A novel ribosomopathy caused by dysfunction of RPL10 disrupts neurodevelopment and causes X-Linked microcephaly in humans, pp. 723–733
Susan S. Brooks, Alissa L. Wall, Christelle Golsio, David W. Reid, Amalia Kondylis, Jason R. Wilier, Christina Botti, Christopher V. Nicchitta, Nicholas E. Katsanis, and Erica E. Davis

This article shows that an X-linked microcephaly syndrome is caused by a novel missense mutation causing loss-of-function of the 60S ribosomal protein L10 (RPL10). In a multigenerational pedigree, the mutation segregated with the disease in an X-linked fashion, and carrier females showed skewed X-inactivation. In zebrafish models, rpl10 suppression decreased head size, accompanied by reduced bulk translation and increased apoptosis in the brain.

Sporadic distribution of prion-forming ability of Sup35p from yeasts and fungi, pp. 605–616

[PSI+] is a prion of Sup35p, a translation termination factor in yeasts and fungi from certain other yeasts can also form [PSI+], which has been interpreted as evidence that the prion-forming ability of Sup35p is conserved, and therefore adaptive. Here, the authors surveyed Sup35p homologs from eleven yeast and fungal species to test whether they form prions in S. cerevisiae. Only four species had Sup35p that forms a [PSI+] prion in S. cerevisiae, suggesting this ability is not widely conserved.

A genome-wide map of mitochondrial DNA recombination in yeast, pp. 755–771
Emilie S. Fritsch, Christophe D. Chabbert, Bernd Klaus, and Lars M. Steinmetz

Mitochondrial DNA recombination is widespread in plants, fungi, protists, and invertebrates. This article describes the first genome-wide mitochondrial recombination map, which was generated using wild-type and mutant yeast strains. These maps will be critical for future mechanistic studies of mitochondrial recombination and genome maintenance.

Identifying causal variants at loci with multiple signals of association, pp. 497–508
Farhad Hormozdiari, Emrah Kostem, Eun Yong Kang, Bogdan Pasaniuc, and Eleazar Eskin

Genome-wide association studies have identified thousands of risk loci for complex traits, but only a handful of causal variants have been found. One drawback to existing methods for predicting which variants are causal is the assumption that only a single such variant exists for each risk locus. In this work, the authors propose an alternative framework that outperforms other methods by allowing for an arbitrary number of causal variants.

Shared genetic pathways contribute to the tolerance of endogenous and low-dose exogenous DNA damage in yeast, pp. 519–530
Kevin Lehner and Sue Jinks-Robertson

Cells can repair damage in double-stranded DNA, but in single-stranded contexts, such damage must be temporarily bypassed. Here, the authors use yeast to examine the contributions of genetic pathways to bypassing low-dose DNA damage from either exogenous damaging agents or spontaneous mutations. The response to these different modes of DNA damage is remarkably similar, showing that low-dose exogenous damage can act as a proxy for the study of endogenous DNA damage bypass.

Genome-wide regression and prediction with the BGLR statistical package, pp. 483–495
Paulino Pérez and Gustavo de los Campos

Incorporating high-dimensional genomic data into statistical models poses important challenges, some of which can be confronted using Bayesian methods. Here, the authors present the R package BGLR, which integrates, in a unified Bayesian framework, various parametric and semi-parametric regression procedures, including shrinkage and variable selection methods. The software supports quantitative (including censored) and categorical outcomes.

Competence for chemical reprogramming of sexual fate correlates with an intersexual molecular signature in Caenorhabditis elegans, pp. 561–575
Elena R Sorokin, Audrey E Gasch, and Judith Kimble

This work explores how a chemical can reprogram sexual fate in adults by investigating small-molecule-induced oogenesis in C. elegans XX “sperm-only” mutants. The authors find that mutants competent for this type of chemical reprogramming have oogenesis-related RNA and protein signatures in the absence of drugs. This intersexual molecular signature may be diagnostic of an intermediate state that poises the adult tissue to switch sexual state in response to environmental cues.

Adaptive fixation in two-locus models of stabilizing selection and genetic drift, pp. 685–697
Andreas Wollstein and Wolfgang Stephan

To what extent do quantitative genetic models of polygenic traits predict selective sweeps? Here, the authors investigate the two-locus model of stabilizing selection to predict the fate of alleles under polygenic adaptation. They found a substantial number of trajectories may lead to fixation if the initial allele frequencies are drawn from a standard neutral frequency spectrum. However, the number of adaptive fixations may be strongly reduced if the population is pre-adapted when it undergoes environmental change.

This Month’s Perspective
Ellis Englesberg and the discovery of positive control in gene regulation, pp. 455–460
Steven Hahn

Ellis Englesberg proposed in 1965 that the bacterial regulatory gene araC was an “activator gene” required for positive control of the ara operon. This challenged the widely held belief in a universal mechanism of negative regulation proposed by Jacob and Monod. For years, Englesberg’s model met with deep skepticism. Despite frustration with the complex ad hoc explanations used to challenge his model, Englesberg persisted until the evidence for positive control in ara and other systems became overwhelming. Englesberg’s pioneering work enriched the original operon model and had a lasting impact in opening new and exciting ways of thinking about transcriptional regulation.

This Month in the American Journal of Human Genetics
Parent of origin, mosaicism, and recurrence risk: probabilistic modeling explains the broken symmetry of transmission genetics, Am. J. Hum. Genet. 95(4): 345–359
Ian M. Campbell, Jonathan R. Stewart, Regis A. James, James R. Lupski, Paweł Stankiewicz, Peter Oflofson, and Chad A. Shaw

Although most de novo mutations affect only one child per generation, the possibility of the mutation being present in the parental germline makes recurrence possible. In this article, Campbell et al. develop a mathematical model for predicting recurrence risk for apparently de novo and somatic mosaic mutations. The authors have developed an online tool, the Recurrence Risk Calculator (http://www.recurrencerisk.org), that provides a user-friendly interface to explore how changes in parameters of their model and parent can affect recurrence estimates. The authors’ work is relevant for researchers who aim to better understand transmission genetics as well as for affected families and their genetic counselors.