HIGHLIGHTS

CELL MIGRATION

Pole position

The association of proteins with lipid rafts — regions of the plasma membrane enriched in cholesterol and glycosphingolipids — is thought to be important for re-distributing specialized molecules to the leading edge of migrating fibroblasts. Reporting in *Proceedings of the National Academy of Sciences*, Santos Mañes and colleagues now show that, similarly to fibroblasts, migrating T lymphocytes asymmetrically redistribute lipid rafts, thereby establishing cell polarity.

The authors studied the distribution of two lipid-raft-associated gangliosides, GM1 and GM3, in the leading edge and rear edge (known as the uropod) of polarized T cells, and found that they are asymmetrically distributed in response to migratory stimuli. GM3 is concentrated mainly at the leading edge and GM1 is found at the uropod. Both gangliosides show colocalization with leading edge- and uropod-specific markers, such as the chemokine receptor, CXCR4, and CD44, respectively.

Further analysis revealed that CXCR4 and CD44, among other markers, were insoluble in detergent, which is typical of raft-associated proteins, but depleting cells of cholesterol increased the solubility of CXCR4 and CD44.

To show that the redistribution of proteins to either pole of the cell is a consequence, rather than a cause, of specific association to the membrane rafts, the authors expressed raft-associated proteins that have no functional significance in polarization and their non-raft mutant counterparts in polarized T cells. The wild-type proteins localized asymmetrically, whereas the mutants were homogenously distributed — despite the fact that GM1 was strongly polarized.

What, then, is the function of these rafts? Mañes *et al.* showed that, following treatment with methyl-β-cyclodextrin (CD), which sequesters membrane cholesterol, the number of polarized T cells decreased. Furthermore, CD treatment inhibited the ability of Jurkat cells to move towards SDF-1α, a chemokine that acts on CXCR4, indicating that leading edge function was impaired. In addition to mediating motility, the uropod functions to recruit bystander T cells — a function that CD treatment also inhibits. Finally, the authors used latrunculin-B — an inhibitor of actin polymerization — to show that an intact actin cytoskeleton is required to distribute the rafts asymmetrically.

So rafts, which in T cells have so far been assigned functions in organizing T-cell receptor signalling and immunological synapse stabilization, may now also be responsible for establishing — through as-yet-unidentified signalling pathways — the redistribution of molecules that are needed for T-cell migration.

Katrin Bussell

References and links

ORIGINAL RESEARCH PAPER Gómez-Moutón, C. *et al.* Segregation of leading-edge and uropod components into specific lipid rafts during T cell polarization. *Proc. Natl Acad. Sci. USA* **98**, 9642–9647 (2001)

FURTHER READING Simons, K. & Toomre, D. Lipid rafts and signal transduction. *Nature Rev. Mol. Cell Biol.* **1**, 31–39 (2000)