

## ISSUE HIGHLIGHTS

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### Cohesin impedes heterochromatin assembly in fission yeast cells lacking Pds5, pp. 127–142

H. Diego Folco, Andrea McCue, Vanivilasini Balachandran, and Shiv I. S. Grewal

Heterochromatin enriched in histone H3 lysine 9 methylation (H3K9me) and HP1 proteins coats chromosomal domains throughout the eukaryotic genome to regulate gene expression and maintain genome stability. How heterochromatin assembly mechanisms are coordinated with other chromosomal processes remains unknown. Folco *et al.* find that loss of cohesin-associated Pds5 enriched throughout heterochromatin domains or the cohesin acetyltransferase Eso1 cause heterochromatic silencing defects. Although cohesin itself is not required for heterochromatin assembly, unacetylated cohesin in cells lacking Pds5 or Eso1 impedes heterochromatin maintenance mechanisms. These findings highlight how heterochromatin assembly can be hindered by a failure in the intricate coordination of fundamental chromosomal activities.

### Predicting phenotypic diversity from molecular and genetic data, pp. 297–312

Tom Harel, Naama Peshev-Yaloz, Eran Bacharach, and Irit Gat-Viks

Uncovering relationships between molecular and phenotypic diversity presents a substantial challenge. Harel *et al.* devised InPhenotype, a computational approach that combines gene-expression and genotype data to predict quantitative traits. The key advance of InPhenotype is its ability to exploit the contiguous nature of molecular data while modeling gene-locus interactions. Application of InPhenotype to synthetic data demonstrates its superiority over existing methods, while application of InPhenotype to mice and yeast data indicates the ability of InPhenotype to detect regulatory interactions between genomic loci and expressed genes that lead to phenotypic diversity.

### Centromere-proximal meiotic crossovers in *Drosophila melanogaster* are suppressed by both highly-repetitive heterochromatin and proximity to the centromere, pp. 113–126

Michaelyn Hartmann, James Umbanhowar, and Jeff Sekelsky

Crossovers are essential for the accurate segregation of chromosomes, but it is important that they be properly positioned. Crossovers must not occur too close to the centromere, but reduced crossover density may extend outward for some distance. Although first described by George Beadle in 1932, this “centromere effect” remains poorly understood. Hartmann, Umbanhowar, and Sekelsky show that centromere-proximal crossover suppression can be separated into two phenomena: complete suppression in highly-repetitive heterochromatin and a centromere effect in which suppression extends into less-repetitive heterochromatin and adjacent euchromatin with a strength that decreases with increasing distance from the centromere.

### The relationship between haplotype-based $F_{ST}$ and haplotype length, pp. 281–296

Rohan S. Mehta, Alison F. Feder, Simina M. Boca, and Noah A. Rosenberg

$F_{ST}$  is a statistic that is frequently used to analyze population structure. Recent work has shown that  $F_{ST}$  depends strongly on the underlying genetic diversity of a locus from which it is computed. Here, Mehta *et al.* consider  $F_{ST}$  computed from sequence-based haplotypes and analyze the effect of haplotype length on  $F_{ST}$ . The authors show that  $F_{ST}$  generally decreases with increasing haplotype length. Using data from the Human Genome Diversity Panel, they find a close correspondence between their theoretical results and observed values of haplotype-based  $F_{ST}$ . They conclude that haplotype length should be considered when interpreting  $F_{ST}$  calculated on haplotypic data.

### Insights into the role of P-bodies and stress granules in protein quality control, pp. 251–266

Regina Nostramo, Siyuan Xing, Bo Zhang, and Paul K. Herman

Nostramo *et al.* identify a potential role for two novel RNA-protein granules, the P-body and stress granule, in the maintenance of normal protein homeostasis. These cytoplasmic granules are members of an ever-growing family of membraneless organelles in eukaryotic cells. These cytoplasmic structures are evolutionarily conserved and have been implicated in the pathology of a number of human diseases associated with defects in protein quality control. These so-called proteinopathies include neurodegenerative disorders like amyotrophic lateral sclerosis. Thus, the results here may provide valuable insight into the role these granules play in the development of these human conditions.

### Plasma membrane integrity during cell-cell fusion and in response to pore-forming drugs is promoted by the penta-EF-hand protein PEF1 in *Neurospora crassa*, pp. 195–212

Marcel René Schumann, Ulrike Brandt, Christian Adis, Lisa Hartung, and André Fleißner

In this study, Schumann *et al.* identify the penta-EF-hand protein PEF1 of the genetic model fungus *Neurospora crassa* as part of the cellular response to different types of membrane injury. By combining molecular genetics, mutant analysis, and fluorescence live cell imaging, the authors show that PEF1 rapidly accumulates at the sites of injury in a  $\text{Ca}^{2+}$  dependent manner and that the lack of PEF1 results in an increased sensitivity against membrane rupture and pore-forming drugs. They propose that PEF1 is part of a membrane repair mechanisms, and that in fungi, membrane repair constitutes an additional line of defense against membrane-targeting drugs.

### Minimal effects of proto-Y chromosomes on house fly gene expression in spite of evidence that selection maintains stable polygenic sex determination, pp. 313–328

Jae Hak Son, Tea Kohlbrenner, Svenia Heinze, Leo Beukeboom, Daniel Bopp, and Richard P. Meisel

Sex determination pathways evolve fast and can even be variable within species. Son *et al.* used the house fly as a model to study the evolution of sex determination because it has a male determining gene on multiple different young Y chromosomes. They characterized the effects of these proto-Y chromosomes on gene expression. Despite evidence that selection maintains the different house fly proto-Y chromosomes, the authors determined that they have minimal phenotypic effects. Amongst those effects, they found some evidence that sex-specific selection acts on the proto-Y chromosomes, which is consistent with population genetic predictions.

### Hybrid decay: a transgenerational epigenetic decline in vigor and viability triggered in backcross populations of teosinte with maize, pp. 143–160

Wei Xue, Sarah N. Anderson, Xufeng Wang, Liyan Yang, Peter A. Crisp, Qing Li, Jaclyn Noshay, Patrice S. Albert, James A. Birchler, Paul Bilinski, Michelle C. Stitzer, Jeffrey Ross-Ibarra, Sherry Flint-Garcia, Xuemei Chen, Nathan M. Springer, and John F. Doebley

Xue *et al.* describe a phenomenon in maize and its nearest wild relative, teosinte, by which backcross progeny of a specific teosinte and maize exhibit a sickly whole-plant phenotype involving changes in morphology, vigor, and viability. The authors characterized the sickly backcross plants and normal control plants by multiple assays including mRNA expression, sRNA expression, genome-wide methylation patterns, karyotype, and changes in genome content. Diverse sequences (some with homology to transposable elements) are increased in copy number and expression, and there is elevated abundance of sRNAs with homology to these sequences. The authors call the phenomenon “hybrid decay” and discuss potential underlying mechanisms.