Nervous chemokines

Guidance molecules from the immune and nervous systems are getting mixed up in each others business. Yan Zhu, Yi Rao (Washington University, St. Louis, MO), and colleagues have found that a leukocyte attractant called stromal-derived factor 1 (SDF-1) is the main factor that entices embryonic cerebellar neurons to their correct location.

SDF-1 is a chemokine—a peptide that attracts leukocytes by activating a G protein signaling cascade. In contrast, neuronal guidance molecules such as the netrins, ephrins, and Slit are proteins that bind single transmembrane receptors linked to a variety of downstream signaling pathways. The two worlds were bridged last year when Rao found that the neuronal repellant Slit could also inhibit leukocyte chemotaxis. Now, he has completed the loop by confirming SDF-1’s function in the brain.

This function was suspected when immunologists made mice lacking SDF-1 and noted a cerebellar defect, whereas others showed that SDF-1 affected either chemotaxis or the motility level of neurons. In Rao’s experiments, collagen blocks embedded with SDF-1 attracted embryonic neuronal precursor cells, and the meninges (the outside lining of the brain) attracted the cells only if the gene encoding SDF-1 had not been knocked out. The meninges thus uses SDF-1 to attract the cells before they go on to form structures involved in motor control and other functions.

The two worlds of chemokines and neuronal guidance may have arisen, says Rao, because “if your assay is set up in a particular way, you get what you are looking for.” But now he thinks that factor participation in both immune and nervous systems will turn out to be “a common thing.” The next place to look may be in blood vessels. Slit is expressed in the endothelium, so it may keep noninflammatory immune cells from escaping the blood.


Plasmid segregation actin’ up

Polymerization of an actin-related protein may drive segregation of a bacterial plasmid, according to Jakob Møller-Jensen, Kenn Gerdes (University of Southern Denmark, Odense, Denmark), and colleagues.

Segregation in bacteria was thought to be a rather passive affair, with DNA attaching to the membrane and getting dragged along as cell growth led to membrane expansion. That model was challenged when DNA replication was found to be localized to one area at the cell center, followed by rapid movement of both plasmids and chromosomal DNA from midcell to more polar sites.

In the meantime, Gerdes had been working on the segregation requirements for the R1 plasmid. He had found that ParR binds to the parC centromere-like site on the plasmid, and that ParM binds to ParR. Then, Møller-Jensen tried detecting native ParM directly, using immunofluorescence, and saw axial filaments in almost half the cells. “We were very excited,” he says, “because this explained a lot of open questions to us.” Filament formation in vivo (and, at lower ParM concentrations, in vitro) required both parC and ParR, suggesting that a parC-ParR complex nucleates the formation of a filament that then drives separation of replicated plasmids. The active nucleator may be dimers of parC-ParR, which form only after replication thanks to the cis-restricted activity of ParR.

ParM filaments can go through multiple cycles of polymerization (which requires ATP) and depolymerization (which requires hydrolysis of the bound ATP). After the majority of the cell’s ParM has polymerized into filaments, a gradual conversion into the ADP form may trigger the fragmentation that the authors saw both in vivo and in vitro.

This very dynamic behavior of ParM makes it very different from MreB, a similar filament-forming bacterial protein that helps maintain cell shape. But the two may not be so different after all. “Being a plasmid molecule, [ParM] may have to make it on its own,” says Møller-Jensen. But MreB, he says, may coopt other proteins to help make it the bacterial equivalent of a mitotic spindle.

Let there be a channel

A newly discovered rhodopsin does double duty as light detector and proton channel, say Georg Nagel (Max-Planck-Institut für Biophysik, Frankfurt am Main, Germany), Peter Hegemann (Universität Regensburg, Germany), and colleagues. Meanwhile, a group led by John Spudich at the University of Texas (Houston, TX) has used RNA interference to show that this and another channel are two rhodopsins that the alga *Chlamydomonas reinhardtii* (Chop 1), came from a database which was named channelrhodopsin-1 phototaxis. His latest candidate, light-detecting chromophore, but they algal proteins that bind retinal, the source. to move closer to or further from a light rhodopsins that the alga has used RNA interference to show that University of Texas (Houston, TX) a group led by John Spudich at the Germany), and colleagues. Meanwhile, Hegemann (Universität Regensburg, Frankfurt am Main, Germany), Peter (Max-Planck-Institut für Biophysik, Toronto, Canada), Keiji Kimura, and Tatsuya Hirano (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY) have found that a single condensin complex can use ATP to wrap two positive gyres of DNA around itself. That packaging, however, may just be the start. Based on previous experiments, Hirano and colleagues had suggested that an individual condensin might span a considerable distance between DNA binding sites and introduce global wrinkles that would twist the DNA into a right-handed solenoid. But direct observation of single complexes on naked DNA by electron spectroscopic imaging has now shown that a single complex is instead tightly wrapped with two turns of DNA. What that means for condensation of cellular chromatin is not yet clear. “We don’t think that the local wrapping per se would account for the massive compaction of chromatin,” says Hirano. There are several models that could explain additional compaction. A single condensin could bring two distantly located DNA segments together, although Hirano has no evidence for such a mechanism. A similar outcome could be achieved if multiple condensins bind to each other, or condensin may wind already compacted DNA around its core. In future experiments, Hirano plans to study the in vitro reaction of condensin with chromatin rather than naked DNA. For now, he favors an old model in which the real function of condensin’s wrapping of DNA is the introduction of compensatory negative supercoils in the surrounding DNA. Such superhelical tension might in turn act as a driving force in coiling up a chromatin fiber.


Condensin wraps it up

Packing DNA into a nucleus is no mean feat. Now, David Bazett-Jones (Hospital for Sick Children, Toronto, Canada), Keiji Kimura, and Tatsuya Hirano (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY) have found that a single condensin complex can use ATP to wrap two positive gyres of DNA around itself. That packaging, however, may just be the start.

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Attack of the waves

A drei Kindzelskii and Howard Petty (Wayne State University, Detroit, MI) have found that self-organizing waves of NAD(P)H can help neutrophils to destroy their targets. When the waves reach the front of the cell, the NAD(P)H donates an electron to NADPH oxidase, which passes it on to oxygen to form reactive oxygen metabolites (ROMs) that help weaken the membranes of bacterial, virus-infected and tumor cells.

The team first described the existence of NAD(P)H waves in a paper in Physical Review Letters in 2000, but this is the first demonstration that the waves can have functional consequences. Petty was able to visualize both NAD(P)H (which autofluoresces) and an indicator for ROMs by using high-speed imaging with an acquisition time in the nanosecond range. Most video microscopy, by contrast, uses millisecond acquisition times and thus would see the NAD(P)H as an indistinct blur.

Self-organizing waves arise from oscillating reactions that are maintained in a nonequilibrium state by metabolic inputs. The self-organizing nature of the NAD(P)H waves distinguishes them from induced calcium waves, but Petty believes that any number of biological molecules may operate in waves. “If neutrophils do it this way,” he says, “what other structures might be observed at high speed?” ■