Sgo stabilizes glue and microtubules

Sister chromosomes in mitosis must stick together even as robust kinetochore microtubules try to pull them apart, with the resulting tension helping to correct attachment errors. Now, Adrian Salic, Jennifer Waters, and Timothy Mitchison (Harvard Medical School, Boston, MA) have found a protein that works on both sides of this glue-and-pull equation.

Using an in vitro assay for proteins that stimulate microtubule formation, the team isolated the human Shugoshin (Sgo) protein. Yeast and fly homologues are essential for mitosis and their loss is known to cause dramatic defects in sister centromere cohesion in meiosis.

In affinity purification experiments, human Sgo brings down tubulin, and the interaction appears to be direct. Sgo localizes to the kinetochore and is degraded by the anaphase-promoting complex before the cell exits mitosis.

Sgo siRNA causes mitotic arrest and failed centromere cohesion; single chromosomes are found scattered over the entire spindle. Any remaining paired kinetochores are closer than normal, indicating a lack of tension, and fluorescently marked kinetochore microtubules turn over much more rapidly. The double function of Sgo as a kinetochore–microtubule stabilizing protein and a cohesion protein is “an interesting twist, but not unbelievable,” says Salic. 

Reference: Salic, A., et al. 2004. Cell. 118:567–578.

Astrocytes orchestrate neuronal synchrony

Astrocytes are known to modulate synaptic communication between neurons. Now, Olivier Pascual (University of Pennsylvania, Philadelphia, PA), Tommaso Fellin, Giorgio Carmignoto (University of Padova, Italy), and colleagues report that astrocytes can elicit slow inward currents outside of synapses and thus activate synchronous responses in multiple neurons.

During periods of intense neural activity, calcium oscillations are triggered in astrocytes, inducing the cells to release glutamate. Fellin et al. find that this glutamate release stimulates neuronal activity in hippocampal slices. Photolysis of caged Ca$^{2+}$ in single astrocytes almost exclusively activates the extrasynaptic NMDA receptors in CA1 pyramidal neurons. Thus, the astrocytes are triggering neural activity by turning on receptors outside of the synaptic junction itself—receptors that are abundant but whose role has been unknown.

Based on electrical activity and fluorescent probes, the team also found that astrocytes induce synchronous responses in multiple neurons. Although they can’t yet say whether a single astrocyte is able to activate multiple neurons, they hypothesize that one glutamate release event may be sufficient to reach the dendrites of several neurons.

“A synchrony is central to information processing,” Carmignoto says. And because the astrocytes only release glutamate when the surrounding neural activity is high, their activation of several neurons at once may be important in memory formation or long-term potentiation. The coordinated activity also hints that the astrocytes may be involved in the pathophysiology that underlies epilepsy, which is characterized by coordinated waves of hyperactive neurons.

Reference: Fellin, T., et al. 2004. Neuron. 43:729–743.