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In This Issue

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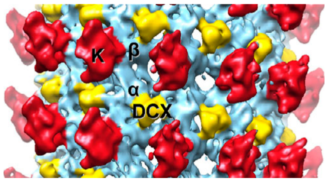
A MAP holds the corners



DCX (yellow) takes up position at the junction of four tubulin dimers.

Microtubule-associated proteins (MAPs) reinforce microtubules (MTs). Fourniol et al. provide the first close-up of a MT-bound MAP, clarifying how it adds stability.

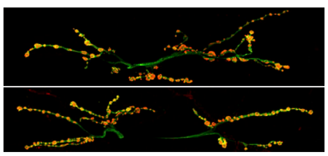
The building blocks of MTs are dimers of one α- and one β-tubulin subunit. These dimers line up end to end to build protofilaments, which in turn align side by side in a ring shape to form a hollow MT. MAPs help fasten the protofilaments together. One type of MAP, known as doublecortin (DCX), fortifies MTs that contain 13 protofilaments, the arrangement in almost all cells. However, researchers haven't been able to get a close enough look at MT-bound MAPs to determine how they strengthen the fibers.

Fourniol et al. used cryo-electron microscopy to create the highest-resolution reconstruction of a MT-bound MAP yet. Using kinesin-1 motors linked to the MTs as landmarks, the researchers nailed down where DCX hooked on. The protein targeted the MT surface at intersections where four tubulin dimers join. In this position, DCX stabilizes the structure laterally and lengthwise.

Thirteen-protofilament MTs contain a seam that forms where α- and β-tubulin subunits fall out of register. The seam runs the length of the MT fiber and is a potential weak spot—some studies suggest that MTs can split open along this fault line. However, the researchers found that DCX avoids the seam, suggesting that it might not require extra stabilization after all. Instead, DCX might act as an on/off switch—its binding to MTs ensuring they grow where the cell needs them. Similar studies should reveal how other MAPs show their support for MTs.

Fourniol, F.J., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201007081.

dRich doesn't take sides



A neuromuscular junction lacking dRich (top) sports fewer boutons (yellow) than one from a control animal (bottom).

Much as a plug fits its socket, the two sides of the neuromuscular junction are complementary. Nahm et al. show that the same protein shapes both sides of this synapse, helping ensure a good match.

Development of the neuromuscular junction is interactive. The postsynaptic side releases a protein called Glass bottom boat (Gbb) that spurs the neuron to grow toward the muscle. A pathway that includes Cdc42 curbs release of Gbb. Previous work suggested that the protein Rich-1 inactivates Cdc42 in other systems, but researchers didn't know whether Rich-1 affected synapse development.

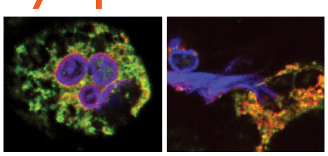
By screening mutants, Nahm et al. found that the fruit fly equivalent of Rich-1, dRich, alters synapse architecture. Flies lacking the protein showed several presynaptic defects. They carried fewer synaptic boutons, for example, and released less neurotransmitter.

The other side of the junction was also flawed in dRich-deficient insects. The subsynaptic reticulum, a network of membranous tubes beneath the postsynaptic membrane, was misshapen. Some subunits of the glutamate receptors that receive synaptic signals were in the wrong location, failing to cluster opposite active zones, the neurotransmitter launching points on the presynaptic terminal. Overall, losing dRich impaired the neuromuscular junction so that stimulating the neuron induced a 50% smaller current than in controls.

The researchers think that dRich exerts it effects on the presynaptic side by blocking postsynaptic Cdc42 and unleashing Gbb. On the postsynaptic side, the protein might alter membrane folding or bring in helpers that renovate the junction.

Nahm, M., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201007086.

Cytoplasmic enzymes cast NETs



The blue-stained nucleus turns purple as neutrophil elastase (red) enters (left), after which the cell ejects its DNA (right).

By unraveling chromatin, two enzymes help neutrophils deploy defensive webs known as NETs, Papayannopoulos et al. reveal.

NETs (neutrophil extracellular traps) not only snare invaders, they are festooned with pathogen-killing proteins, including histones, which are best known for packaging chromatin but also serve as powerful antimicrobial agents. To make a NET, a neutrophil needs to unfurl and jettison its chromatin. The cell starts by cranking up its production of reactive oxygen species, but how this surge leads to chromatin unraveling remains murky.

Neutrophils are difficult to study because they live for only about six hours. So the researchers created a cell-free system that includes neutrophil nuclei and dollops of cytoplasm from the cells. They found that two enzymes stashed in cytoplasmic granules enter the nucleus and join forces to unwind the chromatin. The first to make the move is neutrophil elastase (NE), which promotes chromosome decondensation by breaking down the H1 and H4 histones. Later in the process, myeloperoxidase (MPO) arrives at the nucleus to help NE unravel the chromatin. Exactly how MPO performs its task remains unclear, as its enzyme activity isn't required to decondense chromatin.

The researchers confirmed NE's importance for NET formation by exposing mice to *Klebsiella pneumoniae* bacteria. Neutrophils hustled to the lungs in control mice and in animals lacking NE. But neutrophils from the mice missing NE couldn't produce NETs to snare the bugs.

An important question to answer now, the researchers say, is how NE and MPO travel to the nucleus. The granules could merge with the nuclear membrane or burst and free the enzymes into the cytoplasm, from where they subsequently move to the nucleus.

Papayannopoulos, V., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201006052.