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Probing the Boundaries of Orthology: The Unanticipated Rapid Evolution of *Drosophila Centrosomin*, pp. 903–926

Robert C. Eisman and Thomas C. Kaufman

We expect proteins that carry out important functions to be quite conserved in evolution, but Eisman and Kaufman show that is not the case for *centrosomin*, an essential protein required for early cleavage divisions of *Drosophila* that assists assembly of the centrosome. They found that the *centrosomin* gene is evolving rapidly and observed changes in gene structure and protein sequences that suggest a novel mechanism for rapid evolution of some genes of *Drosophila* and perhaps other organisms.

Genome engineering of *Drosophila* with the CRISPR RNA-guided Cas9 nuclease, pp. 1029–1035

Scott. J. Gratz, Alexander M. Cummings, Jennifer N. Nguyen, Danielle C. Hamm, Laura K. Donohue, Melissa M. Harrison, Jill Wildonger, and Kate M. O'Connor-Giles

This article describes a new method that should make genome engineering of *Drosophila* routine. The authors show that the CRISPR RNA-guided Cas9 nuclease can generate defined deletions and mediate gene replacement by homologous recombination in *Drosophila*, yielding stable mutant lines within a month, from start to finish. The ease of producing sequence-specific RNAs for targeting Cas9 makes this the method of choice for genome engineering.

SLiM: simulating evolution with selection and linkage, pp. 1037–1039

Philipp W. Messer

The neutral theory of molecular evolution assumes that adaptation is rare and that its effect on linked variation—hitchhiking—is negligible. But this assumption may be violated in many species, so we should worry whether population genetic methods, and estimates of key parameters obtained from them, are robust to hitchhiking. This article describes a new tool for simulating hitchhiking on the scale of entire chromosomes and in large populations that will enable modeling the evolution of species with high rates of molecular adaptation.

Genome-wide variation of cytosine modifications between European and African populations and the implications for complex traits, pp. 987–996

Erika L. Moen, Xu Zhang, Wenbo Mu, Shannon M. Delaney, Claudia Wing, Jennifer McQuade, Jamie Myers, Lucy A. Godley, M. Eileen Dolan, and Wei Zhang

The level of cytosine modification, such as DNA methylation, is likely a complex trait influenced by genetic and environmental factors. This study of genome-wide cytosine modification levels in two global populations of Africans and Europeans revealed abundant population-specific CpG sites and the genetic basis underlying their variation. These findings could help explain some previously identified genetic variants associated with gene expression and other complex traits that exhibit racial disparities.

Rates and genomic consequences of spontaneous mutational events in *Drosophila melanogaster,* pp. 937–954

Daniel. R. Schrider, David Houle, Michael Lynch, and Matthew W. Hahn

Knowing spontaneous mutation rates is key to understanding how variation arises. Rates of occurrence of single-nucleotide changes and small insertions and deletions (indels) have been estimated, but little is known about the rate at which larger changes occur. The authors of this study found that far more base pairs are affected by large duplications and deletions than by point mutations, and that 99% of large duplications and deletions are deleterious.

The length of the shortest telomere as the major determinant of the onset of replicative senescence, pp. 847–857

Zhou Xu, Khanh Dao Duc, David Holcman, and Maria Teresa Teixeira

Because telomeres shorten every cell division, they serve as molecular clocks that trigger senescence, something cancer cells avoid. To determine if senescence is stochastic or deterministic, the authors of this article measured telomere length distribution in budding yeast and found that a single dominant telomere controls senescence. They conclude that the length of the shortest telomere in a cell likely determines senescence onset.

This Month's Perspectives

Lamarck, evolution, and the inheritance of acquired characters, pp. 793–805

Richard W. Burkhardt, Jr.

The name of the French biologist Jean-Baptiste Lamarck is tightly associated with the idea that traits acquired during an individual's lifetime can be inherited. This month's Perspectives article revisits Lamarck views of the inheritance of acquired characters, and suggests that the adjective "Lamarckian" could be applied to other ideas, including the idea that behavioral change can be a driving force of change at the organismal level.

This Month in the American Journal of Human Genetics

XLID mutations and associated genes challenged in light of data from large scale human-exome sequencing, Am. J. Hum. Genet. 93(2)

Amelie Piton, Claire Redin, and Jean-Louis Mandel

This article reports reevaluation of the role of 106 genes that have been associated with X-linked intellectual disability (XLID). The authors conclude that ten of the genes are questionably involved in the trait, and fifteen genes require caution when interpreting mutations identified in cases. This study refines the true gene-disease associations in XLID and illustrates the kind of analysis necessary to differentiate real gene-disease associations from rare variants identified in affected individuals in a variety of Mendelian diseases.