IN BRIEF

LEARNING AND MEMORY

piRNA-regulated memory?

Piwi-interacting RNAs (piRNAs) are small non-coding RNAs that have an unclear function. piRNA expression was thought to be limited to germline cells, but in a new study, Kandel and colleagues have detected piRNAs in a microRNA library from the CNS of *Aplysia californica*. Experiments involving knockdown of Piwi in cultured *A. californica* neurons revealed that Piwi–piRNA complexes enhance serotonin-induced long-term facilitation — a form of synaptic plasticity implicated in long-term memory. These complexes exerted their effects through methylation of the promoter region of the gene encoding CREB2, a major transcriptional repressor of memory formation in *A. californica*, leading to a decrease in CREB2 expression.

ORIGINAL RESEARCH PAPER Rajasethupathy, P. *et al.* A role for neuronal piRNAs in the epigenetic control of memory-related synaptic plasticity. *Cell* **149**, 693–707 (2012)

NEURODEGENERATIVE DISEASE

The pyroglutamylated seed

Pyroglutamylated (pE) forms of amyloid-β (Aβ) have been proposed to have a role in the pathogenesis of Alzheimer's disease, but the underlying mechanism is unclear. A new study shows that $A\beta_{3(pE)–42}$ can form short oligomers with $A\beta_{1–42}$ — which is widely implicated in Alzheimer's disease pathogenesis — and that these arrays are more cytotoxic to cultured neurons than oligomers of $A\beta_{1–42}$ alone. This cytotoxicity is tau-depedent. Moreover, oligomers containing 5% $A\beta_{3(pE)–42}$ and 95% $A\beta_{1–42}$, in the presence of monomeric $A\beta_{1–42}$, seem to act as seeds for further cytotoxic oligomer formation, suggesting a means by which pE-Aβ could initiate disease.

ORIGINAL RESEARCH PAPER Nussbaum, J. M. *et al.* Prion-like behaviour and tau-dependent cytotoxicity of pyroglutamylated amyloid-β. *Nature* 2 May 2012 (doi:10.1038/nature11060)

NEURODEGENERATIVE DISEASE

The interneuron link

Cognitive decline and altered network activity are features of Alzheimer's disease, but it is unknown how they are mechanistically linked. Epileptiform discharges, indicating network hypersynchrony, have been detected in a mouse model of this disorder (hAPP mice). Here, the authors show that this hypersynchrony is linked to reductions in gamma oscillatory activity, which is generated by parvalbumin-positive (PV^+) interneurons. In hAPP mice and patients with Alzheimer's disease, PV^+ interneurons showed reduced expression of the voltage-gated sodium channel subunit Nav1.1, and restoration of Nav1.1 expression reduced network hypersynchrony and memory deficits in hAPP mice. Thus, interneuron deficits may link cognitive dysfunction and altered network activity in Alzheimer's disease.

ORIGINAL RESEARCH PAPER Verret, L. *et al.* Inhibitory interneuron deficit links altered network activity and cognitive dysfunction in Alzheimer model. *Cell* **149**, 708–721 (2012)