

IN BRIEF

GLIA

Diffusible danger

The growth of high-grade glioma (HGG) and proliferation of glial precursor cells are enhanced by neuronal activity, but the mechanisms are not known. A new study shows that optogenetic stimulation of cortical neurons in a patient-derived glioblastoma xenograft model in mice increased precursor proliferation. Crucially, a similar effect was obtained by application of conditioned medium from activated neurons to cultured HGG, suggesting that the mitogen responsible was secreted. Indeed, the secreted mitogen was revealed to be neuroligin 3, which, by acting through the phosphatidylinositol 3-kinase–mammalian target of rapamycin pathway, was necessary and sufficient to promote HGG growth.

ORIGINAL RESEARCH PAPER Venkatesh, H. S. *et al.* Neuronal activity promotes glioma growth through neuroligin-3 secretion. *Cell* <http://dx.doi.org/10.1016/j.cell.2015.04.012> (2015)

NEURODEGENERATION

Neurodegeneration takes its TOLL

Sterile- α and TIR motif-containing protein 1 (SARM1) is an essential mediator of axon degeneration, and increased levels of NAD⁺ are neuroprotective, but the link between the two remains unclear. A recent paper showed that, in mice, dimerization of the Toll–interleukin receptor (TIR) domain of SARM1 induced rapid breakdown of NAD⁺ and was sufficient to induce axon degeneration; this effect was reversed by increased synthesis of NAD⁺, suggesting that NAD⁺ loss is a key step in SARM1-mediated axon degeneration.

ORIGINAL RESEARCH PAPER Gerdtz, J. *et al.* SARM1 activation triggers axon degeneration locally via NAD⁺ destruction. *Science* **348**, 453–457 (2015)

COGNITIVE NEUROSCIENCE

Gridlock

Representations of large-scale spaces by grid cells in the medial entorhinal cortex (mEC) requires uniform firing patterns throughout the space being navigated. However, boundaries can disrupt grid-cell firing patterns, suggesting an influence of local environmental cues. Recordings from mEC neurons in a two-compartment chamber showed that, although mEC-cell firing was initially influenced by local cues, firing patterns subsequently formed a single, continuous grid representation that spanned both compartments. Thus, grid cells can uniformly cover the space to be navigated and support large-scale spatial navigation.

ORIGINAL RESEARCH PAPER Carpenter, F. *et al.* Grid cells form a global representation of connected environments. *Curr. Biol.* **25**, 1176–1182 (2015)

GLIA

The devil in the detail

The importance of astrocytic Ca²⁺ fluctuations in synaptic function has been challenged by the finding that mice devoid of inositol-1,4,5-triphosphate type 2 receptors (IP3R2s) — which are enriched in astrocytes — show normal neuronal and vascular responses. Although changes in intracellular Ca²⁺ in astrocyte somata were abolished in mice lacking IP3R2, they were retained in astrocytic processes. Moreover, Ca²⁺ fluctuations were modulated by both neurotransmitter release and pharmacological stimuli, thus providing a possible explanation for the apparently contradictory earlier findings.

ORIGINAL RESEARCH PAPER Srinivasan, R. *et al.* Ca²⁺ signaling in astrocytes from *Ip3r2*^{-/-} mice in brain slices and during startle responses *in vivo*. *Neuron* **18**, 708–717 (2015)