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IN BRIEF

COMPLEX TRAITS

Fine mapping versus replication in whole-genome association studies.

Clarke, G. M. *et al. Am. J. Hum. Genet.* **81**, 995–1005 (2007)

The main weakness of association studies is the poor ability to confirm the association of a variant with disease in an independent study. The authors have developed a theoretical model to determine the best strategy for confirming an association: if markers show only weak linkage with disease, then the most successful route to replication involves performing a local search for both the candidate variants and nearby markers. Conversely, if the initial association was strong, then it is most fruitful to test the initially identified markers.

QUANTITATIVE GENETICS

Linking metabolic QTLs with network and *cis*-eQTLs controlling biosynthetic pathways.

Wentzell, A. M. & Rowe, H. C. *et al. PLoS Genet.* **3**, e162 (2007)

Linking the variation in gene expression on a genome-wide scale with phenotypic consequences remains a challenge. Using two well-defined metabolic pathways in *Arabidopsis thaliana*, these authors show that variation in expression of genes in these pathways can be linked to metabolite variation. This relationship is complex, and regulatory connections can feed back from metabolism to transcripts — candidate-gene analysis indicates that, for one of the pathways, it is the final enzyme that is the key regulator of transcript and metabolite levels.

EVOLUTION

Gene duplication and the adaptive evolution of a classic genetic switch.

Hittinger, C. T. & Carroll, S. B. *Nature* 11 October 2007 (doi:10.1038/nature06151)

The genetic switch that controls the yeast galactose-metabolism pathway involves two paralogues — *GAL3* and *GAL1* — that originated from a single, bifunctional ancestral gene. By precisely replacing sequences in the coding and regulatory regions of these genes, the authors provide evidence that duplication allowed the evolution of new regulatory sequences that were disfavoured when in the same gene, enabling the two duplicates to take on new functions. This work provides a rare example of experimental evidence for how gene duplications allow new gene functions to evolve.

GENOMICS

Islands of euchromatin-like sequence and expressed polymorphic sequences within the short arm of human chromosome 21.

Lyle, R. *et al. Genome Res.* 25 September 2007 (doi:10.1101/gr.6675307)

The Human Genome Project focused on euchromatin, leaving unsequenced the ~6.5% of the genome that is heterochromatic. The authors constructed BAC clones of a region of the heterochromatic short arm of the acrocentric chromosome 21. Sequencing this region uncovered several potential genes, and a surprising amount of copy-number and sequence variation. Expression profiling showed that 10 of the 26 potential genes in this region are expressed in various tissues, although it is not known whether they are genes or pseudogenes.