**Desmosomes sort it out**

Long known for providing strong adhesion, and thus maintenance of tissue architecture, desmosomes are turning up as important regulators of epithelial morphogenesis and cell positioning. Evidence from David Garrod’s laboratory (University of Manchester, Manchester, UK) suggests that desmosomal adhesion may be as important as E-cadherin-mediated adhesion in determining epithelial morphogenesis, at least in the mammary gland, the model system used in these studies. Sarah Runswick, a coauthor of the report, anticipates that these findings may stimulate renewed interest in cross-talk between desmosomes and adherens junctions and how they regulate key cellular events.

Garrod’s group showed that blocking the desmosomal cadherins, desmocollins (Dsc) and desmogleins (Dsg), disrupts normal cellular aggregation and cell positioning of mammary luminal and myoepithelial cells maintained in a rotary culture system.

The newly discovered importance of desmosomal adhesion molecules in morphoregulation and positioning of epithelial cells probably applies well beyond the realm of the mammary gland to a variety of other tissues. The authors speculate that disruption of desmosomal adhesion might contribute globally to tissue disorganization, such as occurs in cancer and other diseases.

Reference: Runswick, S.K., et al. 2001. Nat. Cell Biol. 3:823–830.

**Tagged From birth**

Click! Even as a snapshot records a moment in time, so too do the progeny of neuronal stem cells record and remember the transcriptional regulatory factors present at the time of their birth. For it is these factors that determine the cells’ fate—their temporal identity and spatial destiny.

In the fly, the genes *hunchback* (*hb*), *pdm1/pdm2* (*pdm*), and *castor* (*cas*) are expressed at different times in the embryonic central nervous system and have been suggested to specify temporal identity of neuroblast daughter cells. Now, Chris Doe and colleagues (University of Oregon, Eugene, OR) propose that sequential expression of these factors defines identity in neuroblast lineages.

Doe and colleagues first add the gene *krüppel* (*Kr*) to the proposed temporal cassette, and find that individual lineages sequentially make *Hb*, then *Kr*, then *Pdm*, and finally *Cas*. *Hb* and *Kr* are necessary and sufficient to specify the fate of first- and second-born progeny, respectively.

Birth order, not cell type, correlates with the layered expression of these gene. Thus, the same sequence of gene expression is followed regardless of whether the original progeny cell is a motorneuron, interneuron, or glial cell. First-born progeny express *Hb* and occupy the deepest cortical layers, whereas second-born progeny express *Kr* and reside in the next deepest layer.

A cell-cycle dependent clock, rather than a global timing mechanism, appears to regulate the sequential expression of these genes. If the cell cycle is stopped, the sequence of changes in gene expression also stops.

Reference: Ishiki, T., et al. 2001. Cell. 106:511–521.

**Arp bent out of shape**

Biochemical and kinetic studies have failed to provide a unified view on how the Arp2/3 complex nucleates actin filaments. Does the complex, which mediates actin filament nucleation and branch formation at the leading edge of motile cells, bind to the side of an older actin filament, or does it become incorporated into that filament?

Structural studies now add a new dimension to the discourse, supporting the side-binding, dendritic nucleation model. These studies provide visual evidence that the seven subunit actin-related protein (Arp) complex is not inserted into the mother filament during actin filament nucleation in *Acanthamoeba castellanii* and *Saccharomyces cerevisiae*.

Additionally, and rather unexpectedly, imaging by electron cryomicroscopy provides evidence that the Arp2/3 complex undergoes a major conformational change during branch formation.

“This rearrangement of the complex was “rather surprising to see,” says Dorit Hanein (The Burnham Institute, La Jolla, CA). Hanein describes her work with Niels Volkmann and colleagues as the “first serious attempt to look at the structural changes associated with the mechanism of actin nucleation by Arp2/3 complex.” The group’s approach incorporates various electron microscopy imaging techniques combined with single particle analysis of activated Arp2/3 complexes and image analysis of Arp2/3 in actin filament branch junctions. The structural findings provide direct evidence that Arp2 and Arp3 form the first two subunits of the developing daughter filament.

Reference: Volkmann, N., et al. 2001. Science. 10.1126/science.1063025 http://www.sciencemag.org/cgi/content/abstract/1063025