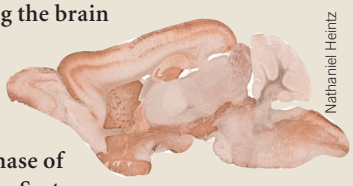
Nervous gene atlas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Neuroanatomical, pharmacological and behavioral approaches to understanding the brain have been profitable but hampered by the organ's complexity. Now Shiaoching Gong and colleagues report the first phase of the Gene Expression Nervous System Atlas (GENSAT), a BAC transgenic project that aims to provide detailed expression information for thousands of genes (*Nature* 425, 917–925; 2003). By creating transgenic lines carrying modified BACs in which the coding region of a particular gene is replaced by an EGFP reporter, the group was able to prepare detailed snapshots of expression patterns in the brain. The results were then confirmed with *in situ* hybridization and immunohistochemistry. The fruit of this effort is important, not just because of the potential to provide expression information on genes in the brain, but also because it simultaneously provides confirmed BAC vectors and animal lines that allow access to specific cell populations. This initial description provides the patterns for 150 genes, offering a taste of the true wealth of information and resources to come. Gene expression data and annotations can be found at http://www.gensat.org. *MS*

Sweet-tasting mice

Compared with rodents, humans are exquisitely sensitive to a broad range of sweet stimuli. To what do we owe our inherent sweet tooth? New work by Charles Zuker and colleagues (*Cell* **115**, 255–266; 2003) identifies a specific taste receptor, T1R2, as a key determinant of mammalian sweet preferences. In one of several interesting studies reported in this paper, Zuker's group generated mice deficient in T1R2 and found that their ability to detect sweet compounds was severely impaired. The authors then introduced human T1R2 into T1R2-deficient mice and found that human T1R2 not only rescued sweet responsiveness but also conferred distinctly humanized sweet preferences. Mouse and human T1R2 show 30% dissimilarity at the protein level, and it is still not known which sequence differences are responsible for the enhanced sweet-detection capacities of human T1R2. It also remains to be seen whether T1R2 sequence variations contribute to individual taste preferences in humans. *KV*

New method for protein knock-down

The phenotype conferred by antisense or RNAi knock-down may be immediate, delayed or undetectable, depending on protein turnover. Turnover depends on the action of the cellular E3 ubiquitin-protein ligases, the best studied of which is the SCF complex comprising Skp1, Cullin 1, a RING domain protein and βTrCP, which acts as the substrate receptor for F box–containing proteins. Jianxuan Zhang and colleagues recently redirected SCF to specifically destroy proteins that were not previously substrates for ubiquitination, by altering the specificity of the receptor, βTrCP, in a way that should provide a general method for protein knock-down (*Proc. Natl. Acad. Sci. USA* advance online publication, 30 October 2003; doi:10.1073/pnas.2233012100). Using part of the human papilloma virus (HPV16) E7 protein in place of the substrate-targeting domain of βTrCP, the authors were able to ablate the whole family of proteins related to tumor suppressor protein Rb. As E7 selects hypophosphorylated forms of Rb, only these forms were proteolytically removed. To make this a general tool, the authors suggest that an antibody Fv chain directed at each desired target might be attached to the βTrCP construct. Because this knock-down technique seems to work stoichiometrically rather than catalytically, regulated expression of the construct should quantitatively reduce any set of target proteins. *MA*

Fly interaction map

Genome sequencing has provided us with a parts list for many organisms, but we still must learn how the many gene products interact in order to move from form to function. One means of achieving this aim is identifying physical interactions between proteins. A massive study of protein interactions in *Drosophila melanogaster* provides the first glimpse of the totality of protein-protein interactions in a multicellular organism (*Science* advance online publication, 6 November 2003; doi:10.1126/science.1090289). Giot *et al.* used yeast two-hybrid screening with 11,282 cDNA-derived baits. Screening against cDNA libraries and a pool of preys yielded 20,439 interactions. High-throughput yeast two-hybrid screening is notoriously littered with false positives; to ameliorate this problem, the authors filtered their data with a statistical model based on previously published interactions in flies and in yeast. The result was a high-confidence interaction map consisting of 4,679 proteins and 4,780 interactions. These interactions were largely consistent with the known cellular localization of the proteins and provide insight into possible cross-compartment interactions. The availability of these data provide ample booty for fly and computational researchers alike. *DG*

KiSS1 sparks puberty

Childhood is a mysterious period during which the signaling axis initiated by the hypothalamus that usually delivers urgent pulses of luteinizing hormone from the pituitary to the gonads goes to sleep, only to reawaken at puberty to trigger sexual maturation. In a large family with three marriages between first cousins, Seminara *et al.* (*N. Engl. J. Med.* 349, 1614–1627; 2003) discovered six individuals with hypogonadism. This condition was linked to mutations in *GPR54*, encoding an orphan receptor of the rhodopsin family. Because these people and experimental mice carrying null alleles of *Gpr54* generated by gene targeting responded similarly to treatment with gonadotropin-releasing hormone with development of their gonads, the authors hypothesized that *GPR54* regulates secretion of gonadotropin-releasing hormone from the hypothalamus. The ultimate trigger of maturation has not yet been spotted. But a good candidate is the peptide ligand KiSS1 that binds GPR54, causing phosphatidylinositol turnover through a G-protein signal transduction mechanism. This would mean there is a conserved vertebrate signal for the onset of puberty. *MA*

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