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Feeding-related traits are affected by dosage of the *foraging* gene in *Drosophila melanogaster*, pp. 761–773

Aaron M. Allen, Ina Anreiter, Megan C. Neville, and Marla B. Sokolowski

The *foraging* gene has been implicated in multiple feeding-related traits. Allen *et al.* precisely deleted the *foraging* gene and used recombineering to re-integrate a full copy, generating the {for^{BAC}} rescue allele. Total loss of *foraging* expression in larvae resulted in reduced larval path length and food intake and increased triglyceride levels. Varying gene dosage demonstrated a linear dose-response of these phenotypes to *foraging* expression levels. These experiments reveal a causal, dose-dependent relationship between the *foraging* gene and its pleiotropic influence on feeding-related traits.

Evidence for amino acid snorkeling from a high-resolution, *In Vivo* Analysis of Fis1 tail anchor insertion at the mitochondrial outer membrane, pp. 691–705

Abdurrahman Keskin, Emel Akdoğan, and Cory D. Dunn

Charged amino acids are often considered unacceptable in protein regions integrated within lipid bilayers. Indeed, algorithms predicting membrane-integrated domains often take amino acid charge into consideration. Previous theoretical work and several *in vitro* studies have suggested that the side chains of lysine and arginine can reach to the bilayer surface, removing the positive charge from the hydrophobic portion of the membrane. This process is called amino acid 'snorkeling'. By examining nearly all amino acid replacements within the membrane anchoring sequence of the mitochondrial protein Fis1, Keskin *et al.* provide *in vivo* evidence for amino acid snorkeling.

Correlated mutations and homologous recombination within bacterial populations, pp. 891–917

Mingzhi Lin and Edo Kussell

Homologous recombination is a critical process in bacterial evolution, yet measuring its basic parameters, such as rates and fragment sizes, remains theoretically challenging as well as computationally expensive. The authors introduce and apply a new population genetic approach for inferring recombination rates from bacterial sequence data. The method is extremely fast and efficient, does not employ phylogenetic inference or other computationally-intensive numerics, and is therefore applicable in many different contexts.

An unexpected regulatory cascade governs a core function of the *Drosophila* PRC1 chromatin protein Su(z)2, pp. 551–558

Son C. Nguyen, Stephanie Yu, Elaine Oberlick, and Chao-ting Wu

Polycomb group (PcG) proteins are major chromatin-bound factors that can read and modify chromatin states to maintain gene silencing throughout development. Nguyen *et al.* reveal that, contrary to previous reports, the essential functions of Suppressor 2 of zeste (Su(z)2), a close homolog of the PcG protein Posterior Sex Combs, do not lie within the C-terminal region. Instead, the region essential for viability lies within the N-terminal end, called the homology region (HR), and this essential activity is controlled by a cascade of inhibitory intramolecular interactions encoded by two subregions of Su(z)2.

The effect of an extreme and prolonged population bottleneck on patterns of deleterious variation: insights from the Greenlandic Inuit, pp. 787–801

Casper-Emil T. Pedersen, Kirk E. Lohmueller, Niels Grarup, Peter Bjerregaard, Torben Hansen, Hans R. Siegismund, Ida Moltke, and Anders Albrechtsen

Pedersen *et al.* use high-depth exome sequencing data to show that the Greenlandic Inuit population has recently undergone a severe 20,000-year-long bottleneck. Such demographic history is the most extreme ever observed for any human population and has therefore led to a markedly more extreme distribution of allele frequencies than seen for any other human population. The authors show that the distribution of deleterious alleles are markedly different and reveal that selection is likely to have been reduced as a consequence of this extended bottleneck. These results suggest there is improved power for finding novel disease associations in the Inuit.

Cooperation between kinesin motors promotes spindle symmetry and chromosome organization in oocytes, pp. 517–527

Sarah J. Radford, Allysa Marie M. Go, and Kim S. McKim

The oocyte spindle in most animal species is assembled without the assistance of the microtubule-organizing centers called centrosomes. Radford *et al.* show that the kinesin-5 KLP61F is required for spindle and centromere symmetry in oocytes. The asymmetry observed in the absence of KLP61F depends on NCD, the kinesin-12 KLP54D, and the microcephaly protein ASP. The authors propose that the activities of several proteins, including NCD, ASP and KLP54D, generate asymmetries within the acentrosomal spindle, while KLP61F balances these forces.

Genetic mechanisms leading to sex differences across common diseases and anthropometric traits, pp. 979–992

Michela Traglia, Dina Bseiso, Alexander Gusev, Brigid Adviento, Daniel S. Park, Joel A. Mefford, Noah Zaitlen, and Lauren A. Weiss

Diseases often show sex differences. Traglia surveyed a number of complex heritable diseases and anthropometric traits for genetic sex differences. They did not find consistent excess genetic risk in the lower-prevalence sex or a disproportionate role for the X chromosome in disease risk, despite sex-heterogeneity on the X for several traits. All anthropometric traits showed sex-differential genetic contributions and the authors find a convincing example of genome-sex interaction in multiple sclerosis. They also describe evidence for hormone-responsive gene enrichment and striking evidence of the contribution of secondary sex characteristic differential associations to common disease risk.

Evolution of resistance against CRISPR/Cas9 gene drive, pp. 827–841

Robert L. Unckless, Andrew G. Clark, and Philipp W. Messer

CRISPR/Cas9 gene drive (CGD) promises a highly adaptable approach to controlling pests or disease vectors by spreading genetically engineered alleles throughout a species. The authors examine the likelihood that resistance to gene drive evolves prior to driver fixation, potentially limiting the ability of the driver to transform whole populations. The results shed light on possible strategies for engineering drivers with lower potential for resistance as well as the potential use of resistance as a mechanism for controlling CGD.

This Month in the American Journal of Human Genetics

Increased *STARD10* expression is associated with defective insulin secretion in humans and mice, Am. J. Hum. Genet. 100(2)

Gaelle R. Carrat, Ming Hu, Marie-Sophie Nguyen-Tu, Pauline Chabosseau, Kyle Gaulton, Martijn van de Bunt, Afshan Siddiq, Mario Falchi, Matthias Thurner, Mickaël Canouil, Francois Pattou, Isabelle Leclerc, Timothy J. Pullen, Matthew C. Cane, Priyanka Prabhala, William Greenwald, Anke Schulte, Piero Marchetti, Mark Ibberson, Patrick MacDonald, Jocelyn E. Manning Fox, Anna L. Gloyn, Philippe Froguel, Michele Solimena, Mark I. McCarthy, and Guy A. Rutter

Type 2 diabetes (T2D) has emerged as a major world-wide health issue. Although genome-wide association analyses have identified dozens of loci associated with T2D risk, the causative variants and mechanism of action remain unclear in most instances. In this paper, Carrat *et al.* explore one such loci, for which two genes, *ARAP1* and *STARD10*, have previously been implicated in T2D etiology. Analysis and experimentation in human and mice supports a model in which reduction of *STARD10* expression in β-cells increases T2D risk. *STARD10* encodes a lipid transfer protein, but little is known about its in vivo function; future work aimed at exploring its ability to influence proinsulin processing could have therapeutic implications.