ISSUE HIGHLIGHTS

Consistent patterns of rate asymmetry and gene loss indicate widespread neofunctionalization of yeast genes after whole-genome duplication, pp. 1341–1350

Kevin P. Byrne and Kenneth H. Wolfe

This article reports evidence that most of the pairs of duplicated genes formed by ancient polyploidization in an ancestor of yeasts have undergone a change of function (neofunctionalization) in one of the gene copies. More than half of the gene pairs have unequal rates of sequence evolution, and this rate asymmetry, seen in more than one species, indicates it was established soon after polyploidization. Furthermore, the faster-evolving gene in each pair tends to be orthologous to the faster-evolving gene in other species. These gene pair members tend to be lost more frequently in other species, approximately four times more often than their slower-evolving paralogs.

Background selection in single genes may explain patterns of codon bias, pp. 1381–1393

Laurence Loewe and Brian Charlesworth

Background selection theory predicts the effects of recurrent deleterious mutations on patterns of variation in linked regions. In particular, background selection results from a reduced effective population size caused by the removal of recurrent deleterious mutations. This article shows the influence of deleterious mutations on a highly localized, intragenic scale: the impact of deleterious mutations on the codon usage of flanking codons in the same gene. It also incorporates the latest estimates of the distribution of deleterious mutational effects into estimates of the reduction of effective population size from background selection. Finally, it suggests reasons for the observed effects of gene length and intron length on codon usage.

Exploring strategies for protein trapping in Drosophila, pp. 1089–1104

Ana T. Quiñones-Coello, Lisa N. Petrella, Kathleen Ayers, Anthony Melillo, Stacy Mazzalupo, Andrew M. Hudson, Shu Wang, Claudia Castiblanco, Michael Buszczak, Roger A. Hoskins and Lynn Cooley

and

The Carnegie protein trap library: A versatile tool for Drosophila developmental studies, pp. 1505–1531

Michael Buszczak, Shelley Paterno, Daniel Lighthouse, Julia Bachman, Jamie Planck, Stephenie Owen, Andrew D. Skora, Todd G. Nystul, Benjamin Ohlstein, Anna Allen, James E. Wilhelm, Terence D. Murphy, Robert W. Levis, Erika Matunis, Nahathai Srivali, Roger A. Hoskins and Allan C. Spradling

To tag endogenous proteins with green fluorescent protein (GFP) the authors modify a transposon-based method for fusing GFP to Drosophila proteins. Splice acceptor and donor sites flank the GFP's coding sequence and thus its expression is dependent on splicing into mRNAs with initiator and stop codons. Using an automated embryo sorter and established lines from GFP-positive animals, the authors screen >78 million embryos for new insertions that express GFP. As a result, the number of different genes with well-characterized GFP fusion lines is increased from ~50 to >400. Additionally, 300 other genes are tagged as GFP-enhancer traps, but the GFP localization is usually nuclear and does not correspond to the site of the endogenous protein. Finally, lines are molecularly characterized at the level of the genome insertion site and many are also characterized with respect to the pattern of RNA splicing downstream from the insertion. Further information about these insertions may be found at the FlyTrap database (http://flytrap.med.yale.edu).

A genetic screen for modifiers of the Delta1-dependent Notch signaling function in the mouse, pp. 1451–1463

Isabel Rubio-Aliaga, Dian Soewarto, Sibylle Wagner, Matthias Klaften, Helmut Fuchs, Svetoslav Kalaydjiev, Dirk H. Busch, Martina Klempt, Birgit Rathkolb, Eckhard Wolf, Koichiro Abe, Stefan Zeiser, Gerhard K. H. Przemeck, Johannes Beckers and Martin Hrabé de Angelis

The Notch signaling pathway is an evolutionary conserved transduction pathway involved in embryonic patterning and regulation of cell fates during development. Because one of the known ligands of the Notch receptors is Delta1, mice homozygous for a loss-of-function allele of the Delta1 gene die during embryonic development. Here the authors present the results of two phenotype-driven modifier screens that generated 35 new mutant mouse lines in which 7 exhibit a phenotype independent of the Delta1 mutation. These lines provide excellent *in vivo* tools for studying the role of Notch signaling in kidney and liver function, cholesterol and iron metabolism, cell-fate decisions, and maturation of T cells in the immune system.

