URLs

Gscl
http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=195333

DiGeorge syndrome
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?188400

Huntington
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?143100

Parkinson disease
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?168600

Gilles de la Tourette syndrome
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?137580

schizophrenia
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?181500

autism
http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?300425

GENE EXPRESSION

Mapping the mouse mind

The Gene Expression Nervous System Atlas (GENSAT) project is an ongoing large-scale screen aimed at creating a digital atlas of gene expression in the mouse central nervous system (CNS). Gong *et al.* now report in *Nature* the first selected findings from this venture, which has so far provided data on ~150 genes and promises to produce detailed expression maps for thousands more in the near future.

The GENSAT project exploits the library of bacterial artificial chromosomes (BACs) associated with the mouse genome sequence. Modified BACs are produced in which a reporter sequence that encodes an enhanced green fluorescent protein (EGFP) is substituted for the coding region of a gene of interest. Transgenic mouse lines are then generated that carry the construct, which allows reporter-gene expression to be systematically analysed during development. The resulting data, which have been verified through mRNA *in situ* hybridization and immunohistochemistry, have been integrated and analysed to create a digital atlas of the mouse brain that can be viewed online and will be updated whenever new data are generated.

This innovative project is allowing gene expression to be correlated with cell type and the elaborate specializations of morphologically complex cells, such as neurons, to be visualized. Furthermore, small groups of cells that express a particular gene can be identified and their development followed over time.

The initial results have provided many insights into gene function and development in neural cells. For example, Gong *et al.* describe how this approach uncovered the highly-specific expression pattern of the goosecoid-like gene (*Gscl*), the absence of which is associated with DiGeorge syndrome, in the developing CNS: the population of neurons that express this gene have been traced back to just two cells that are present in the embryonic day 10.5 mouse embryo.

This screening technique should advance studies of mouse models for neurological disorders such as Huntington disease, Parkinson disease and Gilles de la Tourette syndrome, which result from the effects of specific populations of malfunctioning neurons. Future data might also facilitate studies of disorders such as schizophrenia and autism, in which neurons look normal despite obvious behavioural dysfunction. Prospective therapies for neurological diseases could even be tested in BAC transgenic mice, in which the level of EGFP fluorescence would provide a direct read-out of the effectiveness of a treatment.

So, the BAC library, the library of transgenic mouse lines and the atlas of CNS expression produced by the GENSAT project have opened the door to a range of new investigations, and the value of this resource will grow as more reporter-gene mice are analysed. The use of BAC transgenic reporters to study gene expression in specific cell types will stimulate many fields of biological research and can be readily extended to the analysis of other organs and tissues.

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References and links

ORIGINAL RESEARCH PAPER
Gong, S. *et al.* A gene expression atlas of the central nervous system based on bacterial artificial chromosomes. *Nature* **425**, 917–925 (2003)
FURTHER READING
Heintz, N. BAC to the future: the use of BAC transgenic mice for neuroscience research. *Nature Rev. Neurosci.* **3**, 861–870 (2001)
WEBSITE
GENSAT BAC Transgenic **Project:** http://www.gensat.org