IN THE NEWS

I'm sticking with you

One story that seems to hit the headlines fairly regularly is the continuing investigation into 'stuck-tune syndrome' — that infuriating condition where you can't get a certain tune out of your head. Just when we thought that the story had finally exhausted its news potential, a group in Cincinnati has come up with yet another take on the phenomenon.

It seems that people with neurotic tendencies — as if they didn't have enough to worry about — are more likely to be plagued by a stuck tune than those of a more easy-going disposition. However, researcher James Kellaris reassures us that these people "are not seriously neurotic, but may simply be more prone to worrying and anxiety, and may have neurotic habits like biting pencils or tapping fingernails" (*Reuters*, USA, 24 February 2003).

Health web site WebMD provides a top 10 of the most commonly stuck tunes, presumably to help their readers to empathize with sufferers. Among the offenders in this hellish hit parade are 'Who let the dogs out', the 'Mission Impossible' theme and 'YMCA'. The main criteria for 'sticky' tunes are that they are "relatively simple, repetitive, and contain an element that surprises the listener" (*Reuters*). Kellaris also found that stupid lyrics could contribute significantly to a song's adhesive properties.

So, what's the cure? One common strategy is to try to replace the stuck tune with a more agreeable melody. Alternatively, Kellaris found that "sometimes it helps to sing through the entire song" (*Reuters*), and some people even insist that chewing a cinnamon stick can help them to dislodge a stuck tune. If all else fails, the only option might be to avoid listening to music altogether until the problem goes away.

Heather Wood

CELL BIOLOGY OF THE NEURON

Poles apart

The generation and maintenance of neuronal polarity depends on the differential distribution of key proteins to the axonal or dendritic compartment. This could be achieved in at least two ways — proteins might be specifically targeted to certain projections ('selective delivery'), or they might initially be distributed more evenly through the cell and subsequently become eliminated from certain regions ('selective retention'). In a new paper in *Neuron*, Sampo *et al.* show that both of these systems operate in neurons, and that different mechanisms are employed by different proteins.

The neuronal membrane proteins vesicle-associated membrane protein 2 (Vamp2) and neuron-glia cell adhesion molecule (NgCAM) are both preferentially localized to the axon. Both proteins are transported into dendrites, but very little Vamp2 or NgCAM are detected on the dendritic membrane. Each protein contains an intracellular signal sequence that enables them to undergo endocytosis, so both could potentially be internalized after delivery to the dendritic membrane. Indeed, the behaviour of Vamp2 is consistent with such a model. Sampo *et al.* showed that mutation of the Vamp2 endocytosis signal abolished the polarized distribution of this protein, resulting in equal distribution between axonal and dendritic membrane domains.

By contrast, removal of the NgCAM endocytosis signal had no effect on the subcellular distribution of this protein. However, the authors found that if they removed a series of fibronectin type III-like (FnIII) repeats from the extracellular domain of NgCAM, the molecule could now be incorporated into the dendritic membrane. Furthermore, addition of these repeats to a closely related protein, NrCAM, which does not normally have a polarized distribution, caused this molecule to be directed preferentially to the axonal membrane. This indicates that the FnIII repeats are both necessary and sufficient to ensure that NgCAM is targeted specifically to the axon.

In summary, these findings provide compelling evidence that Vamp2 is eliminated from the dendritic membrane by selective retention, whereas carriers containing NgCAM are prevented from fusing with the dendritic plasma membrane. Sampo *et al.* propose that VAMP2 and NgCAM are transported around the cell by different carrier vesicles, but further experiments will be required to confirm this idea. The answer to this and other questions should provide us with some important new insights into the molecular and cellular mechanisms that underlie neuronal polarity.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Sampo, B. *et al.* Two distinct mechanisms target membrane proteins to the axonal surface. *Neuron* **37**, 611–624 (2003)

WEB SITE

Gary Banker's laboratory: http://www.ohsu.edu/croet/faculty/banker/bankerlab.html

GLIA

A surprising separation

It is possible to dissociate the role of oligodendrocytes in myelination from their involvement in axonal support, according to new research published in *Nature Genetics*. Traditionally, both functions have been thought to be concurrent, but the study of Lappe-Siefke *et al.* shows that knocking out the *Cnp1* gene in mice leads to axonal loss without any apparent effect on myelin structure.

***Cnp1* encodes a cyclic-nucleotide phosphodiesterase (CNP) that seems to participate in RNA metabolism. Although CNP is present in oligodendrocytes and Schwann cells, its function in the nervous system is unknown. The authors knocked out the *Cnp1* gene and failed to see any significant alteration in the biochemical and structural properties of myelin. However, the mutant mice developed progressive motor deficits and died prematurely. More importantly, the brains of the *Cnp1*$^{-/-}$ mice showed marked signs of degeneration that seemed to affect neurons more profoundly than oligodendrocytes. In particular, Lappe-Siefke *et al.* observed profuse axonal swelling that did not result from alterations of the integrity of myelin.**

How CNP participates in the regulation of axonal survival remains an enigma and should be the focus of subsequent studies. But more importantly, these observations indicate that the two main functions of oligodendrocytes can be separated, and establish a double dissociation between them. So, mutations in the gene that encodes the myelin basic protein give rise to the *shiverer* phenotype and are associated with severe demyelination but normal axonal structure.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Lappe-Siefke, C. *et al.* Disruption of *Cnp1* uncouples oligodendroglial functions in axonal support and myelination. *Nature Genet.* 18 February 2003 (doi:10.1038/ng1095)