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Cortical folding of the primate brain: an interdisciplinary examination of the genetic architecture, modularity, and evolvability of a significant neurological trait in pedigreed baboons (Genus *Papio*), pp. 651–665

Elizabeth G. Atkinson, Jeffrey Rogers, Michael C. Mahaney, Laura A. Cox, and James M. Cheverud

Folding of the brain cortex allows for improved neural processing power by increasing cortical surface area for the allocation of neurons. Using a large pedigreed population of ~1000 *Papio* baboons, Atkinson *et al.* address critical questions about the genetic architecture of primate brain folding, the interplay between genetics, brain anatomy, development, patterns of cortical-cortical connectivity, and the potential for future evolution of cortex folding traits. The authors also map variation in these traits to specific genomic regions.

The chromatin and transcriptional landscape of native *Saccharomyces cerevisiae* telomeres and subtelomeric domains, pp. 505–521

Aisha Ellahi, Deborah M. Thurtle, and Jasper Rine

How and why are genes placed near telomeres silenced? Early studies showed that yeast genes near telomeres are silenced in a Sir-protein-dependent manner. However, these studies inserted reporter genes next to truncated, rather than natural, telomeres. Ellahi *et al.* combined ChIP-Seq of Sir proteins with RNA-Seq of wild type and *sir* mutants, and found that, surprisingly, most subtelomeric genes were expressed. Only 6% of subtelomeric genes were silenced in a Sir-protein-dependent manner. While this work provides independent validation of yeast telomere position effects, it also illuminates the mosaic nature of heterochromatin at telomeres and the sparse distribution of genes whose expression is affected by it.

Adaptation, clonal interference, and frequency-dependent interactions in a long-term evolution experiment with *Escherichia coli*, pp. 619–631

Rohan Maddamsetti, Richard E. Lenski, and Jeffrey E. Barrick

Maddamsetti *et al.* reconstructed the dynamics of 42 mutations over 20,000 generations of bacterial evolution. They show that cohorts of multiple beneficial mutations typically accumulated in a lineage before it was able to complete a selective sweep. In one striking case, two bacterial types with different sets of mutations coexisted for thousands of generations. This diversity was reinforced by frequency-dependent ecological interactions, but eventually collapsed after further evolution drove one type extinct.

Allelic imbalance is a prevalent and tissue-specific feature of the mouse transcriptome, pp. 537–549

Stefan F. Pinter, David Colognori, Brian J. Beliveau, Ruslan I. Sadreyev, Bernhard Payer, Eda Yildirim, Chao-ting Wu, and Jeannie T. Lee

It is generally assumed that both alleles of a gene are equally expressed, although examples of allelic imbalance due to epigenetic phenomena are known. Pinter *et al.* measured allele-specific gene expression in hybrid offspring from genetically distinct mice, revealing allelic imbalance in one-fifth of all expressed genes. Genetic differences most likely account for the majority of this phenomenon, but surprisingly some of these genes are also monoallelic in inbred strains.

Efficient CRISPR/Cas9-mediated genome editing in mice by zygote electroporation of nuclease, pp. 423–430

Wenning Qin, Stephanie L. Dion, Peter M. Kutny, Yingfan Zhang, Albert W. Cheng, Nathaniel L. Jillette, Ankit Malhotra, Aron M. Geurts, Yi-Guang Chen, and Haoyi Wang

and

Multiplex conditional mutagenesis using transgenic expression of Cas9 and sgRNAs, pp. 431–441

Linlin Yin, Lisette A. Maddison, Mingyu Li, Nergis Kara, Matthew C. LaFave, Gaurav K. Varshney, Shawn M. Burgess, James G. Patton, and Wenbiao Chen

Two important extensions of CRISPR mutagenesis in vertebrates are reported this month. Qin *et al.* describe the Zygote Electroporation of Nuclease (ZEN) method, which improves the throughput of CRISPR applications in mice by avoiding the bottleneck of manual injection of CRISPR/Cas9 components. Yin *et al.* report a CRISPR system for multiplex conditional mutagenesis of zebrafish in one generation, allowing spatial and temporal control of gene inactivation.

Reconstructing past admixture processes from local genomic ancestry using wavelet transformation, pp. 469–481

Jean Sanderson, Herawati Sudoyo, Tatiana M. Karafet, Michael F. Hammer, and Murray P. Cox

Admixture between long-separated populations is a defining feature of the genomes of many species. As admixed genomes recombine, they produce a mosaic chromosome structure that contains information about when and how the two populations interacted. Sanderson *et al.* describe a new wavelet-based method to reconstruct these admixture processes. The authors show that their method performs well by applying it to simulated genetic data and human genome-wide SNP data from Indonesia. The method is released as the R package *adwave*.

Allele sharing and evidence for sexuality in a mitochondrial clade of bdelloid rotifers, pp. 581–590

Ana Signorovitch, Jae Hur, Eugene Gladyshev, and Matthew Meselson

The view that sexual reproduction is essential for long-term evolutionary success in eukaryotes is challenged by the apparent asexuality of the bdelloid rotifers, invertebrates of ancient origin. Signorovitch *et al.* demonstrate that members of a mitochondrial clade of bdelloids collected in the wild show a striking pattern of allele sharing consistent with sexual reproduction and with an unusual type of meiosis, in which segregation occurs without requiring homologous chromosome pairs.

Massively parallel functional analysis of BRCA1 RING domain variants, pp. 413–422

Lea M. Starita, David L. Young, Muhtadi Islam, Jacob O. Kitzman, Justin Gullingsrud, Ronald J. Hause, Douglas M. Fowler, Jeffrey D. Parvin, Jay Shendure, and Stanley Fields

Genetic tests often reveal missense mutations that are classified as Variants of Uncertain Significance (VUS), a result that is difficult for patients to interpret. Understanding how missense substitutions affect the function of the BRCA1 protein is of vital importance as more women undergo testing of this gene. Starita *et al.* show that the disease relevant cellular activity of BRCA1 variants can be accurately predicted on a large scale using results from massively parallel functional assays.

This Month in the American Journal of Human Genetics

Jump from pre-mutation to pathologic expansion in *C9orf72*, Am. J. Hum. Gent. 96(6)

Zhengrui Xi, PhD, Marka van Blitterswijk, Ming Zhang, PhD, Philip McGoldrick, Jesse R. McLean, Yana Yunusova, Erin Knock, Danielle Moreno, Christine Sato, Paul M. McKeever, Raphael Schneider, Julia Keith, Nicolae Petrescu, Paul Fraser, Maria Carmela Tartaglia, Matthew C. Baker, Neill R. Graff-Radford, Kevin B. Boylan, Dennis W. Dickson, Ian R. Mackenzie, Rosa Rademakers, Janice Robertson, Lorne Zinman, and Ekaterina Rogaeva

The expansion of the *C9orf72* repeat is the most frequent variation associated with amyotrophic lateral sclerosis and frontotemporal lobar degeneration. Some studies have proposed that the expansion has arisen once in human history. However, in this study, Xi *et al.* report a family in which an allele expanded dramatically during the parent-offspring transmission. Although the lower limit for the number of expansions is suggested to be 30 repeats, the unaffected father harbored a 70-repeat expansion that was differentially methylated and expressed compared to his childrens' pathogenic expansion of ~1750-repeats. This observation is consistent with other diseases characterized by expanded repeats where small, nonpathogenic expansions can act as "pre-mutations."