In this issue of Fly

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Rapidly Evolving Heterochromatin-Binding Proteins, pp. 137–41

Most insights into heterochromatin function have emerged from genetic and molecular studies of euchromatin-encoded proteins that affect heterochromatin properties, e.g., positional-effect variegation (PEV). The study of these heterochromatin-bound proteins can reveal the evolutionary forces that may act on the rapidly evolving heterochromatic sequence to which they bind. Over 20 new members of the Heterochromatin Protein 1 (HP1) gene family were recently discovered using 12 sequenced Drosophila genomes. These newly identified HP1 proteins are structurally diverse, lineage-restricted, and expressed primarily in the male germline. In this issue of Fly, Levine and Malik, authors of the original work, address alternative evolutionary models that may drive the constant innovation on HP1 genes.

Smaug and a New Mechanism of Post-Transcriptional Regulation, pp. 142–5

Drosophila Smaug is a sequence-specific RNA-binding protein that can repress the translation and induce the degradation of target mRNAs in the early Drosophila embryo. In this issue of Fly, Pinder and Smibert discuss a newly uncovered mechanism employed by Smaug to repress translation that involved the recruitment of the Agol protein to an mRNA in a microRNA-independent manner. The authors consider the multi-functional nature of Smaug and the suggestion that other RNA-binding proteins are likely to employ a similar mechanism of microRNA-independent Ago recruitment to control mRNA expression.

Neto and Its Role in Synapse Assembly, pp. 146–52

L-glutamate is the primary neurotransmitter at excitatory synapses in the vertebrate CNS and at arthropod neuromuscular junctions (NMJs). Recently, a novel molecule, Neto, was discovered to be essential for clustering of ionotropic glutamate receptors (iGluRs) at Drosophila NMJs. Neto is evolutionary conserved and is the first auxiliary non-channel subunit described in Drosophila that is absolutely required for functional iGluRs. Now, Kim and Serpe review the role of Drosophila Neto in synapse assembly, its similarities with other Neto proteins, and a new perspective on how glutamatergic synapses are physically assembled and stabilized.

UpSET and its Role on Chromatin Structure Modulation, pp. 153–60

Histone acetylation and an open chromatin configuration are key features of transcribed genomic regions and are mainly present around active promoters. Recently, the identification of the SET-domain-containing protein UpSET established a new functional link between the modulation of open chromatin features and the active recruitment of co-repressors. Interestingly, UpSET appears to regulate transcription by modulating chromatin structure through its interactions with histone deacetylases, rather than by histone methylation, like other SET domain-containing proteins do. In an enlightening Extra View article, Rincon-Arano et al. discuss the different scenarios in which UpSET could play key roles in modulating gene expression.

On the Establishment of Embryonic Dorsoventral Polarity, pp. 161–7

Drosophila embryo dorsoventral polarity is established by a maternally encoded signal transduction pathway that controls the activation of the Toll receptor on the ventral side of the embryo. The spatial regulation of this pathway depends upon ventrally restricted expression of the Pipe sulfotransferase in the ovarian follicle during egg formation. In this issue, Stein et al. summarize recent observations that add to the understanding of the mechanisms that regulate the spatially restricted activation of Toll.

The Drosophila KEOPS Complex, pp. 168–72

Recently, p53-related protein kinase (Prpk)-knockdown flies were shown to have phenotypes similar to those found in mutants for positive regulators of the PI3K/TOR pathway. This pathway is able to transduce hormonal and nutritional status into animal growth by regulating the protein synthesis machinery. The human Prpk ortholog has been linked with p53 stabilization in cell culture and its absence in yeast causes a slow-growth phenotype. This protein has also been associated to the KEOPS complex, which has been implicated in telomere maintenance, transcriptional regulation, bud site selection, and chemical modification of tRNAs in other species. Whereas the core constituents of the KEOPS complex are present in Drosophila, their physical interaction has not been reported yet. Now, Rojas-Benítez et al. review the function of this complex in different organisms and present new evidence suggesting a function for Prpk in animal growth.
Steroids and Neuronal Cell Differentiation, pp. 173–83

The generation of neuronal cell diversity is controlled by interdependent mechanisms, including cell intrinsic programs and environmental cues. Recently, pulses of steroid hormone were shown to act as a temporal cue to fine-tune neuronal cell differentiation. In an enlightening Extra View, Kucherenko and Shcherbata now provide evidence that extrinsic JAK/STAT cytokine signaling acts as a spatial code in the process. Particularly, in *Drosophila* mushroom bodies, neuronal identity transition is controlled by steroid-dependent microRNAs that regulate spatially distributed cytokine-dependent signaling factors that, in turn, modulate cell adhesion.

Automating Climbing Behavior Measurements, pp. 184–6

In this issue of *Fly*, Podratz et al. report on a novel model system in *Drosophila melanogaster* to study chemotherapy-induced neurotoxicity in adult flies. The authors have designed an automated fly-counting apparatus that measures 10 samples at a time, with 20 flies per sample. They report that automation of their climbing assay not only reduces variability, but also increases productivity, and enables high-throughput drug screens for neurotoxicity.

A Method for Reversible Drug Delivery, pp. 187–92

As mutations in some critical genes cause early embryonic lethality, it is difficult to study the role of proteins that are essential early in development during later embryonic stages. To address this problem, Schulman et al. have now developed a method to reversibly deliver drugs to internal tissues of stage 15–16 *Drosophila* embryos using a combination of D-limonene and heptane. This method provides a means to disrupt protein function in vivo with temporal specificity, bypassing the complications that arise when the product of the disrupted genes cause early embryonic lethality.

Looking at Mutations in Balancer Chromosomes, pp. 193–203

Balancer chromosomes in *Drosophila melanogaster* are predicted to accumulate numerous deleterious mutations with time. In a Brief Report in this issue of *Fly*, Araye and Sawamura counted the number of recessive lethal mutations on 2 balancer chromosomes from the *In(2LR)SM1/In(2LR)Pm* strain, after making the balancers heterozygous. The authors detected 10 recessive lethal mutations in the balancer *In(2LR)Pm*, which is consistent with the estimated mutation rate, but only 3 in *In(2LR)Pm*. The authors therefore argue that they were able to observe genetic decay over an estimable timescale by using balancers with historical records.

Density Dynamics of Bacterial Endosymbionts, pp. 204–10

Bacterial endosymbionts can have dramatic effects on their hosts, ranging from mutualistic to parasitic. The density of bacterial endosymbiont within the host is critical for the maintenance of the symbiotic relationship, affecting the expression of specific phenotypes and the levels of vertical transmission. In this issue of *Fly*, Haselkorn et al. studied the patterns of Spiroplasma density variation among 3 *Drosophila* species naturally infected with 2 different types of Spiroplasma. Bacterial density varied greatly within and among populations of *Drosophila*, with individuals from the population with the highest prevalence of infection having the highest density. This density variation underscores the complex interaction of Spiroplasma strain and host genetic background in determining endosymbiont density.