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Cathy Holding

Email: cholding@hgmp.mrc.ac.uk

Bacterial artificial chromosomes (BACs) are a large-insert cloning system used in genomic analysis that can carry up to several hundred kilobases of foreign DNA. They are reproducibly expressed in a copy-number - dependent and position-independent manner in mice. The availability of whole organism genome sequences enables, for any gene of interest, the inclusion of flanking regulatory sequences to be confirmed in any particular BAC construct. In the October 30 *Nature*, Shiaoqing Gong and colleagues in the **GENSAT Transgenic Project** at the **Howard Hughes Medical Institute** report the identification of BACs containing complete genes and their regulatory sequences with their modification, by specialized shuttle vectors, for the production of BAC transgenes to produce stable mouse lines (*Nature* 2003, **425**:917-925).

This technique produces reporter gene assays of specific regulatory sequences, identification of their sites of expression at the single cell level, and the labeling of expressing cell lineages that can later be identified morphologically, in the central nervous system (CNS). A valuable resource of transgenic mouse lines, altered BAC clones and high-quality images are freely available to the neuroscience research community that will be of benefit in the fight against - among others - such disorders as Parkinson disease and Huntington disease and that will lead to improved understanding of the mechanisms of development and pathology of the CNS.

Gong *et al.* revealed a major advantage of the BAC constructs to be the ability to visualize small groups of cells expressing a particular gene that could be followed over time to monitor expression during development. The gene *Gscl* (goosecoidlike), involved in DiGeorge syndrome, was expressed in only two cells during embryo development that marked the founders of the lineage of a specific class of neurons, suggesting a functional role not previously envisaged. The technique also revealed roles for the *Sema3b* gene in axon-target interactions, as well as migratory patterns of the genes *Lhx6* and *Pdelc* not previously seen.

"The publication of the initial results of the GENSAT BAC Transgenic Project marks the beginning of a major effort to use genome mapping and sequence information in a directed, large-scale endeavor to advance mammalian neuroscience research. It is our hope that the examples we have discussed and the data we have released will accelerate research in all areas of neuroscience, and that access to the BAC vectors and transgenic lines we have produced will stimulate the fusion of mammalian molecular genetics and functional analysis of CNS cells and circuits," conclude the authors.

References

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