In This Issue

Migration on rafts

The plasma membrane polarizes in moving cells by reorganizing lipid rafts, according to Gómez-Moutón et al. on page 759. This polarization puts migration tools at the correct end of the cell.

The polarization of signaling molecules such as PI3K allows migrating cells to respond directionally to chemotactic signals by forming lamellipodia at the front and uropods at the rear. Gómez-Moutón et al. show that this localized signaling is a result of redistribution of plasma membrane lipid compartments that puts chemokine receptors at the front of cells. Using live migrating white blood cells, the group watched in real time as some rafts moved to the cell’s leading edge, while other rafts moved to the rear. Rafts that moved to the front contained the CCR5 chemotactic receptor.

Wherever CCR5 was found, the authors also saw activated PI3K—a key determinant in the orientation of migration. Disruption of raft polarization, by removing cholesterol, prevented this localized PI3K recruitment and thus stopped directed migration.

So far it is unclear how different rafts choose between the front and rear of the cell. Perhaps activation of a few receptors on one side of the cell initiates the clustering of several receptor-containing rafts. As the actin cytoskeleton is needed for raft polarization, the authors speculate that the PI3K brought to these rafts may activate proteins that alter actin dynamics to recruit more of the appropriate rafts. One of these proteins could be the GTPase Rac1, whose activation at the leading edge is required for cell migration. Rac1 was recently shown to bind to and be activated specifically at lipid rafts (del Pozo, M.A., et al. 2004. Science. 303:839–842).

Other proteins in different rafts might initiate raft movement to the rear. Further insight awaits the characterization of the lipid and protein components of the different rafts.

Lumens laid out by PAR-1

Epithelial cells form the lumens that define the shape and function of several organs. In the intestine, kidney, or pancreas, lumens are created by column-like cells with luminal proteins at their apex. Liver epithelia, however, form lateral bile-secreting lumens between adjacent cells. Microtubules in these different cell types are sensibly organized to transport luminal proteins to the right destination; the microtubule minus ends are found at the top of columnar cells but at the sides of liver epithelia. On page 717, Cohen et al. show that different strengths of the PAR-1 kinase build columnar or liver-like lumens by organizing these microtubule patterns.

Unpolarized epithelia need PAR-1 activity to form lumens. Using RNAi or dominant-negative PAR-1, the authors could prevent lumen generation in both kidney and liver cells and keep microtubules in the radial arrays characteristic of unpolarized cells.

The type of lumen formed depends on the amount of PAR-1 activity. By drastically increasing PAR-1 expression in unpolarized kidney cells, the group created kidney cells with liver-like intercellular lumens and laterally arranged microtubules. Other studies have shown that kidney cells normally pass through such a liver-like phenotype before developing apical lumens. Together, the results suggest that sustained high PAR-1 activity locks liver cells in the liver-like microtubule and lumen arrangement, whereas later lower levels of PAR-1 allow the microtubules in kidney cells to further rearrange to form apical lumens.

Microtubule release from the centrosomes of newly polarizing cells was not affected by the loss of PAR-1, so the kinase probably regulates microtubule capture by the cell cortex. In neurons, PAR-1 phosphorylates the microtubule-associated protein tau, but the group is still searching for the relevant PAR-1 substrates in nonneuronal cells.