IN BRIEF

ION CHANNELS

Distinct contributions of $Na_V1.6$ and $Na_V1.2$ in action potential initiation and backpropagation

Hu, W. *et al. Nature Neurosci.* **12**, 996–1002 (2009)

Both distal and proximal regions of the axon initial segment (AIS) have high concentrations of Na^+ channels; however, action potentials (APs) are initiated mainly in the distal AIS. To understand this disparity, the authors combined immunostaining, electrophysiology and modelling of pyramidal neurons. They found that $Na_V1.6$ channels accumulate at the distal AIS, where their low activation threshold facilitates AP initiation, whereas $Na_V1.2$ channels are concentrated at the proximal AIS and enable AP backpropagation to the soma and dendrites.

NEURODEGENERATIVE DISEASE

Inclusion formation and neuronal cell death through neuron-to-neuron transmission of α-synuclein

Desplats, P. *et al. Proc. Natl Acad. Sci. USA* **106**, 13010–13015 (2009)

Repression of α-synuclein expression and toxicity by microRNA-7

Junn, E. *et al. Proc. Natl Acad. Sci. USA* **106**, 13052–13057 (2009)

Increased levels of α-synuclein and its aggregates characterize many neurodegenerative diseases. Cultured neurons have been shown to secrete α-synuclein that in turn was endocytosed by co-cultured neurons. Desplats *et al.* showed that cultured primary neurons underwent apoptosis when exposed to α-synuclein and tested whether neuron-to-neuron transmission of α-synuclein might underlie the propagation of disease pathology in neurodegenerative disorders. Indeed, neurons expressing human α-synuclein that were engrafted into mice with Parkinson's disease (PD)-like pathology formed inclusion bodies that stained positive for human α-synuclein. In another study, Junn *et al.* found that microRNA 7 (miR-7) is a negative regulator of α-synuclein expression. miR-7 is expressed at high levels in neurons of the substantia nigra — the brain region that is most affected in PD — compared with other brain regions in mice. Treatment with 1-methyl-4-phenylpyridinium, which is used to model PD in mice, reduced miR-7 levels and increased α-synuclein mRNA levels in the substantia nigra. These studies show that α-synuclein might contribute to the spread of neuronal pathology and that miR-7 regulates α-synuclein expression. miR-7 might therefore be a target for drug development.

SYNAPTIC TRANSMISSION

Ca^{2+} and calmodulin initiate all forms of endocytosis during depolarization at a nerve terminal

Wu, X.-S. *et al. Nature Neurosci.* **12**, 1003–1010 (2009)

Following neurotransmitter release, endocytosis completes the vesicle cycle and maintains synaptic transmission by recycling vesicles. Different types of endocytosis can take place, including slow endocytosis, bulk endocytosis and rapid endocytosis; however, what triggers endocytosis and determines the type of endocytosis was unknown. Here, the authors show that Ca^{2+} influx initiates all known forms of vesicle endocytosis through interactions with the Ca^{2+} sensor calmodulin, and that the speed of endocytosis increases as Ca^{2+} influx increases.