

**Simultaneous modeling of disease status and clinical phenotypes to increase power in genome-wide association studies, pp. 1041–1047**

Michael Bilow, Fernando Crespo, Zhicheng Pan, Eleazar Eskin, and Susana Eyheramendy

Jointly modeling clinical phenotype and disease status is a promising way to increase power to detect true associations between genetics and disease in genome-wide association studies. However, standard multivariate techniques fail to effectively solve this problem because their case-control status is discrete and not continuous. Standard approaches to estimate model parameters suffer ascertainment bias in case/control studies. The authors present a novel method that resolves both of these issues for simultaneous association testing of genetic variants that have both case status and a clinical covariate.

**Inferring individual inbreeding and demographic history from segments of identity by descent in *Ficedula* flycatcher genome sequences, pp. 1319–1334**

Marty Kardos, Anna Qvarnström, and Hans Ellegren

Individual inbreeding and historical demography can be estimated by analyzing runs of homozygosity (ROH), which are indicative of identity by descent (IBD). Such analyses have so far been rare in natural populations due to limited genomic resources. Kardos *et al.* analyzed ROH in *Ficedula* flycatchers. The strongest contributors to genome-wide variation in ROH abundance were likely positive selection and increased power to detect ROH in regions with low recombination. The authors identified populations with particularly small effective population size ( $N_e$ ) and estimated the size and founding time of an island population.

**The relative contributions of the X chromosome and autosomes to local adaptation, pp. 1285–1304**

Clémentine Lasne, Carla M. Sgrò, and Tim Connallon

Environmental conditions vary across species' ranges, leading to natural selection for local adaptation. Nevertheless, gene flow constrains population differentiation, and may influence the genetic architecture of locally adapted phenotypes. Lasne *et al.* develop new models that explicitly quantify the roles of the X chromosome and autosomes in adaptation to local environmental conditions. They identify a broad scope for large-X effects in local adaptation, with X-linked inheritance enhancing adaptation to local conditions. The theory yields new predictions about the genetic architecture of local adaptation, and the genomic basis of evolutionary differentiation between populations of geographically widespread species.

**Sexual dimorphism of body size is controlled by dosage of the X-chromosomal gene *Myc* and by the sex-determining gene *tra* in *Drosophila*, pp. 1215–1228**

Kristina Wehr Mathews, Margrith Cavegn, and Monica Zwicky

Sexual dimorphism of body size is prevalent throughout the animal kingdom. *Drosophila* females are larger than males and a central gene of the sex-determination pathway, *transformer* (*tra*), contributes to this difference. The authors have now identified another potent regulator of size dimorphism, showing that dosage of the *Myc* gene regulates sex-specific growth together with *tra*. By escaping dosage compensation, *Myc* confers a growth advantage to females. Since *Myc* is also involved in the activation of *tra*, this gene is a key player in the control of sex-specific body size.

**Nutritional control of chronological aging and heterochromatin in *Saccharomyces cerevisiae*, pp. 1179–1193**

David F. McCleary and Jasper Rine

The role of Siruins in lifespan extension via calorie restriction (CR) in *Saccharomyces cerevisiae* is controversial. The authors measured

chronological lifespan over a higher glucose range than typically used for studying yeast CR in minimal and rich media. In minimal medium, *sir2Δ* extended lifespan in high glucose with little effect in low glucose. In rich medium, *sir2Δ* decreased lifespan in low glucose with little effect in high glucose. In minimal medium, increasing glucose stabilized Sir-based silencing at HML, while, in rich medium, it destabilized silencing.

**Chromatin regulation by the NuA4 acetyltransferase complex is mediated by essential interactions between enhancer of polycomb (Epl1) and Esa1, pp. 1125–1137**

Naomi E. Searle, Ana Lilia Torres-Machorro, and Lorraine Pillus

Uncovering functions for non-catalytic subunits of macromolecular complexes is a major challenge. Enhancer of Polycomb is a deeply conserved protein with clear roles in development and cancer but it is unclear what role it plays *in vivo* within the NuA4 acetyltransferase complex. The authors engineered yeast genetic landscapes for cells to survive without EPL1 and in so doing, define Epl1 as a key co-factor for the essential catalytic enzyme of NuA4, Esa1. Despite having no acetyltransferase activity itself, they show that Epl1 is as critically important as Esa1 in genomic regulation.

**Meiotic crossing over in maize knob heterochromatin, pp. 1101–1112**

Stephen M. Stack, Lindsay A. Shearer, Leslie Lohmiller, and Lorinda K. Anderson

Crossing over is suppressed in the heterochromatin associated with centromeres and nucleolus organizers. But is this characteristic of all heterochromatin? Stack *et al.* examined meiotic recombination in maize knob heterochromatin. They found knob heterochromatin does not suppress crossing over when considered per unit of synaptonemal complex length. However, because the amount of DNA in knob heterochromatin is much higher, crossing over is suppressed in terms of genetic length per DNA amount.

**Efficient estimation of realized kinship from single nucleotide polymorphism genotypes, pp. 1063–1078**

Bowen Wang, Serge Sverdlov, and Elizabeth Thompson

Realized kinship has become an important component of many genetic analyses, including heritability estimation and genomic prediction. It is widely used both in human genetics and in analyses of livestock and plant populations. This paper considers estimators of realized kinship from SNP genotypes, and proposes two new estimators. The authors show that improved estimators are obtained by: optimal weighting of markers, taking physical contiguity of the genome into account, and weighting on the basis of LD.

**This Month in the American Journal of Human Genetics**

**Who's who? Detecting and resolving sample anomalies in human DNA sequencing studies with *peddy*. *Am. J. Hum. Genet.* 100(3); 10.1016/j.ajhg.2017.01.017**

Brent S. Pedersen and Aaron R. Quinlan

Advances in DNA technology have made it possible to answer diverse questions related to human health and history. But as with any process involving human intervention, the potential utility of this technology can be hampered by errors such as contamination or mislabeling. While laboratory best practices certainly are recommended, there is also a need to improve the ability to detect and correct handling errors. In presenting *peddy*, Pedersen and Quinlan do just that. Their fast and user-friendly software analyzes pedigree files for a variety of errors, as well as metrics of poor sequencing quality, and presents results in an interactive format that enables clear communication and rapid remediation of common sequencing pitfalls.