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IN BRIEF

NEURONAL DEVELOPMENT

Forcing axon pathfinding

Developing axons grow through brain tissue to reach their targets — a process termed pathfinding. The regulation of this process involves chemical cues, but it is not known whether the mechanical forces encountered by the axon as it grows through brain tissues also play a part. Here, Koser *et al.* show that, in *Xenopus laevis*, the growing axons of retinal ganglion cells express the mechanosensitive ion channel piezo 1, which detects differences in tissue stiffness and, as a result, promotes the trajectory of axon growth towards softer tissues.

ORIGINAL ARTICLE Koser, D. E. *et al.* Mechanosensing is critical for axon growth in the developing brain. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4394 (2016)

NEUROGENETICS

Accelerating towards mental illness

The human genome contains conserved loci that show accelerated divergence from other species — called human accelerated regions (HARs) — but the effect of mutations in these regions on brain function is poorly understood. Doan *et al.* found that the levels of two types of mutations — *de novo* copy-number variations and biallelic point mutations — were increased in HARs of people with autism spectrum disorder (ASD) compared with healthy individuals. Furthermore, they found that these mutations were located in the enhancer sequences of genes that were previously implicated in this disorder and brain function, suggesting a potential role for mutations in HARs in ASD and cognition.

ORIGINAL ARTICLE Doan, R. N. *et al.* Mutations in human accelerated regions disrupt cognition and social behavior. *Cell* http://dx.doi.org/10.1016/j.cell.2016.08.071 (2016)

SYNAPTIC PLASTICITY

TARP target

Long-term potentiation (LTP) at excitatory hippocampal synapses involves the postsynaptic insertion of AMPA receptors triggered by calcium/calmodulin-dependent protein kinase type II (CaMKII)-mediated protein phosphorylation, but the CaMKII substrate remains unclear. Here, mice expressing a mutant form of auxiliary transmembrane AMPA receptor regulatory protein γ8 (TARP γ8), which lacks CaMKII phosphorylation sites, showed reductions in LTP, postsynaptic AMPA receptor insertion and performance in memory tasks compared with controls. This suggests that TARP γ8 is an important substrate for CaMKII during LTP induction.

ORIGINAL ARTICLE Park, J. *et al.* CaMKII phosphorylation of TARPγ-8 is a mediator of LTP and learning and memory. *Neuron* http://dx.doi.org/10.1016/j.neuron.2016.09.002 (2016)

NEUROIMMUNOLOGY

Waking the immune system

Recent evidence suggests that narcolepsy, a disorder that results from the loss of orexinergic neurons of the lateral hypothalamus, has an autoimmune aetiology, but the underlying mechanisms have not been elucidated. Here, haemagglutinin (which acted as an artificial 'self-antigen') was selectively expressed in mouse hypothalamic orexin-positive neurons, and haemagglutinin-specific T cells were then transferred into these mice. Hypothalamic infiltration by cytotoxic CD8 T cells (CTLs) (but not T helper 1 cells) was associated with destruction of orexinergic neurons and development of a narcolepsy-like phenotype, suggesting a role for CTLs in narcolepsy.

ORIGINAL ARTICLE Bernard-Valnet, R. *et al.* CD8 T cell-mediated killing of orexinergic neurons induces a narcolepsy-like phenotype in mice. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1603325113 (2016)