Tight junctions have turned up in the epidermis. The authors’ analysis of mice lacking the TJ component claudin-1, however, shows that TJs are indeed found in the skin and are at least as necessary there as in simple epithelia.

Claudin-1 belongs to a multigene family that contributes to the backbone of TJ strands, so its deletion should affect simple epithelia. Surprisingly, the major defect in claudin-1−deficient mice is lethally leaky skin: the mice are born normally but die within a day, apparently from dehydration. Permeability assays of the claudin-1−deficient skin show excessive water loss.

In contrast with previous reports, Furuse et al. found continuous TJs in the stratum granulosum, a subset of the epidermis, of both wild-type and mutant mice. The results suggest that functional TJs are required in both types of epithelia and that loss of claudin-1 increases the permeability of the epidermal TJs without disrupting the organization of the keratinocytes.

**An acid invasion**

Intracellular parasites must walk a fine line, invading and exploiting a host cell without killing it too quickly. On page 1029, Glomski et al. show how a single amino acid determines not only the pH optimum of a bacterial hemolysin, but also the virulence of an important pathogen. The data help explain how *Listeria monocytogenes* distinguishes between the membranes of acidic vesicles, which the bacterium must pierce to enter the cytosol, and the plasma membrane, which must remain intact while the parasite reproduces.

The activity of the *L. monocytogenes* pore-forming hemolysin listeriolysin O (LLO) is strongly induced by low pH. By amino acid substitution, the authors determined that changing a single residue largely relieves this pH dependence, but bacteria expressing the pH-independent form of the enzyme are 100-fold less virulent in mice. The virulence defect is not in cellular entry. The mutants escape from acidified phagosomes, grow in the cytosol, and spread from cell to cell. But bacteria expressing the mutant LLO permeabilize the host cell membrane prematurely. The authors propose that the acidic pH optimum of LLO is an adaptation to the parasitic lifestyle, allowing *Listeria* to penetrate acidic vesicles while leaving the plasma membrane intact.

Previously, the authors found that worms with mutations in a muscle-specific ADF/cofilin isoform could not assemble normal myofibrils. ADF/cofilin appears to increase actin turnover, but myofibrils are highly stable structures, suggesting that some additional factor must inhibit ADF/cofilin in order to stabilize the myofibrils. The new study demonstrates that purified tropomyosin and ADF/cofilin compete for binding to purified F-actin, and that ADF/cofilin cannot bind to isolated myofibrils unless the attached tropomyosin is removed from the myofibrils first. RNAi suppression of tropomyosin disrupts myofibril organization in wild-type worms, but not in ADF/cofilin mutant worms. The results suggest that in vivo tropomyosin preserves myofilaments by blocking the destabilizing effects of ADF/cofilin.