Conjunctions of junctions

Like tight junctions in vertebrates, the ladder-like septate junctions found in most invertebrates act as barriers to epithelial permeability. A pair of papers in this issue provide important new insights into the composition and biology of Drosophila septate junctions, and identify new parallels between these structures and intercellular junctions in vertebrates.

The cholinesterase-like molecule gliotactin is required for the formation of the blood–nerve barrier in flies, and Schulte et al. (page 991) examined its localization. Gliotactin is found in the same tissues as other septate junction components, and appears to be required for septate junction formation. At the subcellular level, though, gliotactin specifically localizes to tricellular junctions, points where three epithelial cells meet, rather than being distributed among all septate junctions.

In both vertebrates and invertebrates, each tricellular junction appears to contain a pore, but little was known about this structure. Gliotactin is the first molecular marker identified for tricellular junctions. The authors propose that after septate junctions begin forming, gliotactin links them to the tricellular junction to tighten the structure, generating a mature, impermeable network of septate junctions. An analogous process may occur in vertebrates.

On page 979, Genova and Fehon identify four new components of septate junctions, including the α and β subunits of the Drosophila Na⁺/K⁺ ATPase and neuroglian, a homologue of vertebrate neurofascin. It is puzzling to find a pump in a structure that acts as a diffusion barrier, but the ATPase may help form a scaffold on which the septate junction complex assembles. The presence of neuroglian underscores the molecular and functional homology between invertebrate septate junctions and the vertebrate paranodal septate junctions that form between glial cells and neurons. The authors hope to use the genetically malleable fly system to identify additional components of septate junctions.

Wrong connexin signals cataracts

Besides allowing ions to flow between adjacent cells, gap junctions selectively conduct larger signaling molecules. What determines their selectivity is unknown. Martinez-Wittinghan et al. (page 969) explored this problem by extensively manipulating the genetic loci of the two connexin proteins that make up gap junctions in the lens of the eye. The results show that the developing lens is exquisitely sensitive to changes in the composition of gap junctions, and that alterations in gap junction permeability could underlie human diseases ranging from cataracts to deafness.

In previous studies, mice lacking the connexin 46 gene, which is expressed primarily in fiber cells beneath the lens epithelium, grew lenses of normal size but with severe cataracts. Deletion of the connexin 50 gene, which is expressed in both the lens epithelium and the fiber cells, caused a severe growth defect in the lens but only mild cataracts. The authors have now generated new mouse strains in which the coding sequences of connexins 46 and 50 were deleted from and swapped between their normal genetic loci in a variety of combinations, producing a spectrum of expression patterns.

When connexins 46 and 50 are both expressed in the epithelium as well as the fiber cells, the lens grows to normal size but has severe cataracts. Expressing only connexin 46 in the epithelium and fiber cells prevents cataracts but produces a growth defect. Ionic coupling between lens cells appears to be adequate in the mutants. The authors conclude that connexin 46 maintains lens clarity, and connexin 50 ensures proper lens growth, by determining the permeability of gap junctions not just to ions but to larger biochemical signals.

In humans, mutations in connexin genes are associated with hearing loss, inherited cataracts, and several skin diseases. The new work suggests that these mutations might change the composition of gap junctions, altering their permeability and generating signaling errors during development.