IN THE NEWS

Winning channels

Roderick MacKinnon has been widely tipped to win a Nobel Prize for his groundbreaking work on the structure and function of ion channels — and this year he shares the Chemistry prize with Peter Agre, the discoverer of aquaporins. Unusually, the work for which MacKinnon is honoured was published just five years ago, in 1998.

As the *New Scientist* (8 October) explains: "MacKinnon's breakthrough in laying bare the structure of an ion channel for the first time was achieved by turning to a much simpler example of an ion channel than his competitors." The principles that were revealed by the structure of a bacterial potassium channel could be applied to the more complex channels found in neurons. The Nobel Academy statement said, "Thanks to this contribution we can now 'see' ions flowing through channels that can be opened and closed by different cellular signals."

On the day the prize was announced, MacKinnon was lauded by his colleagues. Talking to the *Baltimore Sun* (9 October), Christopher Miller, MacKinnon's former mentor, described him as "an offscale brilliant scientist" who has "completely changed the field." MacKinnon himself reportedly had trouble accepting the fact that he had won. He described to a press conference how he had been called at his holiday home in Cape Cod with the news. He then searched the internet but, finding no stories to confirm the news, had to wait for another call from Rockefeller. But, he said, "I wanted confirmation from Sweden. I realized after this morning that no one could reach me… I'd better buy a cell phone." (*Reuters*, 8 October.)

Rachel Jones

CELL BIOLOGY OF THE NEURON

Food and fertility

It is well known that starvation reduces fertility, and this makes sense from an evolutionary perspective because it is disadvantageous to produce large numbers of offspring when food supplies are scarce. What is the neurobiological basis of the link between feeding and fertility? Reporting in the *Journal of Neuroscience*, Sullivan *et al.* provide some new insights.

The hypothalamic gonadotropin-releasing hormone (GnRH) neurons provide a crucial neuroendocrine interface between the brain and the reproductive organs. The GnRH neurons receive input from γ-aminobutyric acid (GABA)-releasing neurons. GABA is usually an inhibitory neurotransmitter for adult neurons, but it is excitatory for GnRH neurons.

Sullivan *et al.* initially hypothesized that fasting converts the GABA-mediated excitation of GnRH neurons to inhibition. However, this was not borne out by their findings. After a 48-hour fast in female mice (which is sufficient to halt the progression of the reproductive cycle), $GABA_A$ receptor activation was still excitatory. The authors next asked whether the activity of presynaptic GABA neurons was changed by fasting. After fasting, the GnRH neurons still showed spontaneous GABA-mediated excitatory postsynaptic currents (sPSCs), but the frequency was reduced. Some GABA-releasing neurons express receptors for the satiety hormone leptin, and the authors showed that treating animals with leptin could reverse the effects of fasting on sPSC frequency.

There is also evidence that leptin potentiates the response of GnRH neurons to $GABA_A$ receptor activation. Sullivan *et al.* measured

NEURODEGENERATIVE DISORDERS

Neurodegeneration — it's a snip

Although more than one in every five patients with AIDS develops HIV dementia, the mechanisms by which infection leads to neurodegeneration are unclear. A study published in *Nature Neuroscience* provides evidence for a new neurotoxic pathway that is initiated by HIV-infected macrophages.

Zhang *et al.* found that conditioned medium from human macrophages infected with HIV was toxic to neurons *in vitro*. The medium contained elevated levels of the matrix metalloproteinase precursor pro-MMP2. When pro-MMP2 is added to a neuronal culture, it is activated on the neuronal cell surface by membrane type-1 MMP. The idea that activated MMP2 was causing the neuronal death in culture was supported by the ability of the MMP inhibitor Prinomastat to prevent neuronal death after treatment with pro-MMP2. The same group previously showed that MMP2 can cleave the chemokine stromal cell-derived factor 1α (SDF1), which is expressed by neurons and astrocytes. In the new study, they show that cleaved SDF1 binds to neuronal membranes and induces neuronal apoptosis. Pertussis toxin, an inhibitor of G-protein-coupled receptors, prevented this effect, indicating that cleaved SDF1 acts through a G-protein-coupled receptor.

To investigate whether this pathway was active *in vivo*, the authors implanted cleaved SDF1 into the striatum of mice, where it caused an increase in neuronal loss and gliosis when compared with animals treated with uncleaved SDF1 or vehicle. Similar effects were produced by implantation of conditioned medium from HIV-infected macrophages. Treatment with pro-MMP2 also produced behavioural abnormalities — specifically, the mice rotated towards the site of the