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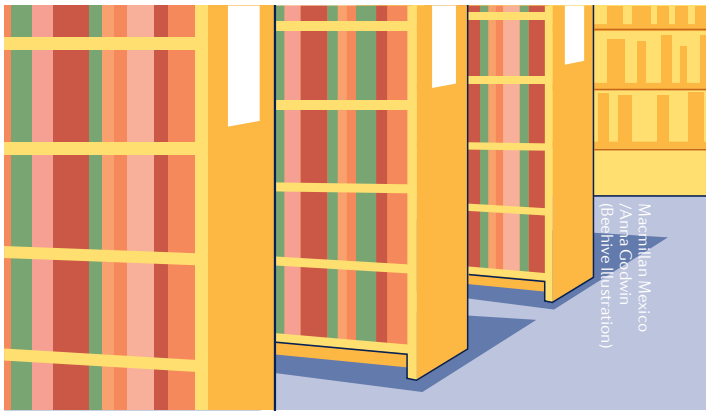
GENOMICS

A catalogue of human gene activity



Furthering the goal of functional annotation of the human genome, two new papers published in *Nature* by the members of the Functional Annotation of the Mammalian Genome (FANTOM) consortium provide catalogues of promoter and enhancer activity across the entire human genome.

In their first study, the researchers mapped transcription start sites in a range of sample types, including human and mouse primary cells, cell lines and tissues. They sequenced cap analysis of gene expression (CAGE) libraries to produce gene expression profiles. This methodology allowed them to analyse multiple promoters related to the same gene and to locate active enhancers, which were presented in the second paper.

These data yield a comprehensive 'atlas' of at least one promoter for more than 95% of annotated protein-coding genes in the human reference genome and provide insights into the properties that regulate cell type specificity of promoters. For example, the atlas revealed that promoters with a higher cell type or tissue specificity evolved more quickly than those that are broadly expressed. In addition, the group found that surprisingly few genes (only 6% of all genes) are 'housekeeping genes'. This encyclopaedia of human gene expression has immediate applications for the design of tissue-specific promoter constructs for mouse models and gene therapy vectors.

In the second study, the consortium identified 43,011 enhancer candidates across 808 human CAGE libraries. The investigators also demonstrated several properties of active enhancers, including the production of bidirectional, unspliced, short RNAs with very different properties compared with those of mRNAs. Validation of randomly selected strong-, medium- and low-activity enhancers by reporter assays showed that CAGE-defined enhancers were more likely to be validated than untranscribed candidate enhancers that were defined by previous methods, such as histone modifications or DNAse hypersensitive sites.

The atlases provide "a major resource for understanding where the genes are in the genome and when or where they are expressed," according to Alistair Forrest of the RIKEN Center for Life Science Technologies in Japan, who is a co-author on both papers. Together, this resource should facilitate further investigation of the molecular and genetic underpinnings of cell specification.

Isabel Lokody

> "this resource should facilitate further investigation of the ... underpinnings of cell specification"

ORIGINAL RESEARCH PAPERS The FANTOM Consortium and the RIKEN PMI and CLST (DGT). A promoter-level mammalian expression atlas. *Nature* **507**, 462–470 (2014) | Andersson, R. *et al.* An atlas of active enhancers across human cell types and tissues. *Nature* **507**, 455–461 (2014)