In This Issue

Location is everything

A specific isof orm of casein kinase 1 (CK1) localizes to the centrosome to promote neurite extension, Greer and Rubin reveal.

The signaling protein Wnt-3a stimulates rapid neurite outgrowth from certain cell lines by activating the e ffector proteins Dishevelled (Dvl) 2 and 3. Dvl proteins’ downstream effects can be modulated by phosphorylation. After finding that Dvl-2 and -3 were phosphorylated during Wnt-3a–induced neurite extension, Greer and Rubin screened a panel of small molecule inhibitors to identify the responsible protein kinases.

IC261, an inhibitor of the closely related CK1 isoforms δ and ε, blocked Wnt-3a–induced neurite outgrowth and Dvl-2/3 phosphorylation. Knocking down either kinase by RNAi also

Connecting the cytokinesis dots

Laporte et al. describe how precursors of the cytokinetic contractile ring assemble at the cell equator.

As fission yeast enter mitosis, protein clusters called cytokinesis nodes form around the cell cortex at the future site of cell division. The nodes eventually coalesce into a contractile ring to separate daughter cells, but little is known about the nodes’ initial assembly, except that their localization at the cell cortex is determined by Mid1, a homologue of the animal–cell cleavage furrow protein anillin.

Laporte et al. analyzed the composition of cytokinesis nodes in different mutant backgrounds to define two protein modules that

Osteoblasts are bone idle without Frizzled-9

The Wnt receptor Frizzled-9 (Fzd9) promotes bone formation. Albers et al. report, providing a potential new target for the treatment of osteoporosis.

Adult bones are maintained by a balance of bone-forming osteoblasts and bone-resorbing osteoclasts. Although Wnt signaling affects this balance in mice and humans, the Wnt receptors involved remain unknown. Albers et al. found that the Wnt receptor Fzd9 was upregulated during osteoblast differentiation and that mice lacking Fzd9 had fragile bones due to low rates of bone formation.

Fzd9-null osteoblasts differentiated normally, but they failed to mineralize their extracellular matrix. The loss of Fzd9 disrupted reduced Dvl-2/3 phosphorylation, yet the two isofoms had opposing effects on neurite formation. Cells lacking CK1δ no longer grew neurites in response to Wnt-3a, whereas CK1ε depletion prompted neurite extension in the absence of Wnt ligand, suggesting that this isoform usually inhibits neurite growth.

Greer and Rubin found that, unlike CK1ε, CK1δ localized strongly to the centrosome, an organelle that controls neurite outgrowth in many types of neurons. Blocking this localization prevented Wnt-3a from inducing neurite extension. CK1δ was targeted to the centrosome by a region in its C terminus; substituting this centrosomal localization signal for the C-terminal domain of CK1ε allowed that isof orm to promote neurite formation in place of CK1δ, indicating that location is the key determinant of the isofoms’ different activities.

Many Wnt signaling pathway proteins localize to centrosomes. The authors now want to investigate whether they cooperate with CK1δ to drive neurite outgrowth and other centrosome functions such as ciliogenesis.

Greer, Y.E., and J.S. Rubin. 2011. J. Cell Biol. doi:10.1083/jcb.2010111111.

assembled around Mid1 at the plasma membrane. The first module consisted of the myosin light chain Cdc4 and the actin-bundling IQGAP protein Rg2, which together recruited the myosin motor protein Myo2. The second module incorporated the membrane-bending F-BAR protein Cdc15. Both modules recruited the actin-nucleating formin Cdc12 into the nodes, Laporte et al. found.

The researchers then used a single-molecule imaging technique called SHREC to examine how these components are organized within each cytokinesis node. Myo2’s head domain points into the cell interior, an orientation that may help it capture and pull actin filaments nucleated from neighboring nodes as the separate clusters condense into a full contractile ring. Senior author Jian-Qiu Wu now wants to examine how the organization of the node proteins changes as they form the contractile ring. He’s particularly interested in whether Myo2 polymerizes into filaments, as has been observed in the contractile ring of other organisms.

Laporte, D., et al. 2011. J. Cell Biol. doi:10.1083/jcb.201008171.

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