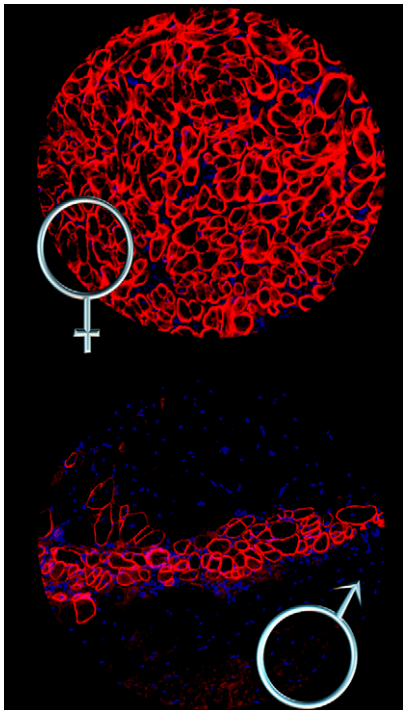
In This Issue



Female muscle-derived stem cells make more skeletal muscle cells (red) than do their male counterparts.

Females' regenerating advantage

Men might build more muscle, but women are better at keeping what they have, if results from Deasy et al. (page 73) are any indication. The group shows that female muscle stem cells are better than their male counterparts at regenerating lost muscle.

The authors were led into the realm of muscle and sex when they realized that they were relying heavily on cell lines derived from female mice to study muscle regeneration. Most of the male lines, by contrast, were stuck away in the freezer. They supposed that the female ones were more popular because they were working better.

The group now shows that female muscle stem cells are indeed better at regenerating diseased muscle in a mouse model. While the male cells proliferated briefly and abruptly differentiated into muscle, the female cells held out. They proliferated more slowly at first, but cycled longer before becoming muscle. By multiplying first, the stem cells can eventually create more fibers.

The female cells also seem better equipped to deal with the hypoxic conditions and reactive oxygen species found in injured and diseased muscle, as they up-regulated more stress-related and antiapoptotic genes. Artificially turning on antiapoptotic Bcl-2 in male stem cells was not enough to improve their regeneration, however.

Hormones may also have some influence, as females were better recipients as well as donors. But estrogen treatments did not prod stem cells of either sex to make muscle more efficiently.

The authors still need to determine the ultimate cause of the female cells' superior regenerating ability. Perhaps a Y chromosome gene encourages quick differentiation. Whatever the cause, biologists should make sure to note cell sex when describing their experimental methods with stem cells of any sort. JCB

Notch remodels junctions

The Notch pathway is renowned for its reign over differentiation. Now, its sway is widened into the realm of morphogenesis and cell–cell adhesion. Grammont (page 139) shows that Notch signaling remodels adherens junctions while cells change shape during development.

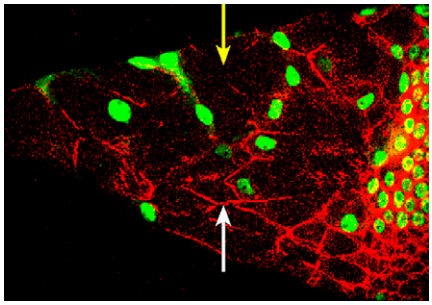
Developmental programs generally require plenty of changes in cell shape. In the developing fly oocyte, a set of cells on the posterior end acquire a columnar shape, whereas anterior cells flatten. Notch has been implicated in several aspects of oogenesis in flies. To better dissect its role, Grammont analyzed developing oocytes with somatic clones mutant for Notch signaling.

The clones revealed that Notch activity is necessary for the anterior cells to take on their new flattened shapes at the proper time. Mutant clones were delayed in changing shape. The delays did not stem from differentiation problems, as cell fates were unaffected. Rather, Grammont noted abnormalities in adherens junction remodeling.

In normal developing oocytes, the flattening cells first disassembled their adherens junctions, starting from the anterior end. Junctions linking three cells were the first to go. Next were two-cell junctions linking a cell to its anterior neighbor. Those that lay parallel to the direction of stretching were maintained.

Junction disassembly was delayed in and just around clones that lacked Notch signaling. These enduring linkages probably prevent cells from taking on their new elongated shape.

Grammont's next big task will be to determine exactly how Notch leads to the remodeling. Its ability to activate transcription was required, but the relevant gene targets are not yet known. Possibilities include myosin II, which accumulated at disassembling junctions and was necessary for flattening. Another putative target is E-cadherin, which is removed from dismantling junctions and added to growing junctions along the anterior–posterior axis. JCB



Clones lacking Notch signaling (green) maintain E-cadherin (red) junctions (white arrow) when normal regions have dismantled them (yellow arrow).

