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IN BRIEF

EPIGENETICS

Genome-wide views of methylation readers

Methyl-CpG binding domain (MBD) proteins have important roles as readers of DNA methylation, but their genome-wide profiling has been impeded by a lack of suitable antibodies for chromatin immunoprecipitation. These authors instead used controlled ectopic expression of tagged MBD proteins. Working with mouse embryonic stem cells and derived neuronal cells, they generated genome-wide profiles for wild-type and mutant forms of all MBD family proteins. Insights were gained into the role of CpG methylation in the binding of these proteins and the functions of their different domains.

ORIGINAL RESEARCH PAPER Baubec, T. *et al.* Methylation-dependent and -independent genomic targeting principles of the MBD protein family. *Cell* **153**, 480–492 (2013)

TRANSCRIPTOMICS

Isoform diversity revealed

Most transcriptomics methods identify only 5′ or 3′ ends of transcripts, so full information about transcript isoforms is lacking. This study describes transcript isoform sequencing (TIF-seq), in which both ends of transcripts are determined. Using TIF-seq, the authors discovered far more isoform diversity in the *Saccharomyces cerevisiae* transcriptome than was previously appreciated. They found an average of more than 26 transcript isoforms per protein-coding gene; these isoforms expand the diversity of proteins that are expressed and differ in their potential for post-transcriptional regulation.

ORIGINAL RESEARCH PAPER Pelechano, V. *et al.* Extensive transcriptional heterogeneity revealed by isoform profiling. *Nature* **497**, 127–131 (2013)

DISEASE GENETICS

Improving GWASs with secondary phenotypes

Genome-wide association studies (GWASs) often measure more than one phenotype that relates to the same underlying trait. These authors develop a statistical approach to harness the power of using secondary phenotypes to improve prioritization of single-nucleotide polymorphisms (SNPs). The approach is based on a scaled marginal model that can be used to assess the affect of common SNPs on the often continuous multiple secondary phenotypes measured. They applied the approach to smoking behaviour phenotypes in a lung cancer GWAS to identify new biologically relevant SNPs.

ORIGINAL RESEARCH PAPER Schifano, E. D. *et al.* Genome-wide association analysis for multiple continuous secondary phenotypes. *Am. J. Hum. Genet.* 2 May 2013 (doi:10.1016/j.ajhg.2013.04.004)

DEVELOPMENT

Testing the threshold-dependent model

The threshold-dependent model predicts that morphogenesis programmes are executed by genetic networks that respond to absolute concentrations of transcription factors. To test this model, Liu *et al.* manipulated the absolute concentration of the transcription factor Bicoid in *Drosophila melanogaster* early embryos. Early on, the Bicoid responsive genetic network shifted in response to altered Bicoid concentration. In subsequent developmental stages, wild-type patterns of network activity were restored, suggesting that later in development, the genetic network integrates information from various inputs counter to the threshold-dependent model.

ORIGINAL RESEARCH PAPER Liu, F. *et al.* Dynamic interpretation of maternal inputs by the *Drosophila* segmentation gene network. *Proc. Natl Acad. Sci. USA* **110**, 6724–6729 (2013)