IN THE NEWS

Hope of a breakthrough?

Excitement is running high over the results of a preliminary clinical trial of a new treatment for Parkinson's disease. Under headlines such as "Drug gave me back my life" (*BBC News Online*, UK, 31 March 2003), the media have been hailing intrastriatal infusions of glial-derived neurotrophic factor (GDNF) as "the most exciting advance in the treatment of Parkinson's disease that has come about in many years" (Michael Zigmond, quoted in *The Globe and Mail*, Canada, 30 March 2003).

The study described five patients who received GDNF infusions. According to the *Globe and Mail*, the trial "surprised scientists when all five patients showed measurable improvement." One of the authors, Clive Svendsen of the University of Wisconsin-Madison, said that the treatment "eliminated the periods of immobility … and reduced or stopped the involuntary movements common to the disease."

Neurosurgeon Steven Gill from Frenchay Hospital in Bristol, UK, led the clinical trial. "We are seeing this as a pretty major step," he told *BBC News Online*. "It needs to be refined, but we have a chance to reverse the progress of Parkinson's."

However, the *New Scientist* (UK, 31 March 2003) sounded a note of caution, pointing out that "more comprehensive studies are needed to determine the drug's efficacy." In the New Scientist, Peter Heywood from Frenchay Hospital, who was also involved in the trial, stressed that this was a small study with no control group, so "there is a vast opportunity for a placebo effect."

Rachel Jones

DEVELOPMENT

Shaping up

Dendrites come in different shapes and sizes, much like most things in this world. In *Drosophila*, the homeodomain protein Cut is crucial for the development of dendrites. In a recent paper in *Cell*, Grueber and colleagues asked how the morphology of a subset of *Drosophila* neurons, the dendritic arborization sensory neurons (DASNs), develop their characteristic branched dendrites.

There are four classes of DASNs (I–IV), which differ in their dendrite morphologies. Class I neurons have the simplest morphology; class II and IV neurons have more complex branching patterns and greater dendritic fields than class I neurons; and class III neurons have a distinctively intricate 'spiked' organization — numerous short terminal branches that extend from the main dendritic trunk.

Drawing from previous studies of DASNs, the authors hypothesized that levels of Cut might correlate with dendritic morphology. This idea was confirmed by their observations. Highly spiked neurons had high levels of Cut, whereas neurons with simple dendrite morphology had low or undetectable levels.

To discern the function of Cut, the authors performed loss-of-function experiments and predicted that, as class III neurons show the highest level of Cut expression, a reduction in Cut levels would lead to a marked change in phenotype. Indeed, class III *cut*$^{-}$ neurons had no higher-order dendritic branching and a reduced number of spikes on the dendrite trunk.

In class IV *cut*$^{-}$ neurons, higher-order branches were lost and overall dendrite length reduced. Loss of Cut function in some class II neurons led to the inhibition of dendritic growth and branching. Interestingly, class I neurons, which showed little or no Cut expression in the wild type, remained unaffected in the *cut*$^{-}$ clones.

If high levels of Cut are responsible for class-specific morphology, then expressing Cut in neurons with low wild-type Cut levels (as in class I neurons) might lead to the development of higher-order dendritic branches. Indeed, the authors found that dendrites of class I neurons that were forced to express Cut (or a mammalian Cut homologue) showed altered morphology that resembled that of class III dendrites.

So, Cut has a role in class-specific dendrite patterning, but how does it perform this function? Does it act in an ON/OFF fashion, switching on the machinery that is required for specific branching? Or, does its function change according to the level at which it is expressed? By increasing levels of Cut in class II and class IV neurons, it was possible to alter the morphologies of their dendrites to become more like those of class III neurons. This ability of neurons to 'jump classes' indicates that Cut functions in a level-dependent manner — the differing levels among neurons being important for their different morphologies.

So, Cut functions to develop the finer morphological features of the specific dendrites. The report indicates that dendrite morphology is not fixed at the time of neuronal birth but rather, it is moulded throughout early development.

Emma Green

References and links

ORIGINAL RESEARCH PAPER Grueber, W. B., Jan, L. Y. & Jan, Y. N. Different levels of the homeodomain protein Cut regulate distinct dendrite branching patterns of *Drosophila* multidendritic neurons. *Cell* **12**, 805–818 (2003)