ISSUE HIGHLIGHTS

Frequency spectrum neutrality tests: One for all and all for one, pp. 249–258

Guillaume Achaz

Under the standard model of evolution, a large body of theoretical results exists, and predictions are made on the expected diversity within the sample of sequences. Taking advantage of these predictions, one can test for the standard model using "neutrality tests." This investigator shows that an entire class of these tests (*i.e.*, tests related to Tajima's *D*) are specific instances of a more general framework that can be applied to build new neutrality tests that are more powerful than previous ones and that can handle experimental biases in the sequences.

Ancestral population genomics: The coalescent hidden Markov model approach, pp. 259–274

Julien Y. Dutheil, Ganesh Ganapathy, Asger Hobolth, Thomas Mailund, Marcy K. Uyenoyama and Marcy K. Schierup

The genealogy varies along the genome of species with close speciation times and large ancestral population sizes. Information on population genetics processes and the speciation process itself can therefore be extracted from genomic alignments, particularly when there is incomplete lineage sorting, *i.e.*, part of the genome has a different tree than the species tree. These authors develop a framework for inferring ancestral population genetics parameters from an alignment of four species, using a hidden Markov model and coalescent arguments. They investigate the properties of the model by extensive simulations and apply it to human-chimp-gorilla-orangutan alignments.

Mitochondrial superoxide radicals differentially affect muscle activity and neural function, pp. 175–184

Tanja Godenschwege, Renée Forde, Claudette P. Davis, Anirban Paul, Kristopher Beckwith and Atanu Duttaroy

Mitochondrial oxygen metabolism engenders reactive oxygen species (ROS), which could cause degenerative disease. These investigators measure the sensitivity of muscles and neurons to ROS attack and find that muscles are more sensitive to superoxide than neurons. Therefore many overt phenotypes observed in animals with high levels of ROS can be directly attributed to the muscle.

***curled* encodes the Drosophila homolog of the vertebrate circadian deadenylase Nocturnin,** pp. 219–232

Sebastian Grönke, Iris Bickmeyer, Roman Wunderlich, Herbert Jäckle and Ronald P. Kühnlein

In 1915, Thomas H. Morgan described the Drosophila mutant *curled*, the founding member of a series of wing marker mutants used daily in fly laboratories worldwide. Despite their widespread use, little is known about their underlying developmental defect. The authors show that *curled* encodes the fly homolog of vertebrate Nocturnins, deadenylases involved in posttranscriptional control of gene expression, initially identified as circadian rhythm-regulated genes.

Alternative splicing of PTC7 in *Saccharomyces cerevisiae* determines protein localization, pp. 185–194

Kara Juneau, Corey Nislow and Ronald W. Davis

Proteome diversity is greatly increased when organisms utilize alternative splicing. Yeast has not been a major player in this field because there are no conclusive examples of functional alternative splicing in *Saccharomyces cerevisiae*. This article reports the first such case: *PTC7* is processed into two mRNAs that express distinct proteins with discrete cellular locations.

Systems-level engineering of nonfermentative metabolism in yeast, pp. 385–397

Caleb J. Kennedy, Patrick M. Boyle, Zeev Waks and Pamela A. Silver

These authors use metabolic modeling to direct their engineering of an important metabolic pathway. Their computational model suggests genes that are not obviously related to one-carbon metabolism, but which, when knocked-out, cause cells to secrete formic acid. Their findings suggest possible modes of regulation of one-carbon metabolism in yeast and demonstrate the successful application of *in silico* models for engineering nonfermentative metabolism in yeast.

A role for nonessential domain II of initiator protein, DnaA, in replication control, pp. 39–49

Kathryn L. Molt, Vincent A. Sutera, Kathryn K. Moore and Susan T. Lovett

Bacteria control DNA replication through a central initiator protein, DnaA. This article describes genetic suppressor analysis that demonstrates a regulatory function of domain II of DnaA, a flexible linker region previously thought to have no function. Mutations in domain II suppress phenotypes of over-initiating mutants by lowering initiation capacity. The authors propose that conformational changes in the domain II linker are required for optimal activation of replication initiation and recruitment of replication machinery.

Temperature-sensitive mutations made easy: Generating conditional mutations by using temperature-sensitive inteins that function within different temperature ranges, pp. 13–22

Guihong Tan, Ming Chen, Christopher Foote and Change Tan

Temperature-sensitive (TS) mutations are powerful tools to study gene function. However, TS alleles are rare and difficult to generate, and this has limited their use in most multicellular organisms. These authors generate and characterize a family of intein switches that can be inserted into proteins to make them temperature-sensitive. The intein switches function in five different temperature ranges, allowing one to choose a TS-intein switch according to the optimal growth temperature of an organism, or to suit a special experimental design.

This Month in Genetics Research

Epistasis and its implications for personal genetics, Am. J. Hum. Genet. **85:** 309–320

Jason H. Moore and Scott M. Williams

Despite easy access to commercial personal genetics services, personalized medicine is not yet here because our knowledge of the genetic architecture of common diseases is still very limited. We simply cannot accurately predict risk for most diseases. This is due to complexities like epistasis and gene-environment interaction and locus heterogeneity. This article provides an introductory review of how epistasis can affect human health and disease and how it can be detected in population-based studies, discusses some implications for personal genetics, and presents some recommendations for improving it.

Diagnosis of miscarriages by molecular karyotyping: Benefits and pitfalls, Genet. Med. **11:** 646–654

Caroline Robberecht, Vicky Schuddinck, Jean-Pierre Fryns and Joris Robert Vermeesch

Spontaneous abortions are common, with 10 to 15% of pregnancies ending in early loss of the fetus. At least half of these events are caused by fetal chromosome abnormalities. However, often no fetal karyotype can be obtained. This article reports that array comparative genomic hybridization is better than karyotyping for diagnosing the chromosomal basis of miscarriage. It also has a much higher level of resolution than conventional karyotyping, bringing many more chromosomal aberrations into view.