Text by Nicole LeBrasseur
lebrasn@rockefeller.edu

Centriolar inequality

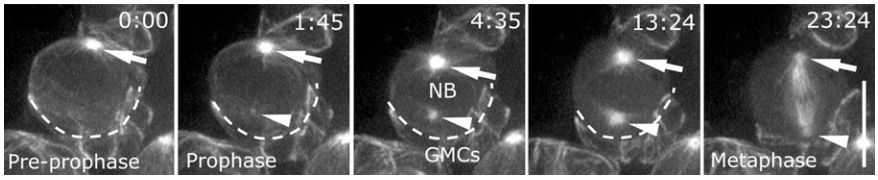
Not all centrosomes are created equal. On page 13, Rusan and Peifer reveal that the separation of a dominant and a secondary centrosome helps define an asymmetric division axis in fly neuroblasts.

Asymmetric divisions in stem cells give rise to one daughter that will differentiate and one that will replace the stem cell. This asymmetry can be set by the orientation of the mitotic spindle through microtubule interactions with the cortex. But Nasser and Peifer find that fly neural stem cells begin to align their spindles before they are even built.

Spindle orientation in male germline stem cells was recently shown to be defined by separation of the mother centrosome, which remains near the stem cell niche, and the daughter centrosome, which travels to the opposite side. In neuroblasts, the authors now find, centrioles similarly separate in interphase to define the division axis.

Whether the traveling centriole is consistently the daughter is not known. But only the stationary centriole retained its microtubule-organizing capacity; the traveler shed its pericentriolar material and microtubules until the following mitosis. The stationary centriole also kept its Polo kinase, which might help provide its unique abilities.

Without centrioles, fly neuroblasts still create spindles, whose interactions with the cortex often resulted in normal orientations. But if the spindle formed too far off-center, cortical cues could not correct the problem, thwarting the asymmetric division. JCB



One centriole (arrow) organizes microtubules (white) throughout the cell cycle, while an apposing centriole (arrowhead) acquires this ability during mitosis.

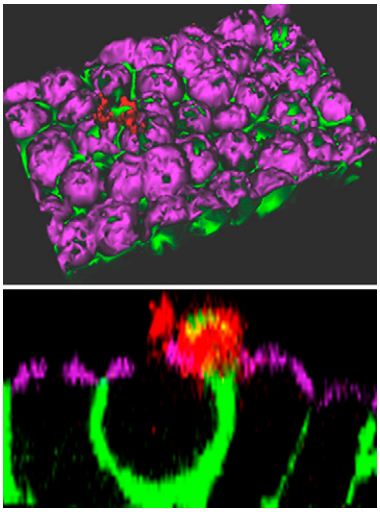
Bug redecorates membrane

A bacterium redecorates its host's membrane to make the host cell more hospitable, reveal Kierbel et al. (page 21). By converting the apical plasma membrane into basolateral membrane, *Pseudomonas aeruginosa* opens up a new cellular entryway for itself.

For unknown reasons, this opportunistic bacterium prefers to enter from the basolateral surface of polarized epithelial cells. A wound provides *P. aeruginosa* with some access to this surface, but in intact epithelia, tight junctions generally block their paths.

Now, Kierbel and colleagues show that *P. aeruginosa* makes the best of the available surface. Given access only to the apical side of a cell, the bug converts the membrane around it into a more basolateral environment.

Conversion starts with phospholipid decorations. The basolateral surface is high in PIP3, which *P. aeruginosa* induces in the apical membrane by recruiting PI3K to its binding sites (usually just above the tight junctions).



Binding of *P. aeruginosa* (red) increases apical PIP3 (green) and displaces apical proteins (purple).

The PIP3 then creates actin-filled protrusions that surround and eventually take in the bacterium. The protrusion membranes contain basolateral proteins instead of their previous apical occupants. This exchange also seems to be PIP3 driven: the authors previously found that exogenous apical PIP3 redirects the recycling of basolateral material to the apical surface. How this interference is achieved is not known, but the new arrivals apparently displace the former apical residents. JCB

A myosin for basolateral sorting

The first motor for AP-1B–dependent polarized sorting in epithelial cells is identified by Au et al. on page 103. An isoform of myosin VI, the group shows, helps set basolateral proteins apart from the rest.

Myosin VI works in a complex containing optineurin and Rab8, according to the new results. Rab8 is important for the sorting of basolateral proteins from the Golgi, which the authors now find also relies on a myosin VI isoform. Deletion of the shortest of four myosin VI isoforms sent basolateral proteins that are sorted by AP-1B to the apical membrane instead.

Polarized transport is generally associated with microtubules and their motors, whereas myosins run along actin tracks. The authors suspect that myosin VI, which was concentrated with AP-1B around endosomes, is important during short range movements near these and other organelles, where microtubules are scarce and actin dominates.

Within the myosin family, only myosin VI moves toward actin's minus ends. Minus ends point away from the plasma membrane and from phagosomes, but whether they also point away from the Golgi or endosomes is unknown. If actin is in the right orientation, myosin VI might help create basolateral transport vesicles by pulling membrane away from these organelles. JCB