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One cyclin for adult neurogenesis

In recent years, scientists have found evidence that new neurons arise in the brains of adult mammals, but little is known about the underlying mechanisms. Now, on page 209, Kowalczyk et al. find that in neurogenic regions of the adult brain only one cyclin D protein, cyclin D2, is required for neural precursors to enter the cell cycle. To determine which cyclins were required for adult neurogenesis, the team analyzed mice lacking either the cyclin D1 or D2 gene. Neuronal proliferation in the hippocampus, which is the region required for memory formation, was completely inhibited in cyclin D2 mutants, but was unaffected in cyclin D1 mutants. Astrocytes continued to proliferate in mice lacking D2, albeit to a limited extent, suggesting that the gene is absolutely required for neurogenesis but not for glial cell proliferation.

By contrast, dividing neural precursors isolated from mouse pups contain all three cyclin D proteins, 1, 2, and 3. Thus, there is a mechanistic distinction between adult and developmental neurogenesis. The researchers hope to use cyclin D2’s newly defined role in adult neurogenesis to test how neural proliferation relates to the formation or extinction of memories in adult animals. JCB

One protein, two pools

The cytoplasmic protein β-catenin is essential for both intercellular adhesion and intracellular Wnt signaling. Invertebrates have multiple genes to cover the multiple functions, but on page 339 Gottardi and Gumbiner propose that vertebrate cells make do with one gene by maintaining different pools of protein for the different roles. Different folding may distinguish the adhesion and proliferative signaling functions.

Cofractionation experiments showed that β-catenin that interacts with cadherin is in a heterodimer with α-catenin, but Wnt signaling induces a monomeric form of β-catenin that interacts with a transcription factor complex. After enrichment for cadherins, β-catenin can be detected using antibodies to either NH$_2$-terminal or COOH-terminal regions; but in the cadherin-free fraction only the NH$_2$-terminal antibody binds. The team hypothesizes that the β-catenin protein is folded back on itself in its monomeric form and, as such, is available for transcription complex binding but not for adhesion duties.

Gottardi speculates that a post-translational modification is responsible for the conformational change but does not yet know what that modification is. Furthermore, she thinks this sort of molecular segregation may be a common mechanism cells use to allow one protein to do multiple jobs, without the more common function soaking up all the protein required for a temporally regulated one. JCB

Vesicle biogenesis potentiation

The AP-3 adaptor protein exists in two forms, A and B. Loss of the ubiquitously expressed AP-3A complex leads to widespread problems in lysosome functions. Now, on page 293, Nakatsu et al. show that loss of neuronal-specific AP-3B function causes defects in hippocampal function in mice, increases the magnitude of long-term potentiation, and makes the animals susceptible to seizures.

The team generated mice lacking the 3B-specific subunit μ3B. The animals had no gross morphological brain defects, but were prone to spontaneous and triggered seizures. At hippocampal synapses, the number and size of synaptic vesicles was reduced, although baseline release of the neurotransmitters GABA and glutamate were normal. However upon neural stimulation, the mutants released less GABA, the inhibitory neurotransmitter, than did wild-type animals. Nakatsu et al. found that synaptic vesicles had reduced integration of the GABA-specific transporter VGAT but normal levels of the glutamate transporter VGLUT.

The team hypothesizes that AP-3B is critical for the biogenesis of a subset of synaptic vesicles in hippocampal neurons and that VGAT may be a specific cargo for AP-3B. Also, because there is more glutamate than GABA available in the system, a reduction in glutamate vesicle biogenesis may be compensated for by efficient vesicle recycling at the plasma membrane. JCB

Adult neurogenesis is absent in a cyclin D mutant (top) but normal in wild-type progeny (bottom).