Multiple levels of redundant processes inhibit Caenorhabditis elegans vulval cell fates, pp. 2001–2012
Erik C. Andersen, Adam M. Saffer and H. Robert Horvitz
Many mutations cause obvious abnormalities only when combined with other mutations, often because the genes are redundant. The synthetic multivelva (synMuv) genes of Caenorhabditis elegans fall into several classes that redundantly inhibit vulval cell fates. Animals with mutations in any two classes have a multivelva phenotype, whereas animals with one or more mutations of the same class develop normally. But with sensitive assays, these authors can show that mutations in most synMuv genes within a single synMuv class enhance each other. In the few cases where no enhancement was observed, the authors suggest that the protein products of those genes function together in vivo and in at least some cases interact physically. The approach of genetic enhancement can be applied more broadly to identify potential protein complexes as well as redundant processes or pathways.

Bayesian quantitative trait loci mapping for multiple traits, pp. 2275–2289
Sanmprit Banerjee, Brian S. Yandell and Nengjun Yi
There is a lack of comprehensive genomic approaches to search strategies to detect multiple pleiotropic quantitative trait loci (QTL). The composite model approach is extended to jointly analyze multiple correlated traits. Multiple traits are modeled using seemingly unrelated regression models (QTL SUR models) that detect either the same or different QTL for each pair of traits. The QTL SUR models include the traditional multivariate model and single trait-by-trait model as special cases. These authors develop and benchmark computationally efficient Markov chain Monte Carlo algorithms for performing joint analysis.

Histone H3 K56 hyperacetylation perturbs replisomes and causes DNA damage, pp. 1769–1784
Ivana Celic, Alain Verreault and Jef D. Boeke
Why is deacetylation of histone H3 K56, regulated by the sirtuins Hst3p and Hst4p, critical for maintenance of genome stability? These authors find that hyperacetylation of H3 K56 leads to hallmarks of spontaneous DNA damage, such as activation of the checkpoint kinase Rad53p and upregulation of DNA-damage inducible genes, and enhances the effects of mutations that cripple genes involved in DNA replication and DNA double-strand break repair. The effects of hyperacetylation are suppressed by overexpression of the PCNA clamp loader Rfc1p and by inactivation of alternative clamp loaders.

Defective break-induced replication leads to half-crossovers in Saccharomyces cerevisiae, pp. 1845–1860
Angela Deem, Krista Barker, Kelly VanHulle, Brandon Downing, Alexandra Vayl and Anna Malkova
Break-induced replication (BIR) has been implicated in the restart of collapsed replication forks as well as in various chromosomal instabilities. The authors investigate the genetic control of BIR using a yeast experimental system. They find that a deletion of POL32, which encodes a nonessential subunit of polymerase δ, significantly reduces the efficiency of BIR and leads to the formation of half-crossovers. The authors propose that these half-crossovers resulted from aberrant processing of BIR intermediates and that they are analogous to nonreciprocal translocations (NRTs) described in mammalian tumor cells.

A complex genetic basis to X-linked hybrid male sterility between two species of house mice, pp. 2213–2228
Jeffrey M. Good, Matthew D. Dean and Michael W. Nachman
The X chromosome often plays a central role in speciation, but few studies have examined the early stages of reproductive isolation. These authors use a reciprocal introgression experiment to evaluate X-linked hybrid male sterility between two species of mice. Introgression of the Mus musculus X chromosome into M. domesticus produced male sterility involving at least four X-linked factors. By contrast, introgression of the M. domesticus X chromosome did not cause sterility. These results reveal complex and asymmetric genetic bias to hybrid male sterility during the early stages of speciation in mice.

