevin B. Jacobs, et al.

Understanding the frequency of somatic mosaicism in healthy populations has many implications for the management of disease and genetic counseling. In this study, Machiela *et al.* use both a recently genotyped cohort of almost 25,000 individuals as well as a combined meta-analysis of 127,000 individuals to identify the frequency of somatic mosaicism of large structural autosomal alterations. Across these groups, they observe large autosomal changes in approximately 0.7% of individuals. There appeared to be higher levels of mosaicism in men and lower levels of mosaicism in African Americans. Additionally, an increase in mosaicism was observed in a subset of individuals that were re-analyzed six years later.