

ISSUE HIGHLIGHTS

Mek1 suppression of meiotic double-strand break repair is specific to sister chromatids, chromosome autonomous and independent of Rec8 cohesin complexes, pp. 771–782

Tracy L. Callender and Nancy M. Hollingsworth

Mistakes in chromosome segregation during meiosis, which can lead to infertility and birth defects, may result if homologs are not physically connected by crossovers. The Mek1 protein kinase acts to promote recombination between homologs in yeast by suppressing recombination between sister chromatids. This article describes how Mek1 acts to regulate recombination during meiosis. It is important to understand the constraints on Mek1 function because that may facilitate identification of Mek1 substrates involved in suppressing intersister chromatid recombination.

Genome-wide association studies and the problem of relatedness among advanced intercross lines and other highly recombinant populations, pp. 1033–1044

Riyan Cheng, Jackie E. Lim, Kaitlin E. Samocha, Greta Sokoloff, Mark Abney, Andrew D. Skol and Abraham A. Palmer

Studies of model organisms offer the potential to elucidate the genetic architecture of complex traits, but few studies have been able to map the critical loci accurately enough to implicate specific genes. These investigators studied mice from a 34-generation advanced intercross line (AIL) and implemented a statistical procedure that tests the association between genotypes and phenotypes and accounts for the complex familial relationships. Using this approach, they are able to implicate small genetic intervals while retaining many of the key advantages of model organisms.

Specific α - and β -tubulin isotypes optimize the functions of sensory cilia in *Caenorhabditis elegans*, pp. 883–896

Daryl D. Hurd, Renee M. Miller, Lizbeth Núñez and Douglas S. Portman

Primary cilia serve as cellular signaling centers that detect multiple extracellular cues. All primary cilia are built around a microtubule axoneme. Do specific tubulin isoforms specialize the function of this axoneme? By studying the primary cilia of the dendrites of *Caenorhabditis elegans* sensory neurons, the authors of this article find that tubulins are more than generic building blocks. When cilium-specific tubulin genes are mutated, cilia can form, but their morphology, makeup, and mission are often upset. Thus, specialized tubulins build axonemes that are optimized for the needs of primary cilia.

Fine mapping in 94 inbred mouse strains using a high-density haplotype resource, pp. 1081–1095

Andrew Kirby, Hyun Min Kang, Claire M. Wade, Chris Cotsapas, Emrah Kostem, Buhm Han, Nick Furlotte, Eun Yong Kang, Manuel Rivas, Molly A. Bogue, Kelly A. Frazer, Frank M. Johnson, Erica J. Beilharz, David R. Cox, Eleazar Eskin and Mark J. Daly

The genetics of phenotypic variation in inbred mice has long been a primary weapon in the medical research arsenal. Understanding the relationship between phenotypic variation and genetic variation in the inbred mouse strains requires understanding the genetic relationships between strains in each region of the genome. This article reports a dense map of genetic variation gleaned from 94 mouse strains containing more than 10 million genotypes over 121,433 single nucleotide

polymorphisms. This resource should facilitate effective designs of both human and mouse studies for dissecting the genetic basis of complex traits.

Genotype-by-diet interactions drive metabolic phenotype variation in *Drosophila melanogaster*, pp. 1009–1019

Laura K. Reed, Stephanie Williams, Mastafa Springston, Julie Brown, Kenda Freeman, Christie E. DesRoches, Marla B. Sokolowski and Greg Gibson

Metabolic syndrome is a complex disease that is influenced by interactions between genes and the environment. Its prevalence is increasing, and this might be due to a global shift in the population mean of underlying genetic variants or to increased variance underlying endophenotypes (such as body weight) in response to changing lifestyles. Using inbred lines of *Drosophila melanogaster* raised with different diets, the authors of this article show that population level genotype-by-diet interactions are pervasive and result in changes in both the population mean and the variance of metabolic phenotypes.

The rate and spectrum of spontaneous mutations in a plant RNA virus, pp. 983–989

Nicolas Tromas and Santiago F. Elena

RNA viruses are well known for their tremendous evolutionary potential. The lack of a proofreading ability of their RNA replicases contributes to this evolvability. These authors sought to estimate the mutation rate of a plant RNA virus and characterize the spectrum of spontaneous mutations. They find that the mutation rate is lower than that of animal RNA viruses.

Expression quantitative trait loci: Replication, tissue- and sex-specificity in mice, pp. 1059–1068

Atila van Nas, Leslie Ingram-Drake, Janet S. Sinsheimer, Sanna S. Wang, Eric E. Schadt, Thomas Drake and Aldons J. Lusis

Mapping genes that control transcript abundance has proven useful for modeling networks underlying complex traits such as obesity and diabetes. However, neither the reproducibility of these expression quantitative trait loci (eQTL) nor their tissue- and sex-specificity have been thoroughly evaluated. This article reports the analysis of these characteristics in four tissues from two large genetic crosses in mice. The conclusion is that local eQTL—the ones near the gene encoding the transcript and likely acting in *cis*—are highly reproducible, but distal, *trans*-acting eQTL are only modestly reproducible.

This Month in Genetics Research

Spoiling the whole bunch: Quality control to preserve the integrity of high throughput genotyping, *Am. J. Hum. Genet.* 87(1): DOI: 10.1016/j.ajhg.2010.06.005.

Anna Pluzhnikov, Jennifer E. Below, Anuar Konkashbaev, Anna Tikhomirov, Emily Kistner-Griffin, Cheryl A. Roe, Dan L. Nicolae and Nancy J. Cox

Successful genome-wide association studies (GWASs) require navigating the shoals of undetected genotyping errors, which will likely loom larger as investigators tap existing public databases for GWAS control samples. This article describes how to deal with this problem by utilizing additional sources of information, including raw signal intensity data.