

NEUROGENETICS

Mapping gene expression in the human brain

Although all cells in the human body have the same genetic code, they vary hugely in their structures and functions. At the crossroads between the genome and the phenotype is the transcriptome — a list of the mRNA transcripts that are found in a given cell or tissue type — which reflects differences in gene expression between different cells. A new publication from the Allen Human Brain Atlas describes the adult human brain transcriptome in unprecedented anatomical detail.

The study of tissue-specific transcriptomes has become increasingly widespread, but the size and complexity of the human brain, coupled with the scarcity of post-mortem samples, has made it difficult to carry out detailed transcriptome analysis of the brain. However, an international collaboration has now succeeded in

“ ... the Allen Human Brain Atlas describes the adult human brain transcriptome in unprecedented anatomical detail ”

generating a comprehensive atlas of the brain's transcriptome based on brains from two individuals (whose transcriptomes were highly correlated).

The laboratories involved in this effort carried out careful anatomical dissection to obtain tissue from about 900 defined anatomical sites within the human brain. They then isolated RNA from each sample and analysed it using microarrays to identify the transcripts that were present at each site. This process generated a detailed map of transcript expression throughout the brain, and the data are publicly accessible online (see <http://www.brain-map.org>).

The transcriptome data can be used in various ways to investigate the molecular organization of the brain. For example, in their study, the authors graphically illustrate how the transcripts for genes involved in dopaminergic signalling are expressed across the brain, with peaks in structures such as the striatum and substantia nigra. They also looked at the distribution of transcripts for 740 genes that had previously been identified as being expressed in the postsynaptic density and found that 31% of these transcripts showed highly differentiated regional expression, presumably reflecting regional specializations in synaptic structure or function. Among these differentially expressed transcripts were those encoding neurofilament proteins (*NEFL*, *NEFM* and *NEFH*), which are found in long-range projection neurons. These proteins were selectively enriched in the primary motor cortex, from which the projection neurons with the longest ranges originate.

Surprisingly, there were no statistically significant differences in

transcript expression between the two hemispheres, despite the considerable functional differences between the left and right hemisphere. The authors suggest that hemispheric differences might depend more on subtle differences in structure or connectivity between the two sides of the brain than on molecular differences.

The authors also used weighted gene co-expression network analysis to group transcripts into 'modules' that show strongly co-varying patterns of expression. Among the modules identified were those containing transcripts that are expressed in different types of glial cell and others in which transcripts were particularly enriched for genes involved in neuron-specific functions and energy metabolism; these latter modules were associated with the neocortex, as might be expected given the high energy needs of cortical neurons. At a more local level, discrete subdivisions within the hippocampus could be discriminated by their transcriptomes. Overall, variation in the transcriptome across anatomical sites tended to reflect the cellular make-up of different brain regions, with greater similarity among different cortical regions than between different subcortical structures.

This publicly available resource will no doubt be invaluable for comparing transcription between species or at different developmental stages and also for investigating disease-related alterations in transcription in neurological and neuropsychiatric disorders.

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ORIGINAL RESEARCH PAPER Hawrylycz, M. J. et al. An anatomically comprehensive atlas of the adult human brain transcriptome. *Nature* **489**, 391–399 (2012)



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