GENETICS, Vol. 209, August 2018, Copyright © 2018

The effect of strong purifying selection on genetic diversity, pp. 1235–1278

Ivana Cvijović, Benjamin H. Good, and Michael M. Desai

Negative selection is a ubiquitous evolutionary force, but its effects on diversity in large samples are poorly understood. Cvijović, Good, and Desai obtain simple analytical expressions for the whole population site frequency spectrum at a nonrecombining genetic locus experiencing recurrent neutral and deleterious mutations. They show that negative selection can lead to substantial distortions in diversity in large samples that are not seen in small samples. These signatures can potentially mimic those of other evolutionary events, such as population expansions or positive selection.

Chromatin that guides dosage compensation is modulated by the siRNA pathway in *Drosophila melanogaster*, pp. 1085–1097

Nikita Deshpande and Victoria H. Meller

A family of X-linked repetitive elements enhances dosage compensation of nearby genes in male flies. Here, Deshpande and Meller show that chromatin around these repeats is modified in a siRNA-dependent manner. Proteins that interact with the siRNA effector protein Argonaute2, including Su(var)3-9, also contribute to dosage compensation. Su(var)3-9 deposits H3K9me2 at the X-linked repeats, and this siRNA-directed H3K9me2 enrichment at repeats correlates with increased expression of genes up to 100 kb away, thus linking the siRNA pathway to repeats on the X chromosome and X recognition.

Determinants of base-pair substitution patterns revealed by whole-genome sequencing of DNA mismatch repair defective *Escherichia coli*, pp. 1029–1042

Patricia L. Foster, Brittany A. Niccum, Ellen Popodi, Jesse P. Townes, Heewook Lee, Wazim MohammedIsmail, and Haixu Tang

and

The spectrum of replication errors in the absence of error correction assayed across the whole genome of *Escherichia coli*, pp. 1043–1054

Brittany A. Niccum, Heewook Lee, Wazim MohammedIsmail, Haixu Tang, and Patricia L. Foster

Proofreading during DNA replication and post-replication mismatch repair are two major defenses against mutations. Foster et al. and Niccum *et al*. used mutation accumulation and whole genome sequencing to assemble a database of thousands of mutations across the *Escherichia coli* genome, revealing that error correction by each of these pathways is biased and that the local DNA context strongly influences replication fidelity. *E. coli*'s DNA replicative polymerase has an intrinsic bias for converting G:C to A:T basepairs, but the two error-prevention pathways work together to maintain a low mutation rate of 1 per 1000 generations and a genomic G:C content of ≈50%.

Genetic modifiers of neurodegeneration in a *Drosophila* model of Parkinson's Disease, pp. 1345–1356

Sierra Lavoy, Vinita G. Chittoor-Vinod, Clement Y. Chow, and Ian Martin

Mutations in LRRK2 (leucine-rich repeat kinase 2) cause Parkinson's disease through poorly understood mechanisms. Lavoy *et al*. performed a genome-wide screen to identify genetic modifiers of LRRK2 G2019S-induced locomotor dysfunction in *Drosophila*. Genes involved in the outgrowth and regulation of neurites were enriched in this screen, and several candidates were shown to similarly affect age-related dopamine neuron loss. These results describe novel candidate modifier genes for LRRK2 G2019S that may provide insight into the link between LRRK2 and neuronal degeneration via neurite defects.

A crucial caste regulation gene detected by comparing termites and sister group cockroaches, pp. 1225–1234

Yudai Masuoka, Kouhei Toga, Christine A. Nalepa, and Kiyoto Maekawa

Acquisition of a sterile caste is a key step in insect eusocial evolution; however, the molecular mechanisms associated with sterile caste development are unclear. To help resolve the issue, Masuoka *et al*. focused on soldiers—the first acquired sterile caste of termites—comparing them with their sister group within cockroaches. Since juvenile hormone is the primary factor in inducing soldier differentiation, they analyzed its expression and signaling pathway in both groups, finding that ecdysone signaling and the nuclear receptor gene *HR39* were crucial for soldier differentiation.

Initiation of meiotic development is controlled by three posttranscriptional pathways in *Caenorhabditis elegans*, pp. 1197–1224

Ariz Mohammad, Kara Vanden Broek, Christopher Wang, Anahita Daryabeigi, Verena Jantsch, Dave Hansen, and Tim Schedl

A major transition in germ cell development is the switch from mitotic cell cycling to entry into the meiotic developmental pathway. Mohammad *et al*. report that the SCF^{PROM-1} substrate-specific E3 ubiquitin ligase complex is a new regulator of meiotic entry in *Caenorhabditis elegans*, functioning to both downregulate mitotic cell cycle protein levels including cyclin E and to promote homologous chromosome pairing as a positive regulator of CHK-2. They demonstrate that three posttranscriptional pathways function in parallel to coordinate the transition to meiotic development in *C. elegans*.

Dual roles for yeast Sti1/Hop in regulating the Hsp90 chaperone cycle, pp. 1139–1154

Michael Reidy, Shailesh Kumar, D. Eric Anderson, and Daniel C. Masison

Hsp70/Hsp90 co-chaperone Sti1/Hop bridges Hsp70 and Hsp90 to facilitate client transfer. Many Hsp90 mutations make Sti1 necessary for viability, implying the Hsp90-Hsp70 interaction is essential. These mutations cluster in regions important for interaction with Hsp70 (SdN) or clients (SdC). Reidy *et al*. find Hsp90 SdN mutants depend on Sti1 to promote an essential Hsp70 interaction, while SdC mutants need Sti1 to establish an Hsp90 conformation crucial for capturing clients and progressing through the reaction cycle. Their findings show Sti1/Hop coordinates Hsp70 binding and client transfer with progression of the Hsp90 reaction cycle.

Human-mediated introgression of haplotypes in a modern dairy cattle breed, pp. 1305–1317

Qianqian Zhang, Mario Calus, Mirte Bosse, Goutam Sahana, Mogens Sandø Lund, and Bernt Guldbrandtsen

Domestic animals provide a robust model system to understand complex evolutionary processes and their genomic consequences. Zhang *et al*. use full re-sequenced genomes of modern dairy cattle to identify haplotypes in the genomes of an admixed modern dairy breed introgressed from high yielding breeds that affect important economic traits such as milk and production traits. Their findings show that hybridization events are detectable in the genome, adding to our understanding of genomic alterations resulting from hybridization and adaptive selection.

This Month's Perspectives

Developmental bias and evolution: a regulatory network perspective, pp. 949–966

Tobias Uller, Armin P. Moczek, Richard A. Watson, Paul M. Brakefield, and Kevin N. Laland

A recurrent theme in evolutionary biology is to contrast natural selection and developmental constraint – two forces pitted against each other as competing explanations for organismal form. Despite its popularity, this juxtaposition is deeply misleading. Characters often evolve through changes in how genes, cells, and tissues regulate each other. This paper explains why such regulatory interactions not only limit evolution, but also may facilitate the capacity to adapt and diversify. Recent theoretical and empirical research is now beginning to reveal how evolution of the evolutionary process itself contributes to diversification and adaptation.