Why cells shrink from a swell time

The ability of cells to regulate their volume when exposed to anisotonic environments is important for cellular homeostasis. Hypotonic environments cause cells to swell through osmosis but many vertebrate cells quickly shrink back to normal by what is known as regulatory volume decrease (RVD). Marina Jendrach and co-workers now report that TRPV4, a member of the vanilloid subfamily of transient-receptor-potential channels, directly participates in RVD (see p. 2345). They show that RVD in HaCaT cells, a TRPV4-expressing human keratinocyte cell line, involves a significant Ca2+ influx. Both RVD and the Ca2+ influx are blocked by Gd3+, which inhibits TRPV4. Then, the authors express a TRPV4-EGFP fusion protein in CHO cells, which do not normally express TRPV4 or undergo RVD under hypotonic conditions. These engineered cells undergo RVD after a Ca2+ influx, and this is reduced by Gd3+. Together, these results suggest a model in which cellular swelling caused by osmosis increases tension in the cell membrane and activates TRPV4; this mediates a Ca2+ influx, which activates the signalling cascades that lead to RVD.

Smoothing out muscle

Smooth muscle cells line the walls of hollow organs such as the airways and control their dimensions and mechanical functions. As in striated muscle cells, actomyosin interactions produce sliding of actin and myosin filaments but, because there are no obvious repeating contractile units of myofibrils (sarcomeres) in smooth muscle cells, it is not clear how filament sliding translates into cell shortening. Chun Seow and co-workers now link structure to function in porcine airway smooth muscle and propose that smooth muscle cells have a malleable sarcomeric structure composed of contractile units assembled in series and parallel (see p. 2381). The authors measure force, velocity and power in muscle cells adapted to different lengths and examine their ultrastructure under different conditions. Their results fit a model in which the geometric organization of the contractile units within smooth muscle cells and the dimensions of individual units alter when the muscle cells adapt to different lengths. This flexibility, the authors conclude, underlies the unique functional and structural characteristics of smooth muscle.

Co-Arperative mRNA transport

The seven-subunit, Arp2/3 complex localizes to the leading protrusions of migrating cells, where it nucleates actin assembly. On p. 2425, Gang Liu and colleagues hypothesize that an efficient way to target such a large, stable complex to a specific region of the cell might be to localize the mRNAs for its component subunits to the same region. By using sensitive FISH techniques, the authors show that, as predicted, all the mRNAs for the Arp2/3 complex are targeted to the leading protrusions of chick embryo and human foreskin fibroblasts. This localization depends on serum factors, which suggests that it represents a cellular response to extracellular stimuli, and on actin filaments, microtubules and the presence of myosin motors. How the Arp2/3-complex mRNAs are localized to the leading protrusions of fibroblasts and then anchored is not yet known, but these results provide the first evidence for localization of all the mRNAs of a multisubunit protein complex to its site of assembly and function.

Traffic signals for myelin

The transmission of electrical impulses along the axons of the nervous system is only possible because each axon is surrounded by an insulating coat of myelin made by the oligodendrocytes and Schwann cells. How myelin-specific proteins are targeted to this specialized multilamellar membrane is poorly understood. Now, on p. 2415, Mikael Simons and colleagues report that palmitoylation is an important sorting determinant for protein transport to the myelin membrane. Using a primary oligodendrocyte culture system in which there is excessive deposition of myelin-like membranes (MLMs), the authors show that palmitoylation-deficient mutants of a major myelin protein, proteolipid protein (PLP/DM20), are less efficiently targeted to MLMs than wild-type PLP/DM20. The N-terminal 13 residues of PLP/DM20, which are palmitoylated at three sites, are sufficient to target a fluorescent fusion protein to the MLMs, as are palmitoylation signals from Ha-Ras and neuraminidase. However, note the authors, palmitoylation is probably only one of a hierarchy of sorting determinants that together generate the full complexity of the myelin membrane.

Development in press

Patterning embryos from the outside in

The anterior-posterior (AP) axis in mammalian embryos is established by interactions between the embryonic and extra-embryonic tissues. The extra-embryonic anterior visceral endoderm (AVE) is needed for anterior patterning in mice. However, little is known about what induces AVE formation at the embryo’s distal tip or what directs its migration to the embryo’s anterior. In paper published in Development, Rodriguez and colleagues now report that these processes are regulated by the extra-embryonic ectoderm (ExE). By using microsurgery, grafting and video imaging, they show that the ExE restricts AVE induction to the distal tip of the mouse embryo and is required to initiate AVE migration to the prospective anterior of the embryo. The ExE also induces mesoderm markers in the posterior epiblast. Thus, the ExE has a critical role in AP specification in the mouse by patterning both extra-embryonic and embryonic tissues.