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**Energy-dependent modulation of glucagon-like signaling in *Drosophila* via the AMP-activated protein kinase, pp. 457–466**

*Jason T. Braco, Emily L. Gillespie, Gregory E. Alberto, Jay E. Brenman, and Erik C. Johnson*

How organisms maintain energetic homeostasis is unclear. These authors show that the actions of a known cellular sensor of energy—the AMP-activated protein kinase (AMPK)—cause release of a glucagon-like hormone in *Drosophila*. They further show that AMPK regulates secretion of adipokinetic hormone. This suggests new roles and targets for AMPK and suggests metabolic networks are organized similarly throughout Metazoa.

**The relation of codon bias to tissue-specific gene expression in *Arabidopsis thaliana*, pp. 641–649**

*Salvatore Camiolo, Lorenzo Farina, and Andrea Porceddu*

This article reports systematic differences in usage of synonymous codons in *Arabidopsis thaliana* genes whose expression is tissue specific. The authors propose that codon bias evolves as an adaptive response to the different abundances of tRNAs in different tissues.

**Integrity and function of the *Saccharomyces cerevisiae* spindle pole body depends on connections between the membrane proteins Ndc1, Rtn1, and Yop1, pp. 441–455**

*Amanda K. Casey, T. Renee Dawson, Jingjing Chen, Jennifer M. Friederichs, Sue L. Jaspersen, and Susan R. Wente*

Budding yeast face an unusual challenge during cell division: they must segregate their chromosomes while the nuclear envelope remains intact. Consequently, mitosis begins with insertion of the duplicated spindle pole body (a.k.a. centrosome) into the nuclear envelope, a process that parallels the generation of new nuclear pore complexes. These authors report data that suggest new mechanisms for linking nuclear division and transport.

**Cellular memory of acquired stress resistance in *Saccharomyces cerevisiae*, pp. 495–505**

*Qiaoning Guan, Suraiya Haroon, Diego González Bravo, Jessica L. Will, and Audrey P. Gasch*

Cells can retain memory of prior experiences that influence future behaviors. Here, the authors show that budding yeast retains a multifaceted memory of prior stress treatment. Cells pretreated with salt retain peroxide tolerance for several generations after removal of the initial stressor. This is due to long-lived catalase, produced during salt treatment and distributed to daughter cells. These cells also display transcriptional memory dependent on the nuclear pore subunit Nup42 that functions to promote reacquisition of stress tolerance in future stress cycles.

**Genomic variation in natural populations of *Drosophila melanogaster*, pp. 533–598**

*Charles H. Langley, Kristian Stevens, Charis Cardeno, Yuh Chwen G. Lee, Daniel R. Schrider, John E. Pool, Sasha A. Langley, Charlyn Suarez, Russell B. Corbett-Detig, Bryan Kolaczkowski, Shu Fang, Phillip M. Nista, Alisha K. Holloway, Andrew D. Kern, Colin N. Dewey, Yun S. Song, Matthew W. Hahn, and David J. Begun*

This article greatly extends studies of population genetic variation in natural populations of *Drosophila melanogaster*, which have played an important role in the development of evolutionary theory. The authors describe genome sequences of 43 individuals taken from two natural populations of *D. melanogaster*. The genetic polymorphism, divergence, and copy-number variation revealed in these data are presented at several scales, providing unprecedented insight into forces shaping genome polymorphism and divergence.

**Estimating allele age and selection coefficient from time-serial data, pp. 599–607**

*Anna-Sapfo Malaspinas, Orestis Malaspinas, Steven N. Evans, and Montgomery Slatkin*

The relative importance of the four fundamental processes driving evolution—genetic drift, natural selection, migration, and mutation—remains undetermined. These authors propose a new approach to estimate the selection coefficient and the allele age of time serial data. They apply their methodology to ancient sequences of a horse coat color gene and demonstrate that the causative allele existed as a rare segregating variant prior to domestication. This illuminates the debate on the relative importance of new *vs.* standing variation in adaptation and domestication.

**DNA replication origin function is promoted by H3K4 di-methylation in *Saccharomyces cerevisiae*, pp. 371–384**

*Lindsay F. Rizzardi, Elizabeth S. Dorn, Brian D. Strahl, and Jeanette Gowen Cook*

What defines a DNA replication origin? It is becoming increasingly apparent that post-translational modifications of nucleosomes near replication origins help mark them and control their activity. The genetic analysis presented in this article implicates di-methylated histone H3 lysine 4 (stimulated by histone H2B monoubiquitination) as part of the definition of active replication origins. Since these histone modifications are highly conserved, these findings are relevant to genome organization in other eukaryotes.

**Comparative oncogenomics implicates the Neurofibromin 1 gene (*NF1*) as a breast cancer driver, pp. 385–396**

*Marsha D. Wallace, Adam D. Pfefferle, Lishuang Shen, Adrian J. McNairn, Ethan G. Cerami, Barbara L. Fallon, Vera D. Rinaldi, Teresa L. Southard, Charles M. Perou, and John C. Schimenti*

This study of a mouse model of genomic instability indicates that NF1 (Neurofibromin 1) deficiency can drive breast cancer. ~ 63,000 people in the United States annually will develop breast cancer with an NF1 deficiency. Together with evidence that NF1 depletion confers resistance of human breast cancer cells to tamoxifen, these findings suggest therapeutic strategies for patients with *NF1*-deleted tumors.

## This Month in the American Journal of Human Genetics

**Homeotic Arm to Leg Transformation Associated with Genomic Rearrangements at the PITX1 Locus, Am. J. Hum. Genet. 91(4)**

*Malte Spielmann, Francesco Brancati, Peter Krawitz, Peter N. Robinson, Daniel Ibrahim, Martin Franke, Jochen Hecht, Silke Lohan, Katarina Dathe, Anna Maria Nardone, Paola Ferrari, Antonio Landi, Lars Wittler, Bernd Timmermann, Danny Chan, Ulrich Mennen, Eva Klopocki, and Stefan Mundlos*

Homeotic transformations –the conversion of one body part into another in development –are most familiar in *Drosophila*, but they occur in humans, too. This article explains one of these cases –Liebenberg syndrome, which causes partial homeotic transformations in which the arms acquire some features of legs. Spielmann *et al.* identify causative chromosome structural variations upstream of PITX1 associated with Liebenberg syndrome in three families. These variants likely affect expression of PITX1: a heterozygous deletion brings limb-specific enhancers near PITX1. Indeed, expression of hs-1473-Pitx1 in mice recapitulates Liebenberg syndrome.