Discovery of mutations in *Saccharomyces cerevisiae* by pooled linkage analysis and whole-genome sequencing, pp. 1127–1137
Shanda R. Birkeland, Natsuko Jin, Alev Cagla Ozdemir, Robert H. Lyons, Jr., Lois S. Weisman and Thomas E. Wilson

Mutations can often be difficult or impossible to locate using standard genetic approaches, especially for those contributing to complex traits. Next-generation sequencing is rapidly changing how such mutations are identified. This article describes an experimental approach and computational platform for rapidly identifying a mutation of interest among the large excess of background alterations and polymorphisms invariably observed in a genome sequence.

The genetic basis for male × female interactions underlying variation in reproductive phenotypes of *Drosophila*, pp. 1355–1365
Clement Y. Chow, Mariana F. Wolfner and Andrew G. Clark

Interactions between males and females can determine the reproductive success of a mating pair. These investigators dissect the genetic architecture of interactions between the sexes in Drosophila and find significant interactions between the third and X chromosomes for several important reproductive phenotypes. This study has implications for evolution by showing how high levels of variation can be maintained and how genes of males and females are coevolving.

Phenotypic consequences of aneuploidy in *Arabidopsis thaliana*, pp. 1231–1245
Isabelle M. Henry, Brian P. Dilkes, Eric S. Miller, Diana Burkart-Waco and Luca Comai

Aneuploidy [extra copies of chromosome(s)] in humans is lethal or highly deleterious, but plants are more tolerant of aneuploidy. These investigators identify strong relationships between the number of copies of specific chromosomes and aneuploid phenotypes (symptoms) in the plant *Arabidopsis thaliana*. Interestingly, plants that no longer carry extra chromosome(s) still display irregular development, as if they have a memory of aneuploidy in their progenitors.

Exploiting natural variation in *Saccharomyces cerevisiae* to identify genes for increased ethanol resistance, pp. 1197–1205
Jeffrey A. Lewis, Isaac M. Elkon, Mick A. McGee, Alan J. Higbee and Audrey P. Gasch

*Saccharomyces cerevisiae* thrives in diverse climates around the globe, but strains from different niches often display unique phenotypes. These authors use natural variation in yeasts’s response to ethanol to identify genes required for ethanol tolerance. They phenotype 47 *S. cerevisiae* strains for their ability to acquire tolerance to a high level of ethanol after a mild ethanol pretreatment. They compare gene expression of several wild strains and identify genes whose expression is correlated with the ability to acquire ethanol tolerance. They identify new genes and processes not previously linked to ethanol tolerance, revealing new engineering targets for improved biofuel production.

The role of replication bypass pathways in dicentric chromosome formation in budding yeast, pp. 1161–1173
Andrew L. Paek, Hope Jones, Salma Kaochar and Ted Weinert

Errors during DNA replication often lead to chromosomal rearrangements. For example, when replication forks stall and switch to the wrong template, dicentric chromosomes result. These authors show that the post replication repair pathway prevents these switching events and that the lagging strand polymerase and associated proteins are likely involved in switching events.

General epistatic models of the risk of complex diseases, pp. 1467–1473
Yun S. Song, Fulton Wang and Montgomery Slatkin

SNPs associated with higher disease risk account for only a small fraction of the inherited risk of disease. One explanation for this “missing heritability” is that interactions among causative alleles conceal their true contribution to heritability. This article describes a theoretical study of this possibility and examines the extent to which gene interactions (epistasis) account for the missing heritability. The conclusion is that epistasis can substantially increase the heritability of disease risk, an effect that increases with the number of causative alleles. Hence, gene interactions may account for some of the missing heritability of complex diseases.

The rate of fitness-valley crossing in sexual populations, pp. 1389–1410
Daniel B. Weissman, Marcus W. Feldman and Daniel S. Fisher

How do populations acquire complex adaptations that require multiple mutations before providing a fitness benefit? This is one of the oldest problems in evolutionary theory. The authors investigate the dynamics of complex adaptation across a broad range of population parameters and find expressions for the rate of adaptation. They find that while frequent recombination can render complex adaptation effectively impossible, lower recombination rates can greatly increase the rate of complex adaptation relative to that in an asexual population.

Bulk segregation mapping of mutations in closely related strains of mice, pp. 1139–1146
Yu Xia, Sungyong Won, Xin Du, Pei Lin, Charles Ross, Diantha La Vine, Sean Wiltshire, Gabriel Leiva, Silvia M. Vidal, Belinda Whittle, Christopher C. Goodnow, James Koziol, Eva Marie Y. Moresco and Bruce Beutler

Mouse geneticists will be happy to read this article, which describes a genome-wide panel of DNA markers for mapping mutations in two popular, closely related inbred laboratory mouse strains. The authors use these markers to map two N-ethyl-N-nitrosourea (ENU)-induced mutations by bulk segregation analysis, a method that is more time- and cost-efficient than traditional mapping.