

## EDITORIAL

# Acting on Impulse: Neuronal Function and Dysfunction

The basic events involved in the passage of nerve impulses through the nervous system have been broadly understood for many decades. However, advances on many fronts in recent years have added considerably to our knowledge of this process and revealed a remarkable complexity in the contributing molecular interactions. This complexity is apparent in the multiple families and subtypes of receptors that mediate the cellular responses to neurotransmitters and in the sophisticated molecular machinery responsible for the synthesis, release and termination of action of these substances. Ongoing studies are identifying a highly developed capacity for the control and modulation of neurotransmission at multiple levels. Furthermore, alterations in the strength of interactions between neurones mediated by modifications of the molecules involved in chemical transmission are now recognised as common responses to normal stimuli. They are widely considered to be important contributors to the development of complex behaviours. These recent advances in understanding normal function of the nervous system have been accompanied by new insights into the molecular basis of debilitating neurological diseases, including stroke, Alzheimer's disease and Parkinson's disease, in which neurotransmission is disrupted.

This issue's Showcase on Research presents four mini-reviews that explore important aspects of neuronal function in health and disease. The first two articles focus on features of normal neurotransmission that also have potential relevance for studies of the functions of some proteins in non-neural cells. Peter Dunkley and Phillip Dickson examine the role of protein phosphorylation in ensuring that the intracellular levels of catecholamine neurotransmitters and hormones are restored

following exocytotic release. This review discusses the likely contribution of hierarchical phosphorylation of the enzyme tyrosine hydroxylase as a modulator of this process. The mini-review by Ann Mitrovic and Robert Vandenberg discusses aspects of the structure and function of glutamate transporters. This family of transporters is essential for rapidly terminating the action of glutamate, the major neurotransmitter of the mammalian central nervous system. Failure of glutamate uptake modifies neurotransmission and can lead to neuronal degeneration. The article examines the structural basis for the transport function of these proteins and particularly addresses the surprising finding that they are also chloride channels.

The other two articles discuss aspects of abnormal neuronal function. The venom of cone shells has provided a rich source of toxins that target proteins including receptors, ion channels and transporters involved in many facets of neurotransmission. Richard Lewis summarises the properties and targets of the cone snail toxins and discusses their use in the development of novel treatments for pain and other neurological conditions. In the final article, David Small, Dusan Losic, Lisa Martin, Bradley Turner, Anna Friedhuber and Marie-Isabel Aguilar discuss the implications of recent findings on the pathogenesis of Alzheimer's disease. Altered neurotransmission due to modification or death of brain neurones is a major contributor to the devastating symptoms of this disorder. This article examines possible novel avenues for treatment that have arisen from advances in understanding the molecular basis of this disease.

These articles provide a small sample of some recent insights into neuronal function. Despite the progress, much remains to be learned. This makes it an exciting time to be involved in molecular neuroscience research.

**Neil Sims**

*Department of Medical Biochemistry and Centre for Neuroscience, School of Medicine, Flinders University, SA 5042*

### Cover Illustration – Coeliac ganglion PJ.

*This image shows sympathetic neurons in a mouse coeliac ganglion. The cells, after fixation, were triple-labelled using antisera against tryptophan hydroxylase (red), neuropeptide Y (green) and vasoactive intestinal peptide (blue). Image supplied by Phil Jobling, Judy Morris and Ian Gibbins, Centre for Neurosciences, Flinders University, Adelaide.*

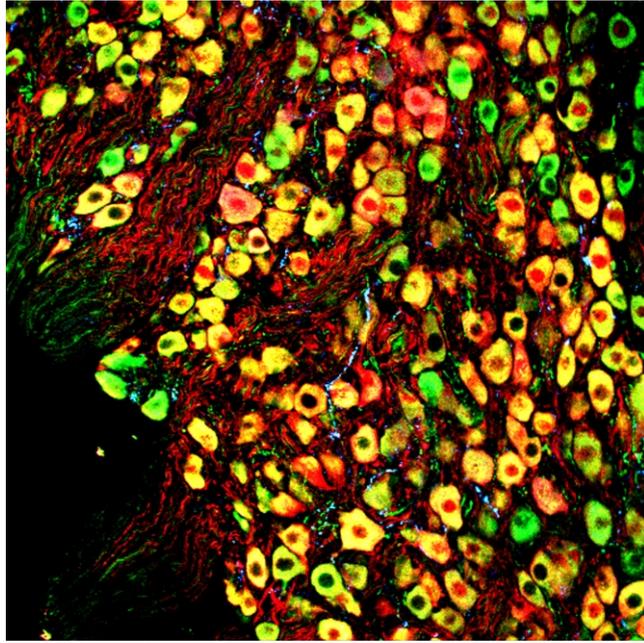
### Acting on Impulse: Neuronal Function and Dysfunction

**Guest Editor: Neil Sims**

- 5 Catecholamine Synthesis: A Hierarchy of Controls?  
*Peter Dunkley and Phillip Dickson*
- 8 Glutamate Transporters: Redefining the View of a Transporter  
*Ann Mitrovic and Robert Vandenberg*
- 12 Conotoxins as Selective Inhibitors of Neuronal Ion Channels, Receptors and Transporters  
*Richard Lewis*
- 15 New Strategies for the Treatment of Alzheimer's Disease  
*David Small, Dusan Losic, Lisandra Martin, Bradley Turner, Anna Friedhuber and Marie-Isabel Aguilar*

### In the Next Issue...

In April, Showcase on Research will be on **DNA Replication and Repair** – Guest Editor: Nick Dixon



Front Cover Image