Fibronectin for branching

Branched organs are shaped when epithelia make their own paths, according to a study by Takayoshi Sakai, Melinda Larsen, and Kenneth Yamada (National Institutes of Health, Bethesda, MD). The pathmaker in this process is fibronectin (FN), which tells cells to let go of their neighbors and instead grab hold of the underlying matrix.

Organs such as the lung and kidney gain surface area by forming numerous branches, which are generated by cycles of budding and cleft formation in epithelial cells. Branching is known to involve growth factor–regulated interactions between the epithelium and mesenchyme, but the authors wanted to know how individual cells respond during branching. Using the developing mouse salivary gland as a model, the group now reports that epithelia change their architecture by secreting FN fibrils in newly forming clefts.

Although cleft-initiating signals are not yet known, cleft formation was induced by FN expression in cells bordering the cleft. Inhibition of FN mRNA expression in the epithelium or antibody inhibition of FN or its integrin receptor inhibited branching and cleft formation. In contrast, exogenous expression of FN induced excess branching in cultured salivary glands. FN fibrils suppressed local levels of the cell–cell adhesion molecule cadherin in nearby epithelial cells. Cadherin loss, which occurs via both local redistribution and mRNA suppression, probably releases the epithelial cells from each other as they attach to the matrix FN.

Lung and kidney epithelia also have cleft FN pools that function as in salivary glands, suggesting that FN is widely used for branching. “We wonder whether this kind of local developmentally regulated appearance of fibronectin is possibly a general strategy in tissue remodeling,” says Yamada.

Reference: Sakai, T., et al. 2003. Nature. 423: 876–881.

Spare the Mbl, spoil the rod?

New results from Richard Daniel and Jeff Errington (University of Oxford, Oxford, UK) indicate that bacteria have different strategies to control cell shape through cell wall deposition, depending on the presence of an actin-like protein.

Distant homologues of eukaryotic actin were only recently identified in bacteria. In the rod-shaped Bacillus subtilis, these proteins, members of the MreB family, form helical cables along the cell axis and are required for the maintenance of proper cell shape. Daniel and Errington now show that MreB proteins direct the deposition of cell wall material.

The authors probed for new cell wall material in Bacillus by labeling precursors inserted into peptidoglycan (PG), the major component of the cell wall. New PG was inserted in a helical pattern matching that of an MreB family member, called Mbl. Mutation of Mbl led to loss of the helical pattern in the cell cylinder. It is not clear how Mbl controls PG synthesis, but the authors believe that the MreC and MreD membrane proteins may connect the cytoplasmic cables to the external cell wall machinery.

Additional transient PG synthesis was found at sites where cell division occurred. Cells lacking Mbl survived by acquiring mutations that allowed them to maintain growth from finished division sites. They continued to grow as long as cell division was not inhibited.

Round bacteria such as Streptococcus lacked MreB proteins and inserted new wall material only at sites of division. Two groups of rod-shaped bacteria also lacked MreB-type proteins. The group found that one of these bacteria, Corynebacterium, relied entirely on continuous growth from cell division sites, just like the B. subtilis mbl mutants. MreB-directed wall synthesis allows cells to grow more rapidly, since new material can be added throughout the growing cell. But polar-growing cells may have the advantage of a static wall that can be reinforced by additional modifications to increase its strength.

Reference: Daniel, R., and J. Errington. 2003. Cell. 113:767–776.