Genomewide screen for negative regulators of sirtuin activity in Saccharomyces cerevisiae reveals 40 loci and links to metabolism, pp. 1933–1944
Ryan M. Raisner and Hitten D. Madhani
Sirtuins are conserved proteins implicated in myriad key processes including gene control, aging, cell survival, metabolism, and DNA repair. This article describes a genomewide screen for factors that negatively regulate sirtuin activity in yeast that identified 40 loci, including 20 that have not been previously described to regulate sirtuin. These include factors that control histone acetylation, mRNA metabolism, as well as proteins (such as the PAS kinase Psk2p) linked to general metabolism.

The relationship between homozgyosity and the frequency of the most frequent allele, pp. 2027–2036
Noah A. Rosenberg and Mattias Jakobsson
This article describes the mathematical connection between two of the most basic properties of a polymorphic locus—its homozgyosity and the frequency of its most frequent allele. The close relationship between these two quantities, illustrated with human data, may help guide intuition about population-genetic results involving these quantities. Notably, it provides a basis for understanding the performance of the Hudson haplotype test of neutrality, the haplotype diversity test, and the use of extended haplotype homozgyosity in identifying the signature of partial selective sweeps.

The Arp2/3 activators WAVE and WASP have distinct genetic interactions with Rac GTPases in Caenorhabditis elegans axon guidance, pp. 1957–1971
M. Afaf Shakir, Ke Jiang, Eric C. Struckhoff, Rafael S. Demarco, Falshutrui B. Patel, Martha C. Soto and Erik A. Lundquist
This article defines the role of WASP, WAVE, and Rac in axon guidance. These proteins have been extensively studied in vitro; this article elucidates the roles these molecules play in developmental processes and reveals new and unpredicted interactions between WASP, WAVE, and Rac signaling in axon guidance.

Exchangeable models of complex inherited diseases, pp. 2253–2261
Montgomery Slatkin
The genetic architecture of fairly common diseases such as schizophrenia, with high twin concordance (30–50%) and recurrence risk (5–10%) but which lack strong SNP associations, continues to challenge geneticists. This article explores a class of models of the genetic basis of complex inherited disease and then uses these models to predict the disease prevalence and risk to relatives of affected individuals. For diseases with a prevalence of 1% and moderate twin concordance and recurrence risk, the models show that risk must increase rapidly with the number of disease-associated alleles to be consistent with the data.

Two new Y-linked genes in Drosophila melanogaster, pp. 2325–2327
Maria D. Vibranovski, Leonardo B. Koerich and A. Bernardo Carvalho
Heterochromatic regions of chromosomes are poorly annotated, mainly because their repetitive DNA makes the sequence difficult to assemble. So, the identification of genes in heterochromatin is cause to celebrate. This article describes two novel Y-linked genes in Drosophila melanogaster, raising the number of genes on this chromosome to 12. One of these genes may correspond to the long sought fertility factor kl-1.

Maternal phosphatase inhibitor-2 is required for proper chromosome segregation and mitotic synchrony during Drosophila embryogenesis, pp. 1823–1833
Weiping Wang, Claire Crommiller and David L. Brautigan
The inhibitor-2 protein, a regulator of protein phosphatase-1, is highly conserved among all eukaryotic species. It has been well characterized biochemically, but little is known about its in vivo function. These authors find that embryos derived from mothers without inhibitor-2 function have faulty chromosome segregation and lose mitotic synchrony in cleavage stage embryos. Thus, inhibitor-2 regulates chromosome segregation during early embryogenesis.

Molecular basis of sculptural tuning in the red- and green-sensitive (M/LWS) pigments in vertebrates, pp. 2037–2043
Shozo Yokoyama, Hui Yang and William T. Stamer
How do visual pigments achieve sensitivity to various wavelengths? Since the late 1980s, the mechanism of the spectral tuning of visual pigments has been studied using contemporary pigments. This article describes a genomewide screen for factors that negatively regulate sirtuin activity in yeast that identified 40 loci, including 20 that have not been previously described to regulate sirtuin. These include factors that control histone acetylation, mRNA metabolism, as well as proteins (such as the PAS kinase Psk2p) linked to general metabolism.