

Uncovering natural longevity alleles from intercrossed pools of aging fission yeast cells, pp. 733–744

David A. Ellis, Ville Mustonen, María Rodríguez-López, Charalampos Rallis, Michał Malecki, Daniel C. Jeffares, and Jürg Bähler

Chronological lifespan of non-dividing yeast cells is a quantitative trait that reflects cellular aging. By monitoring allele frequencies in aging segregant pools, Ellis *et al.* uncover regulatory variants in the 5'-untranslated regions of two genes that become enriched in old cells; allele replacements confirm that these variants contribute to longevity. These results raise the possibility that two cellular processes previously implicated in longevity-nutrient signaling and spermidine homeostasis-function together to modulate chronological lifespan, thus associating regulatory changes in two genes with the complex genetics of cellular aging.

From "the worm" to "the worms" and back again: the evolutionary developmental biology of nematodes, pp. 397–433

Eric S. Haag, David H. A. Fitch, and Marie Delattre

Biologists have long appreciated natural variation in the nematode phylum. The development of *Caenorhabditis elegans* as a model organism has provided a rich set of specific genetic and cellular mechanisms that have been subjected to comparative analysis at various phylogenetic scales. Here, Haag, Fitch, and Delattre chronicle important insights from comparative studies of nematode development. Despite the outwardly similar forms of nematodes, their development evolves rapidly due to adaptive changes that support the emergence of novel phenotypes and developmental systems that drift in the face of stabilizing selection.

Accurate genomic prediction of human height, pp. 477–497

Stephen Hsu, Louis Lello, Steven G. Avery, Laurent C. A. M. Tellier, Gustavo A. de los Campos, and Ana Ines Vazquez

Hsu *et al.* used advanced methods from machine learning to analyze almost half a million genomes. They produced, for the first time, accurate genomic predictors for complex traits such as height, bone density, and educational attainment. Height predictions are accurate to roughly one inch, meaning the height of an adult can be predicted from DNA alone to within an inch or so. These methods can also be used to estimate how much genomic data is required to "solve" other complex traits, such as disease risks; indeed, some results in this direction have already started to appear in the literature.

Inferring population structure and admixture proportions in low depth NGS data, pp. 719–731

Jonas Meisner and Anders Albrechtsen

Meisner and Albrechtsen present two methods for inferring population structure and admixture proportions in low depth next-generation sequencing (NGS). NGS methods provide large amounts of genetic data but are associated with statistical uncertainty, especially for low-depth sequencing data. The authors propose a method for inferring population structure through principal component analysis in an iterative heuristic approach of estimating individual allele frequencies and demonstrate improved accuracy in samples with low and variable sequencing depth for both simulated and real datasets.

Extraordinary genome instability and widespread chromosome rearrangements during vegetative growth, pp. 517–529

Mareike Möller, Michael Habig, Michael Freitag, and Eva H. Stukenbrock

The ability to rapidly adapt to changing environments is crucial for the success of pathogens infecting plants and animals. In some eukaryotic pathogens, rapid evolution can be mediated by genome rearrangements, which are often associated with sexual reproduction and meiotic recombination. However, many eukaryotic pathogens inhabit pronounced phases of asexual reproduction and use other mechanisms to generate genetic novelty. Here, Möller *et al.* demonstrate extreme rates of chromosome loss and genome rearrangement during mitotic propagation in the fungal pathogen *Zymoseptoria tritici*, indicating an important role for asexual propagation in generating genome variability.

Bimodal expression of the *salmonella* typhimurium *spv* operon, pp. 621–635

Ioannis Passaris, Alexander Cambré, Sander K. Govers, and Abram Aertsen

Passaris *et al.* show that the well-studied *spv* virulence operon of *Salmonella* Typhimurium displays a bimodal expression pattern. Using quantitative single-cell fluorescence microscopy, they demonstrate that this expression pattern originates in the bimodal expression of the SpvR activator and reveal that SpvA protein can impart negative feedback on *spvABCD* expression without affecting *spvR* expression. These results present new insights into the regulation of the *spv* operon, adding it to the growing list of virulence factors exhibiting marked expression heterogeneity in *S.* Typhimurium.

Geometry of the sample frequency spectrum and the perils of demographic inference, pp. 665–682

Zvi Rosen, Anand Bhaskar, Sebastien Roch, and Yun S. Song

Numerous studies in population genetics have been based on analyzing the sample frequency spectrum (SFS) summary statistic. Most SFS-based inference methods can display pathological behavior in optimization: some demographic model parameters can degenerate to 0 or diverge to infinity, and they show undesirable sensitivity to perturbations in the data. Rosen *et al.* investigate the geometry of the set of expected SFS, demonstrating that such a study can greatly facilitate understanding of the key challenges associated with SFS-based statistical inference.

This Month's Perspectives**How Mendel's interest in inheritance grew out of plant improvement, pp. 347–355**

Peter J. van Dijk, Franz J. Weissing, and T. H. Noel Ellis

Gregor Mendel's crossing experiments in pea are the foundation of classical genetics, but since the importance of his 1866 paper was not understood until long after his notebooks were burned, we know little about the background of his experiments. Van Dijk, Weissing, and Ellis report on the discovery of two 1861-newspaper articles that describe Mendel's activities as a plant breeder and horticulturist. Based on this new information, they argue that Mendel was initially concerned with applied problems but with time became more interested in fundamental biological questions about inheritance, fertilization, and natural hybridization.