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Detecting rare variant associations by identity-by-descent mapping in case-control studies, pp. 1521–1531

Sharon R. Browning and Elizabeth A. Thompson

A number of methods are available for detecting genomic segments that are identical by descent between individuals due to common ancestry within the past ~25 generations. Is identity-by-descent (IBD) mapping (population-based linkage analysis) powerful as a strategy for detecting association between genetic variation and disease? This article reveals that IBD mapping can have higher power than SNP-based association testing in some cases, especially when multiple rare causal variants are clustered in a gene. However, the power of IBD mapping tends to be low for common complex diseases in outbred populations.

High-resolution genome-wide analysis of irradiated (UV and γ-rays) diploid yeast cells reveals a high frequency of genomic loss of heterozygosity (LOH) events, pp. 1267–1284

Jordan St. Charles, Einat Hazkani-Covo, Yi Yin, Sabrina L. Andersen, Fred S. Dietrich, Patricia W. Greenwell, Ewa Malc, Piotr Mieczkowski, and Thomas D. Petes

This article shows that even low doses of radiation induce mitotic recombination surprisingly frequently. Using DNA microarrays and high-throughput DNA sequencing, the authors examine recombination events throughout the yeast genome. This is the first high-resolution genome-wide analysis of DNA damage-induced loss of heterozygosity events in a eukaryote.

Ecological genomics of *Anopheles gambiae* along a latitudinal cline: A population-resequencing approach, pp. 1417–1432

Changde Cheng, Bradley J. White, Colince Kamdem, Keithanne Mockaitis, Carlo Costantini, Matthew W. Hahn, and Nora J. Besansky

The malaria mosquito *Anopheles gambiae* carries polymorphic chromosomal rearrangements whose frequencies vary along latitudinal clines in response to spatially varying selection. This article describes genomic resequencing of mosquitos along a cline of aridity in Cameroon. The interplay between natural selection, migration, and gene flux—even across inverted regions of the genome—allows the authors to identify several candidate genes responsible for the match between inversion frequency and environmental variables.

Allelic ratios and the mutational landscape reveal biologically significant heterozygous SNVs, pp. 1225–1233

Jeffrey S.-C. Chu, Robert C. Johnsen, Shu Yi Chua, Domena Tu, Mark Dennison, Marco Marra, Steven J. M. Jones, David L. Baillie, and Ann M. Rose

Whole-genome sequencing is powerful, but there are still technical limitations, such as how to confidently identify biologically significant heterozygous mutations. This article describes an effective way of doing so by taking advantage of allelic ratios and the mutational landscape of EMS-induced mutations to efficiently identify coding regions with lethal mutations. Application of this method to *Caenorhabditis elegans* identified a lethal mutation in the essential gene *let-504*, which encodes NKAP, a protein implicated in a wide range of biomedically important functions.

Surrogate genetics and metabolic profiling for characterization of human disease alleles, pp. 1309–1323

Jacob A. Mayfield, Meara W. Davies, Dago Dimster-Denk, Nick Pleskac, Sean McCarthy, Elizabeth A. Boydston, Logan Fink, Xin Xin Lin, Ankur S. Narain, Michael Meighan, and Jasper Rine

As DNA sequencing rapidly catalogs differences between human genomes, uncharacterized gene variants now greatly outnumber defined ones. To separate benign from disease-causing sequences, these investigators use a surrogate assay in *Saccharomyces cerevisiae* to analyze 84 disease-associated alleles of the human gene cystathionine β-synthase (CBS), providing a quantitative assessment of the effect of each allele.

Accuracy of genomic selection methods in a standard data set of loblolly pine (*Pinus taeda* L.), pp. 1503–1510

M. F. R. Resende, Jr., P. Muñoz, M. D. V. Resende, D. J. Garrick, R. L. Fernando, J. M. Davis, E. J. Jokela, T. A. Martin, G. F. Peter, and M. Kirst

Genomic selection will dramatically improve the genetic improvement of plant species, particularly those whose breeding cycle extends over several decades. These investigators evaluate the performance of standard methods of genome-wide selection for 17 growth, developmental, and disease-resistance traits. They show that the performance of most methods is comparable in all traits evaluated.

The abundance of deleterious polymorphisms in humans, pp. 1579–1583

Sankar Subramanian

This study shows that up to 48% of nonsynonymous SNPs (nSNPs) specific to a single genome are deleterious, underscoring the abundance of deleterious polymorphisms in humans. It reveals a gradual increase in the proportion of nSNPs from root to tip of the human population tree.

A Bayesian antedependence model for whole genome prediction, pp. 1491–1501

Wenzhao Yang and Robert J. Tempelman

Animal and plant breeding programs have been transformed by statistical models that jointly infer overall effects associated with each marker. These methods show promise for improving genomic predictions in human health. This article demonstrates substantial gains in accuracy of genomic predictions and genome-wide association studies from modeling spatial dependencies between adjacent SNP effects using nonstationary covariance specifications. These advantages increase as the average linkage disequilibrium between adjacent SNP markers increases.

This Month in the American Journal of Human Genetics

A "Copernican" reassessment of the human mitochondrial DNA tree from its root, Am. J. Hum. Genet. 90(4)

Doron M. Behar, Mannis van Oven, Saharon Rosset, Mait Metspalu, Eva-Liis Loogväli, Nuno M. Silva, Toomas Kivisild, Antonio Torroni, and Richard Villems

Mitochondrial DNA phylogeny informs the history of humans, but the reference mtDNA sequence that has been used belongs to a recently coalesced European haplogroup, resulting in misinterpretation and errors. This article describes a new reference sequence that incorporates data from Neanderthal mitogenomes, and over 18,000 human mtDNA sequences. It provides the most phylogenetically valid mtDNA reference sequence for human population genetics studies.