In the nervous system, guidance molecules called semaphorins bind to receptors called plexins to induce motility and regulate axonal pathfinding. Now, Swiercz et al. (page 869) show that plexin-B1, after binding its ligand semaphorin 4D (Sema4D), forms a heterodimer with the tyrosine kinase ErbB2. This raises the intriguing possibility that the semaphorins and the EGF-like ligands of ErbB receptors may affect each other’s signaling abilities.

Swiercz et al. used a number of different kinase inhibitors to block the RhoA activation seen downstream of Sema4D binding to plexin-B1. These findings revealed that one or more proteins in the ErbB family was involved. Of the four members of the ErbB family, only a dominant-negative ErbB2 mutant showed significant effects on RhoA activation. Unlike other family members, ErbB2 is not activated by a ligand. Rather it acts in trans via association with other tyrosine kinases. Likewise, Swiercz et al. found that plexin-B1 and ErbB2 form a heterodimer in which activated ErbB2 phosphorylates plexin-B1. This phosphorylation is required for plexin-B1 signaling via PDZ-RhoGEF/LARG to RhoA.

Competition experiments between Sema4D and EGF (which stimulates and activates ErbB1/ErbB2 heterodimers) resulted in an overall inhibition of plexin-B–mediated signaling by EGF. But, at the same time, Sema4D is able to activate the ErbB2 pathway, which may under some circumstances lead to tumor promotion.

contractile actin ring does most of the work during cytokinesis, but microtubule-to-membrane anchoring is also needed as two cells pinch away from each other. Tomas et al. (page 813) now show that a protein called annexin 11 may act as a bridge during this last separation event by interacting with both the microtubule-binding CHO1 kinesin-like protein and membranes.

Annexins are Ca\(^2\)^+-dependent proteins that function in a variety of cellular processes. The team finds that cells lacking annexin 11 fail to separate during division and die via apoptosis. Annexin 11–depleted cells remained joined via long thin extensions that do not resemble the functional midbodies characteristic of cells going through a normal cytokinesis. Annexin 11 and CHO1 coimmunoprecipitated and colocalized to the midbody in wild-type cells.

Annexin 11 has membrane fusogenic activity in vitro and so could be involved in the fusion of membrane vesicles at the cleavage furrow. But direct evidence for such an in vivo function is lacking, leading the authors to suspect that CHO1 and annexin 11 bring together microtubules and the cell membrane to execute the final phase of cell division.

Stuck in the divide

Mixed guidance

Cell growth is controlled, in part, by the extracellular matrix and the intracellular signals that it elicits. No matrix usually means no growth. But, as reported by Yang et al. (page 881), some cancerous cells can probably get by with very little matrix by making their own costimulator.

That costimulator is melanoma chondroitin sulfate proteoglycan (MCSP). MCSP is known to be an early cell surface marker during melanoma progression, and to stimulate tumorigenesis. When Yang et al. transfected MCSP into a melanoma cell lacking MCSP, the cells exhibited an increased propensity to undergo spreading, which was mediated in large part by focal adhesion kinase (FAK). Integrin-mediated activation of both FAK and ERK 1/2 were increased by MCSP expression, and activation of ERK 1/2 remained even when FAK activity was inhibited.

MCSP is up-regulated early in melanoma (even in precancerous lesions), and its expression is maintained in the vast majority of melanomas throughout progression. The authors speculate that MCSP may function to lessen the requirement by tumor cells for ligands in the tumor microenvironment, giving cells that express this cell surface proteoglycan a selective advantage.

Stuck in the divide

Mixed guidance

Tumors make do with less matrix