Mei-P26 mediates tissue-specific responses to the Brat tumor suppressor and the dMyc proto-oncogene in *Drosophila*, pp. 249–258

Ana Ferreira, Laura Boulan, Lidia Perez, and Marco Milian

TRIM-NHL proteins are a family of translational regulators that control cell growth, proliferation and differentiation during development. In *Drosophila*, loss-of-function of two TRIM-NHL proteins, Brat and Mei-P26, leads to tumorous phenotypes in neural and germline stem cell lineages, respectively. These phenotypes are caused, at least in part, by the expression of dMyc. Here, the authors show that in the wing epithelium, dMyc overexpression or Brat depletion do not cause tissue overgrowth because Mei-P26 is up-regulated. Thus, Brat and Mei-P26 act as context-dependent tumor suppressors.

A defined Zebrafish line for high-throughput genetics and genomics: NHGRI-1, pp. 167–170

Matthew C. LaFave, Gaurav K. Varshney, Meghana Vemulpalli, James C. Mullikin, and Shawn M. Burgess

In zebrafish, substantial genetic variation between strains complicates the use of CRISPR, morpholinos, RNAseq, and other methods that depend on precise knowledge of the target sequence. To facilitate such molecular studies in the absence of robust inbred lines, the authors generated a healthy zebrafish strain with a completely defined background, NHGRI-1. The founder parents were sequenced to a depth of approximately 50x to identify the portions of the genome that match the reference sequence, along with identifying most of the variants. The authors also developed several browser tools to make the strain useful to the entire research community.

Genome-wide linkage-disequilibrium profiles from single individuals, pp. 269–281

Michael Lynch, Sen Xu, Takahiro Maruki, Xiaqian Jiang, Peter Pfaffelhuber, and Bernhard Haushold

In this work, the authors show that the genome of a single diploid individual can yield highly informative patterns of linkage disequilibrium (LD) via the spatial distribution of heterozygous sites. The new parameter level related to conventional population-level measures of LD, but is agnostic to allele frequencies and hence likely less prone to outlier artifacts. Application of the method to several vertebrate species reveals that more than 80% of recombination events are resolved by gene- conversion-like processes unaccompanied by crossovers. As a consequence, the recombination rate between sites is nonlinearly related to distance.

Influence of gene interaction on complex trait variation with multi-locus models, pp. 355–367

Aiko Miki-Tanila and William G. Hill

Considerable controversy surrounds the importance of epistasis and epistatic variance for complex traits. For example, genetic interactions may be important in understanding the genetic architecture of human disease, but that does not imply that interacting loci will contribute much epistatic variance. Here, the authors consider the potential magnitude of epistatic variance using a range of models. They conclude that theoretical predictions are concordant with experimental observations of low epistatic variance, suggesting it is not a likely source of missing heritability or a major influence on selection responses.

Fine-mapping nicotine resistance loci in *Drosophila* using a multiparent advanced generation intercross population, pp. 45–57

Tara N. Marriage, Elizabeth G. King, Anthony D. Long, and Stuart J. Macdonald

Nicotine is a potent herbivory-defense chemical and a widely used addictive drug. Here, the authors identify *Drosophila* loci underlying variation in nicotine resistance using a large panel of inbred lines from a recombinant multiparental population. Together, the mapped QTL contribute almost 70% of variation for the trait, and one region alone explains around half of the heritability. Gene expression implicates three strong candidate causal genes, all of which are members of established families of detoxification enzymes. It is likely these genes harbor regulatory polymorphisms responsible for much of the variation in nicotine resistance in *Drosophila*.

Asymmetric neuroblast divisions producing apoptotic cells require the cytohesin GRP-1 in *Caenorhabditis elegans*, pp. 229–247

Jerome Taillere, Shaun Cordes, Aakanksha Singhvi, Karla Takavera, and Gian Garriga

Although much is known about how apoptosis is executed, less is known about how a given cell makes the decision to live or die. In *C. elegans*, this decision is tied to asymmetric cell divisions that produce one small dying cell and one large surviving sister. Here, the authors identified a regulator of cell death by screening for mutants with extra neurons of a type normally generated by such asymmetric divisions. The authors showed that the regulator, cytohesin GRP-1, controls Arf GTPase activity at the cell surface to generate daughter cell size asymmetry.

Identification of a novel gene for diabetic traits in rats, mice and humans, pp. 17–29


Multiparental populations allow fine mapping of QTL to within a few Mb. Using expression and sequence analysis of lines from a multiparental rat population, the authors identified a gene, Tpcn2, that is involved in regulating glucose and insulin levels. This role is supported by studies of Tpcn2 knockout mice and associations between human Tpcn2 variants and fasting insulin levels. These findings suggest that Tpcn2 is a likely causal gene that may play a role in diabetes.

Genetic diversity in introduced populations with an Allee effect, pp. 299–310

Meike J. Wittmann, Wilfried Gabriel, and Dirk Metzler

Newly founded populations are often so small that individuals have difficulty finding partners for mating or cooperation. At the population level, this can lead to reduced population growth and higher extinction probabilities, a phenomenon called the Allee effect. Here, the authors show that this effect can either increase or decrease genetic diversity depending on the average founder population size. These results are important for understanding the evolutionary potential of newly founded populations and for inference of demographic parameters from genetic data.

This Month in the American Journal of Human Genetics

**Neu-Laxova syndrome is a heterogeneous metabolic disorder caused by defects in enzymes of the L-Serine biosynthesis pathway, Am. J. Hum. Genet. 95(3)**


Neu-Laxova syndrome (NLS) is a rare, multisystemic disorder that causes prenatal or early postnatal lethality. The genetic causes of the disease remained unknown for some time, but the recent identification of homozygous *PHGDH* mutations in affected individuals pointed to defects in serine metabolism as a cause. Now, Acuna-Hidalgo et al. confirm and expand this finding, identifying mutations in all three enzymes involved in *de novo* serine biosynthesis. Less severe mutations in these genes cause a much milder spectrum of phenotypes, and no link between NLS and these disorders had been suspected based on phenotype alone. Thus, this work highlights the power of sequencing to uncover unexpected allelic disorders.