WEB WATCH

The Human Brain Project
The recent publication of the human genome sequence constitutes a milestone for the Human Genome Project. Sequencing the genome has been heralded as one of the major scientific breakthroughs in history, a statement that cannot be dismissed as an exaggeration. Looking at this resounding success, we cannot help but ask ourselves what neuroscientific accomplishment would match the impact of the human genome sequence. Although it is hard to come up with a satisfactory answer, it is reassuring to know that, just as there is a Human Genome Project, there is also a multidisciplinary research effort known as the Human Brain Project (HBP).

The HBP was launched in 1993 as a reaction to the explosive growth of the neurosciences and our concomitant inability to maintain an integrated view of the brain. The goal of this initiative is to create a series of Internet-based databases and data-management tools that will help us to analyse the available neuroscientific data. The different neuroscience databases will be fully interoperable with other resources such as genome and protein databases, but their ultimate goal is to provide more than just a collection of information. The HBP hopes that scientists will use the databases to gain a deeper understanding of brain structure and function across every level of analysis.

Although the HBP has not yet reached the notoriety of the Human Genome Project, significant progress has already been made on some fronts. A visit to the HBP website (in particular, to the 'Research Grants' page) will give you a feel for the kind of research projects that are supported, as well as their current status. Hopefully, it won't be long before one of them is also proclaimed as an extraordinary breakthrough in our understanding of the human species.

Juan Carlos López

ION CHANNELS

A mul-TRP-PLIK-ation of channel functions

How many everyday utensils have dual functions? A watch/calculator. A bottle opener/corkscrew. A Swiss Army knife, the ultimate multifunctional gadget. Cells also use this trick to increase the functional repertoire of their constituents and it is not unheard of for a single molecule to do more than one job. Ion channels are the latest addition to the list of multifaceted molecules following the discovery of TRP-PLIK, an ion channel protein with kinase activity.

TRP-PLIK is a protein expressed in the brain, as well as in many other organs, including heart, kidney, liver and lung. The sequence of TRP-PLIK shows similarity to channels of the transient receptor potential (TRP) type, which are involved in many processes ranging from phototransduction in *Drosophila* to osmosensitivity in *C. elegans*. Indeed, TRP-PLIK does form ion channels that are cation-selective and permeable to calcium, indicating that it might contribute to membrane depolarization and to the regulation of intracellular calcium levels.

But the carboxy-terminal region of TRP-PLIK shows similarity to the catalytic domain of a very different molecule: eukaryotic elongation factor 2 kinase, a member of the atypical α-kinase family. In fact, this homologous domain is functional in TRP-PLIK, as the channel can phosphorylate itself, as well as other substrates. Moreover, if the kinase activity is abolished, then TRP-PLIK currents are reduced, indicating that auto-

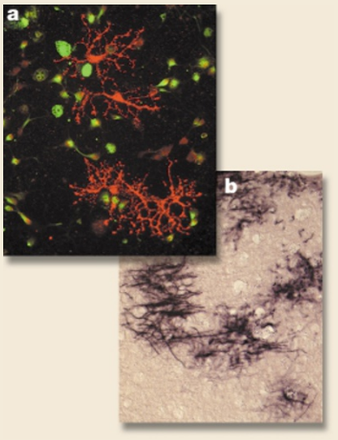
DEVELOPMENT

Sonic boom in oligodendrogenesis

The signalling protein sonic hedgehog (Shh) is pivotal to many aspects of vertebrate neural development, including dorsoventral patterning and specification of motor neurons and ventral interneurons. In the spinal cord, Shh also specifies oligodendrocytes, and Nery *et al.* have questioned whether it might have a similar role in the brain. As they report in *Development*, there is now evidence that Shh promotes oligodendrogenesis in the mammalian telencephalon.

To determine whether the telencephalon can produce oligodendrocytes in response to Shh, the authors used a viral vector to express human *SHH* in this region from embryonic day 9.5. After five days, regions of *SHH* expression showed ectopic activation of the early oligodendrocyte markers *Olig2* and *PDGFRα*. However, in mice allowed to develop to adulthood, some cells expressing *SHH* failed to express mature oligodendrocyte markers (for example, myelin basic protein (MBP) and 2′,3′ cyclic nucleotide 3′ phosphodiesterase (CNPase)), particularly in regions where myelinating oligodendrocytes are usually absent, such as the grey matter. Therefore, although Shh might impose an early oligodendrocyte identity on telencephalic cells, additional locally derived signals might be required to complete the differentiation pathway. Nery *et al.* also showed that localized Shh inhibition reduced the number of cells entering the oligodendrocyte differentiation pathway. In *Nkx2.1* knockout embryos, which lack *Shh* expression in the medial ganglionic eminence, *PDGFRα* and *Olig2* were downregulated in the telencephalon and ventral diencephalon. In other regions of the telencephalon where *Shh* expression was unaffected, including the prospective amygdala, early oligodendrocyte markers were retained. This was a particularly important observation because the amygdala had not previously been identified as a source of oligodendrocytes.

Some additional observations argue against Shh as an absolute requirement for oligodendrogenesis. First, telencephalic cells from *Shh* null mice can generate oligodendrocytes *in vitro*. To explain this observation, Nery *et al.* propose that Shh acts *in vivo* to override negative regulation of the oligodendrocyte differentiation pathway. A different mechanism that results in the same net loss of the hypothesized inhibitory signal might operate *in vitro*. Second, in the *Nkx2.1* mutant telencephalon, *PDGFRα* expression was restored



a | Oligodendrocytes (red) derived *in vitro* from *Shh*-null neural tissue. The green cells are neurons. **b** | PLAP reporter gene expression in brain tissue infected with SHH-expressing virus. Photographs courtesy of Gord Fishell, Skirball Institute, New York University, USA.