IN BRIEF

SYNAPTIC TRANSMISSION

GABA receptor crosstalk

The inhibitory neurotransmitter GABA activates both ionotropic type A GABA receptors ($GABA_A$Rs) and metabotropic $GABA_B$ receptors ($GABA_B$Rs). Two independent studies in rat brain slices now show that activation of postsynaptic $GABA_B$Rs enhances signalling through extrasynaptic $GABA_A$Rs. Activity-dependent changes in GABA concentration activate postsynaptic $GABA_B$Rs leading to slow inhibition, whereas high-affinity $GABA_A$Rs at extrasynaptic sites are activated tonically by ambient GABA. This tonic inhibitory tone has been implicated in synaptic integration, anxiety-related behaviours and seizure susceptibility. Tao *et al.* show that activation of postsynaptic $GABA_B$Rs enhances $GABA_A$R-mediated currents caused by exogenous GABA or the $GABA_B$R agonist baclofen in dentate gyrus granule cells (DGGCs) but not in CA1 pyramidal neurons or cortical layer 2/3 pyramidal neurons. Connelly *et al.* report similar crosstalk in thalamocortical neurons of the ventrobasal thalamus and cerebellar granule cells as well as in DGGCs.

ORIGINAL RESEARCH PAPERS Tao, W. *et al.* Postsynaptic $GABA_B$ receptors enhance extrasynaptic $GABA_A$ receptor function in dentate gyrus granule cells. *J. Neurosci.* **33**, 3738–3743 (2013) | Connelly, W. M. *et al.* $GABA_B$ receptors regulate extrasynaptic $GABA_A$ receptors. *J. Neurosci.* **33**, 3780–3785 (2013)

SIGNAL TRANSDUCTION

JACOB reveals the origin of NMDAR signals

Signalling through NMDA receptors (NMDARs) can trigger cell death or survival depending on whether activation of such receptors occurs at extrasynaptic or synaptic sites, respectively. It is unclear how these opposing signals are communicated to and discriminated by the nucleus, but the authors of this study show that differential phosphorylation of JACOB relays the origin of the NMDAR signal to the nucleus. Synaptic NMDAR activation induces phosphorylation of JACOB at Ser180 by ERK1/2 (extracellular receptor-activated MAP kinase 1 and 2) and ERK1/2-dependent nuclear translocation. During nuclear transit, phosphorylated JACOB associates with the intermediate filament protein α-internexin, which hinders dephosphorylation. Once in the nucleus, phosphorylated JACOB inactivates the transcription factor cyclic AMP-responsive element-binding protein (CREB) to promote cell survival and enhance synaptic plasticity.

ORIGINAL RESEARCH PAPER Karpova, A. *et al.* Encoding and transducing the synaptic or extrasynaptic origin of NMDA receptor signals to the nucleus. *Cell* **152**, 1119–1133 (2013)

NEUROPROTECTION

Neuronal immune signatures

Little is known about why certain types of neurons are more susceptible to microbial infection than others. Diamond and colleagues examined the differential permissivity of neurons from distinct brain regions to infection by several positive-stranded RNA viruses, such as West Nile virus, *ex vivo* and *in vivo*. They found that granule cell neurons have a higher basal level of expression of type I interferon-inducible genes than cortical neurons, making them more resistant to infection by such viruses. Furthermore, the epigenetic state and microRNA-mediated regulation of these interferon-stimulated genes correlated with the enhanced antiviral response of granule cell neurons. These unique, innate immune signatures may explain why neurons from evolutionarily distinct brain regions have different susceptibility to infection.

ORIGINAL RESEARCH PAPER Cho, H. *et al.* Differential innate immune response programs in neuronal subtypes determine susceptibility to infection in the brain by positive-stranded RNA viruses. *Nature Med.* 3 Mar 2013 (doi:10.1038/nm.3108)