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INVESTIGATIONS

The *Neurospora crassa* genome is a graveyard of transposon relics due to its efficient genome defense. "Meiotic silencing by unpaired DNA" (sometimes called MSUD) is one post-transcriptional defense mechanism that silences unpaired genomic segments during karyogamy. The authors discovered a novel DNA transposon family (called *Sly*) with multiple copies in several lab strains that are absent from most wild isolates. This is the first demonstration of an intact and likely active DNA transposon in the genus *Neurospora*. Here, small RNAs are required for meiotic silencing in order to suppress spreading of transposons.

Children with Down syndrome (DS) have 2000-fold elevated risk of developing atrioventricular septal defects (AVSD), a severe congenital heart abnormality. To uncover the genetic architecture behind this elevated risk, Ramachandran *et al.* conducted a genome-wide association study on 210 cases with DS and complete AVSD and 242 controls with DS and documented structurally normal hearts, making this the largest heart study conducted to date on a trisomic background. No common variant of large effect size (odds ratio > 2.0) was identified, thus supporting a complex and multifactorial etiology for AVSD even in the sensitized DS population.

The fruit fly *Drosophila sechellia* is narrowly adapted to the fruit of *Morinda citrifolia*, which is toxic to its sibling species, *Drosophila simulans*. The authors combined a high-throughput, high-resolution genomic tool with QTL mapping to detect evolved genomic regions that confer resistance to *M. citrifolia* in *D. simulans-D. sechellia* hybrids. Their analysis shows that *M. citrifolia* resistance is conferred by two large effect loci that act with multiple smaller-effect regions. The discovery of novel, major effect loci is an important first step towards identifying the molecular basis of adaptation in a multicellular organism.

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2137–2154 SUMO-Enriched Proteome for *Drosophila* Innate Immune Response
Mithila Handu, Bhagyashree Kaduskar, Ramya Ravindranathan, Amarendranath Soory, Ritika Giri, Vijay Barathi Elango, Harsha Gowda, and Girish S. Ratnaparkhi

Handu *et al.* measured the changes to the SUMO proteome in *Drosophila* cells in response to an immune challenge and find global changes, with protein domains, cellular pathways, and protein complexes responding to immune stress. A confident set of 710 proteins is identified as the immune-induced SUMO proteome that contains *bona fide* SUMO targets such as Caspar, Jra, Kay, cdc42, 14-3-3ε, p38b, and also cellular proteins with diverse functions, such as prosβ4, Rps10b, SmD3, Tango7, and Arginyl tRNA synthetase. This study will help increase understanding of the roles for SUMO modification in the host response to pathogens.

2155–2164 A Genomic Selection Index Applied to Simulated and Real Data
J. Jesus Ceron-Rojas, José Crossa, Vivi N. Arief, Kaye Basford, Jessica Rutkoski, Diego Jarquín, Gregorio Alvarado, Yoseph Beyene, Kassa Semagn, and Ian DeLacy

Genomic selection is now a standard method to predict breeding values and to select individuals as parents to the next generation. A genomic selection index (GSI) is a linear combination of genomic estimated breeding values of individuals used to select parents in an unobserved testing population, for which there is only marker information. In this article, the authors propose a GSI and compare its efficiency with that of the Smith phenotypic selection index (PSI). They used simulated and real data sets to compare the efficiency of the GSI and the PSI.

2165–2176 Similar Efficacies of Selection Shape Mitochondrial and Nuclear Genes in Both *Drosophila melanogaster* and *Homo sapiens*
Brandon S. Cooper, Chad R. Burrus, Chao Ji, Matthew W. Hahn, and Kristi L. Montooth

Nonrecombining genomes, such as the mtDNA and heteromorphic Y/W chromosomes, are predicted to accumulate deleterious mutations. Prior studies comparing samples of mitochondrial and nuclear genes have largely supported the idea that selection is less effective at removing deleterious variants from mitochondrial relative to nuclear genes. Using large samples of mitochondrial and nuclear whole-genome data from fruit flies and humans, Cooper *et al.* find little evidence that mitochondrial genes, on average, harbor more nonsynonymous polymorphism than do nuclear genes. Their findings challenge the current understanding of animal mitochondrial evolution and will lead to investigations of how selection maintains protein sequence in nonrecombining genomes.

2177–2186 Identification and Correction of Sample Mix-Ups in Expression Genetic Data: A Case Study
Karl W. Broman, Mark P. Keller, Aimee Teo Broman, Christina Kendziorski, Brian S. Yandell, Śaunak Sen, and Alan D. Attie

In a large mouse eQTL study with 500 intercross mice and genome-wide gene expression data on six tissues, the authors identified a high proportion (18%) of sample mix-ups in the genotype data, as well as a smaller number of mix-ups in the expression data for each tissue. They describe a simple and practical approach for identifying and correcting such problems. The approach has been implemented in the R package R/lineup, which is available at https://github.com/kbroman/lineup.

2187–2197 Genetic Networks Required to Coordinate Chromosome Replication by DNA Polymerases α, δ, and ε in *Saccharomyces cerevisiae*
Marion Dubarry, Conor Lawless, A. Peter Banks, Simon Cockell, and David Lydall

Genome replication is an important, complex, and difficult task. In eukaryotes, DNA replication depends principally on three DNA polymerase activities. Dubarry *et al.* used systematic genetic approaches to investigate DNA replication when each polymerase is defective. They identify hundreds of genetic interactions affecting replication. Comparison of fitness profiles between defective DNA polymerase strains allows them to distinguish factors that affect different aspects of replication. New online tools facilitate access and interaction with these data, which should improve the understanding how eukaryotic DNA replication is coordinated.

MUTANT SCREEN REPORT

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