Of coilin and Cajal bodies

Cajal bodies (CBs), until recently known as coiled bodies, are revealed by silver staining as prominent spots in nuclei. Their purpose has been mostly a mystery since their discovery 98 years ago. They look similar to nucleoli, the cell’s ribosome factories, and often lie close to them. Small nuclear ribonucleoproteins (snRNPs), components of the pre-mRNA splicing machinery, are known to be concentrated in the bodies. Although the presence of CBs is not required for splicing, cells that are particularly active in transcription have CBs.

For the last decade, cell biologists have used the protein coilin as a marker for CBs. It is the only molecule known to be uniquely concentrated in the bodies, although it is also expressed diffusely throughout the nucleus, in all tissues. Tucker et al. (page 293) knocked out coilin in mice, and were surprised to find that at least some of the mutants are viable and appear normal. When they studied cells derived from the mutant mice, they found what they term “residual CBs.” These foci contain some of the typical proteins found in CBs, but they fail to stain brightly when treated with silver, and lack two complexes that are normally prominent components of CBs: snRNPs and the SMN (survival motor neuron) protein complex. The authors conclude that coilin is necessary for recruiting these factors to CBs. Indeed, when they transiently expressed wild-type coilin in the mutant cells, bodies formed that contain both the previously missing factors.

A dystroglycan ligand in the brain

Dystroglycans are present on the surfaces of cells throughout the body, anchoring cells in the matrix that surrounds them. This function is conspicuously important for muscle cells. Defects in the protein dystrophin, which is connected to dystroglycan, destabilize the connection of muscle cells to their matrix and cause muscular dystrophy. Dystroglycans are abundant in the brain as well, even though neurons are not embedded in a classical extracellular-matrix mesh of proteins, so the role of dystroglycans on neurons and on supporting glia cells has not been clear. Sugita et al. (page 435) find that instead of anchoring cells to the outside matrix, dystroglycans in the nervous system bind to the membrane proteins neurexins, and therefore may help connect cells to each other.

Neurexins are a family of cell-surface proteins specific to neurons. Three genes encode neurexins, but rampant alternative splicing creates hundreds, if not thousands, of forms of the proteins. In a sample of 100 neurons, each neuron could have a different set of neurexins. The authors speculated that these diverse cell-surface proteins may regulate the formation of connections within the brain.

The study describes the search for the natural binding partners of neurexins. The black widow spider toxin is one known ligand for neurexins. The authors showed that the toxin competes with dystroglycan for binding to neurexins. Multiple other lines of evidence imply that in the brain dystroglycan and neurexin are connected. The connection may be regulated by alternative splicing, which can change the surfaces of repeated domains in neurexin, thereby affecting dystroglycan binding.

The asymmetric bond between these two types of cell-surface proteins could play an important part in the organization of synapses. The study also has implications for muscular dystrophy, which is often associated with cognitive defects. Although the relevant proteins have not yet been localized to synapses, it is possible that a dystrophin deficiency could destabilize dystroglycan–neurexin links and thus disturb connections between neurons in the brain.