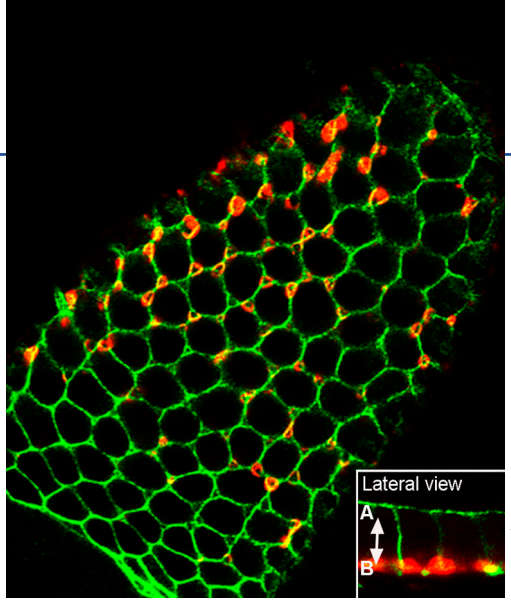
Research Roundup

Plasma membrane in Golgi costume

Stretching cells hold tight by allowing integrins to sidestep the Golgi, suggest Hans Schotman, Leena Karhinen, and Catherine Rabouille (University Medical Centre, Utrecht, Netherlands). The group uncovers a specialized section of Golgi-like plasma membrane that draws in integrins directly.

The hybrid membrane appeared in remodeling epithelial cells that cover the developing fly oocyte. The cells begin as columns that attach to each other at the sides and to the matrix on their basal side. But as the oocyte grows, the cells are stretched and flattened. The group found that these forces pulled the cells apart slightly, exposing the matrix to membrane that was previously attached to other cells.



RABOUILLE/ELSEVIER

The *grasp* RNA (red) is translated near membrane regions that are being pulled apart from neighboring cells and newly attaching to the matrix.

This newly matrix-adjacent membrane soon harbored GRASP, which is normally a bona fide Golgi marker. As the epithelial cells were pulled apart, *grasp* RNA was translated near the exposed membrane region. Two other Golgi proteins, GM130 and Gos28, were also found in this membrane region. "Our idea is that the plasma membrane is disguising itself as the Golgi," says Rabouille, "so that carriers from the ER fuse there instead of with the Golgi."

These lured carriers, the group imagines, harbor integrins that attach the membrane to the matrix. Insertion of one integrin subunit into these membrane sections was indeed insensitive to inhibitors of Golgi transport. And in the absence of GRASP, the integrin was instead retained within the cell. The resulting lack of adhesion caused epithelial disorganization.

It is not clear why the cells do not use the standard Golgi trafficking pathway. Posttranslational modifications that occur at the Golgi can make integrins less sticky. Bypassing this organelle might thus create more adhesion for these highly stressed cells.

The *Dictyostelium* version of GRASP has been shown to drive another unusual secretion pathway, which sends proteins directly from the cytosol to the extracellular space. Rabouille's group now wants to determine how the fly bypass is activated; since integrins are thought to be mechanosensors, they might trigger their own retargeting in response to stretching. JCB

Schotman, H., et al. 2008. *Dev. Cell.* 14:171–182.

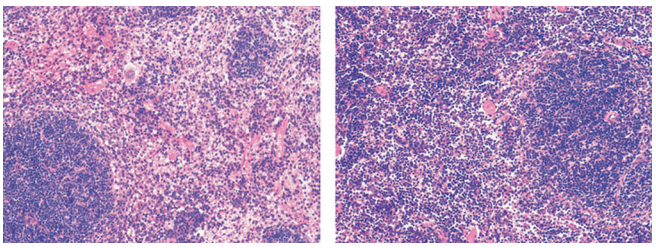
Rb turns up mitochondria

New results suggest that escape from the cell cycle is hooked to mitochondrial performance, say Vijay Sankaran, Stuart Orkin, and Carl Walkley (Harvard Medical School, Boston, MA). The group finds that both escape and performance are controlled by Rb in differentiating red blood cells.

The precursors to red blood cells, like many cell types, must stop proliferating before they can differentiate. Previous work showed that the precursors of red blood cells must also boost mitochondrial activity, perhaps to generate enough ATP for the impending onslaught of globin synthesis. In the new work, the authors reveal that Rb-mediated exit from the cell cycle allows differentiation by providing this mitochondrial boost.

In several cell types, Rb is necessary for the transition from G1 to S phase. But reports on its function in red blood cell development were conflicting. Sankaran et al. eliminated some of the complications that afflicted previous studies by knocking out Rb activity only in the cell lineage that produces red blood cells in mice.

The mutant precursors failed at a late stage of differentiation, when exit from the cell cycle is needed. Gene expression patterns revealed that S phase genes were maintained at high levels in the mutants. Several of these genes were targets of the E2F transcription factor—a known substrate of Rb's inhibitory powers. As a result, whereas normal precursors escaped proliferation at this G1 stage, the mutants pushed forward into another S phase.



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Red blood cell precursors proliferate uncontrolled when they lack Rb (right) and enough mitochondrial activity to differentiate.

Loss of Rb also impaired mitochondrial biogenesis, electron transport, and oxidative phosphorylation. These pathways were up-regulated just before differentiation in normal precursors but remained flat in the mutants.

One transcription factor that promotes mitochondrial biogenesis in muscle and fat, called PGC, was reduced in the Rb mutants. The authors imagine that PGC levels are kept low by the mutant cells' high levels of S phase cyclin-dependent kinases, one of which has been shown to block PGC function. JCB

Sankaran, V., et al. 2008. *Genes Dev.* 22:463–475.