Epigenetic modifications of distinct sequences of the *p1* regulatory gene specify tissue-specific expression patterns in maize, pp. 1059–1070

Rajandeep S. Sekhon, Thomas Peterson and Surinder Chopra

Regulation of gene expression in eukaryotes is controlled by molecular mechanisms that can restrict the expression to a specific signal, developmental stage, tissue, or a cell. Because tissue-specific patterns of expression can be maintained as both stable and unstable alleles or epialleles, it is desirable to study those alleles that respond to known genetic factors/modifiers, which heritably alter the alleles' expression pattern. This study presents epigenetic behavior of a multicopy, tandemly repeated gene that encodes a Myb transcription factor in maize and demonstrates that distinct sequences can undergo epigenetic modifications to generate tissue-specific expression patterns.

Evolution of different Y chromosomes in two medaka species, *Oryzias dancena* and *O. latipes*, pp. 1335–1340

Yusuke Takehana, Diana Demiyah, Kiyoshi Naruse, Satoshi Hamaguchi and Mitsuru Sakaizumi

In verterbrates, only two sex-determining genes have been isolated: *Sry* from mammals and *DMY* from the medaka (*Oryzias latipes*). Although *Sry* has a widespread distribution, *DMY* is not conserved even in closely related species. This article shows that although another medaka species (*O. dancena*) does not possess *DMY*, it does have an XX/XY sex-determination system. Comparitive analysis reveals that Y chromosomes of *O. dancena* and *O. latipes* are not homologous, thus suggesting that not only do *O. dancena* and *O. latipes* have an independent origin of their Y chromosomes, but also a novel sex-determining gene controls the sex in *O. dancena.*

Haplotype probabilities for multiple-strain recombinant inbred lines, pp. 1267–1274

Friedrich Teuscher and Karl W. Broman

This article develops a method for calculating haplotype probabilities in recombinant inbred lines (RILs) derived from multiple founder strains. It expands past work that has established the power of such crosses for the genetic dissection of complex traits. Through theoretical analysis of the predicted structure of variation across a set of RILs, it is possible to design efficient experiments for quantitative trait analysis. This article also extends the results for RILs founded with multiple parental strains, including the case of multiple-strain intermated recombinant inbred populations.

Genetic evidence for a *SPO1*-dependent signaling pathway controlling meiotic progression in yeast, pp. 1213–1227

Gela G. Tevzadze, Jessica V. Pierce and Rochelle Easton Esposito

SPO1, which encodes a meiosis-specific phospholipase B (PLB) homolog, is required at MI, MII, and spore formation in yeast. On the basis of suppression and complementation analyses and binding of specific phosphatidylinositol (PI) species to Spo1, a model is presented in which phosphatidylinositol monophosphates (PIPs), known lipid signaling molecules, negatively regulate successive stages of meiotic progression. The authors suggest that Spo1, a PIP-specific PLB, promotes gametogenic development by cleaving PIPs. These findings suggest the existence of a novel Spo1-dependent signaling pathway required at multiple stages of meiotic progression.

The cloning and characterization of the histone acetyltransferase human homolog Dmel\TIP60 in *Drosophila melanogaster*: Dmel\TIP60 is essential for multicellular development, pp. 1229–1240

Xianmin Zhu, Neetu Singh, Christopher Donnelly, Pamela Boimel and Felice Elefant

This article describes the first identification and developmental characterization of the human histone acetyltransferase (HAT) homolog in Drosophila Dmel\TIP60. To decipher developmental HAT function, the authors create an inducible and targeted HAT RNAi knockdown system in Drosophila. Their results demonstrate that Dmel\TIP60 is essential for multicellular development and, specifically, muscle formation in the developing fly. This system has implications for future study of these and other chromatin regulators in multicellular development and epigenetic-based disorders.