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The chromatin remodeler Isw1 prevents CAG repeat expansions during transcription in *Saccharomyces cerevisiae*, pp. 963–976

Melissa R. Koch, Nealia C. M. House, Casey M. Cosetta, Robyn M. Jong, Christelle G. Salomon, Cailin E. Joyce, Elliot A. Philips, Xiaofeng A. Su, and Catherine H. Freudenreich

CAG/CTG trinucleotide repeat expansions cause several degenerative neurological and muscular diseases. Koch *et al*. show that the chromatin remodeling protein Isw1 prevents CAG expansions in budding yeast. They propose that Isw1 is important for resetting chromatin structure after transcription, thus preventing the formation of DNA structures that induce inappropriate excision repair. Their results suggest a new function for ISWI chromatin remodeling activity in maintaining chromatin structure during transcription to limit CAG repeat expansions.

The modERN resource: genome-wide binding profiles for hundreds of *Drosophila* and *Caenorhabditis elegans* transcription factors, pp. 937–949

Michelle M. Kudron, Alec Victorsen, Louis Gevirtzman, LaDeana W. Hillier, William W. Fisher, Dionne Vafeados, Matt Kirkey, Ann S. Hammonds, Jeffery Gersch, Haneen Ammouri, Martha L. Wall, Jennifer Moran, David Steffen, Matt Szynkarek, Samantha Seabrook-Sturgis, Nader Jameel, Madhura Kadaba, Jaeda Patton, Robert Terrell, Mitch Corson, Timothy J. Durham, Soo Park, Swapna Samanta, Mei Han, Jinrui Xu, Koon-Kiu Yan, Susan E. Celniker, Kevin P. White, Lijia Ma, Mark Gerstein, Valerie Reinke, and Robert H. Waterston

The model organism Encylopedia of Regulatory Elements (modERN) project was designed to generate genome-wide binding profiles for the majority of transcription factors in *Drosophila* and *Caenorhabditis elegans*. Here, Kudron and Victorsen *et al*. report the *in vivo* binding sites for hundreds of such transcription factors. This mapping of transcription factor activity reveals conserved and specialized developmental and homeostatic regulatory networks that will be broadly useful to the community.

The hidden genomic and transcriptomic plasticity of giant marker chromosomes in cancer, pp. 951–961

Gemma Macchia, Marco Severgnini, Stefania Purgato, Doron Tolomeo, Hilen Casciaro, Ingrid Cifola, Alberto L'Abbate, Anna Loverro, Orazio Palumbo, Massimo Carella, Laurence Bianchini, Giovanni Perini, Gianluca De Bellis, Fredrik Mertens, Mariano Rocchi, and Clelia Tiziana Storlazzi

Neocentromeres contribute to cancer progression by mitotically stabilizing acentric chromosomes containing amplified oncogenes. Macchia *et al*. show that neocentromeres on giant chromosomes from cancer samples are formed from complex patchworks of multiple short amplified sequences. These expand during tumor progression, likely providing a selective advantage to cancer cells. The authors also report extensive neocentromere "sliding" giving rise to closely mapping epialleles. The results shed light on how cancer evolution is influenced by the extraordinary complexity and plasticity of neocentromeres.

Estimating barriers to gene flow from distorted isolation-by-distance patterns, pp. 1231–1245

Harald Ringbauer, Alexander Kolesnikov, David L. Field, and Nicholas H. Barton

Ringbauer *et al*. introduce a novel method to estimate barriers to gene flow in a two-dimensional population. Their inference scheme utilizes geographically localized allele frequency fluctuations: a classical isolation-by-distance signal. The strength of these local fluctuations increases on average next to a barrier, and there is less correlation across it. The authors use a framework of diffusion of ancestral lineages to model this effect and provide an efficient numerical implementation to fit their results to geo-referenced biallelic SNP data. This inference scheme can robustly estimate strong barriers to gene flow, as tests on simulated data confirm.

Impact of homologous recombination on silent chromatin in *Saccharomyces cerevisiae*, pp. 1099–1113

Kathryn J. Sieverman and Jasper Rine

One of the best-studied domains of heterochromatin is the silent mating-type locus *HML* in baker's yeast. Sieverman and Rine report that DNA transactions required for homologous recombination within *HML* can disrupt its silencing, revealing changes to the chromatin environment at *HML* that occur after it acts as a template for double-strand break repair. Remarkably, homologous recombination involving *HML* can also occur without disturbing transcriptional silencing. This study sheds light on the complex nature of silenced chromatin domains and raises awareness of the potential for genome editing to alter chromatin domains and epigenetic states.

A role for monomethylation of histone H3-K27 in gene activity in *Drosophila*, pp. 1023–1036

Liangjun Wang, Preeti Joshi, Ellen L. Miller, LeeAnn Higgins, Matthew Slattery, and Jeffrey A. Simon

N-terminal histone tails emanate from the chromatin fiber—providing docking surfaces for regulatory proteins—and are commonly modified by lysine methylation. The functional impact of these modifications depends on which lysines are modified and how many methyl groups are added. H3-K27 trimethylation features prominently in silent chromatin, but less is known about other H3-K27 states. Here, Wang *et al*. show that H3-K27 monomethlyation (me1) is enriched at active *Drosophila* genes and that boosting it triggers desilencing, thus linking H3-K27me1 to transcriptional activity.

A population phylogenetic view of mitochondrial heteroplasmy, pp. 1261–1274

Peter R. Wilton, Arslan Zaidi, Kateryna Makova, and Rasmus Nielsen

The mitochondria contained within the human body are genetically diverse. This type of variation, called heteroplasmy, is emerging as an important factor in human health, but information surrounding heteroplasmy transmission between generations and distribution within the body is still sparse. Wilton *et al*. introduce a statistical model that employs ideas from population genetics and phylogenetics to provide insights into the inheritance and ontogenesis of heteroplasmy. By applying the model to a dataset of heteroplasmy frequencies in humans, they corroborate previous studies of the mitochondrial bottleneck during oogenesis and find evidence for subsequent tissue-specific bottlenecks during early somatic development.

Regulation of circadian behavior by astroglial microRNAs in *Drosophila*, pp. 1195–1207

Samantha You, Tudor A. Fulga, David Van Vactor, and F. Rob Jackson

You *et al*. describe the first genome-wide analysis of glial microRNAs in the context of circadian behavior. They identified multiple miRNAs whose manipulation in glial cells results in arrhythmic circadian behavior. At least two of these miRNAs are required in adult astrocytes, and the authors describe candidate RNA targets for one of them. Most of these miRNAs have not been studied in any context, so the results provide an important resource for further analysis of glial miRNA function.