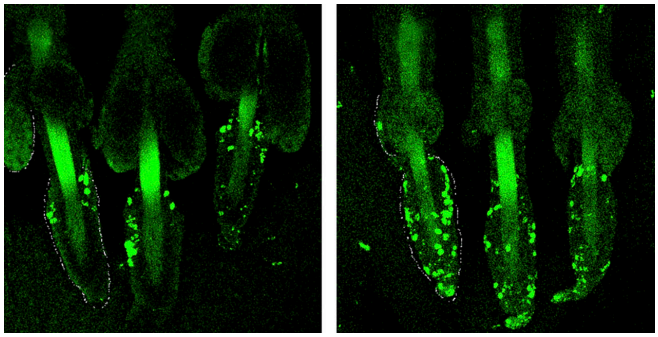
In This Issue

Stem cell slowdown

Stem cells become sluggish in a disease that resembles premature aging, as Espada et al. show. The work is the first in vivo study to link the disease to stem cell abnormalities.

In some ways, children with Hutchinson-Gilford progeria syndrome (HGPS) resemble their grandparents. They lose their hair, their bones weaken, and they develop atherosclerosis, which usually kills them as teenagers. HGPS patients manufacture a defective version of lamin A, a key component of the nuclear lamina. Two years ago, Paola Scaffidi and Tom Misteli strengthened the link between aging and HGPS, showing that healthy people accumulate faulty lamin A at the edge of the nucleus as they age. One hypothesis suggests that mutant lamin A causes some infirmities of HGPS and aging by hampering stem cells.



Slowly dividing follicle stem cells (green specks) are more abundant in mice lacking Zmpste24 (right).

Espada et al. tested this idea using a mouse model of HGPS. The animals fashion faulty lamin A because they lack an enzyme, Zmpste24, that helps trim the protein into its functional form. The team first measured the abundance of the skin's follicle stem cells, which promote wound healing and hair growth. To the researchers' surprise, the Zmpste24-deficient mice harbored more of these stem cells than did controls. However, these more numerous cells were reluctant to divide. In culture, stem cells from the mutant mice spawned smaller colonies than did cells from normal animals.

The researchers also found that abnormal lamin A disrupts the Wnt/β-catenin pathway that helps control the proliferation of stem cells. Zmpste24-lacking mice contained less of the active form of β-catenin and less cyclin D1, one of the division-promoting targets of the pathway.

Last month, Scaffidi and Misteli reported that mutant lamin A disrupted differentiation of mesenchymal stem cells (Scaffidi, P., and T. Misteli. *Nat. Cell Biol*. doi:10.1038/ncb1708). However, Espada et al. found that the follicle stem cells differentiated normally.

The mutant mice didn't show increased apoptosis by stem cells. But the suicide rate was higher among neighboring cells, whose signals nudge the stem cells to divide. The researchers conclude that abnormal lamin disrupts not just stem cells but also the surrounding cells that help control their behavior. The next step, the researchers say, is to look for similar defects in other stem cell types, such as hematopoietic stem cells. JCB

Espada, J., et al. 2008. *J. Cell Biol.* 181:27–35.

Career change for a mitotic protein

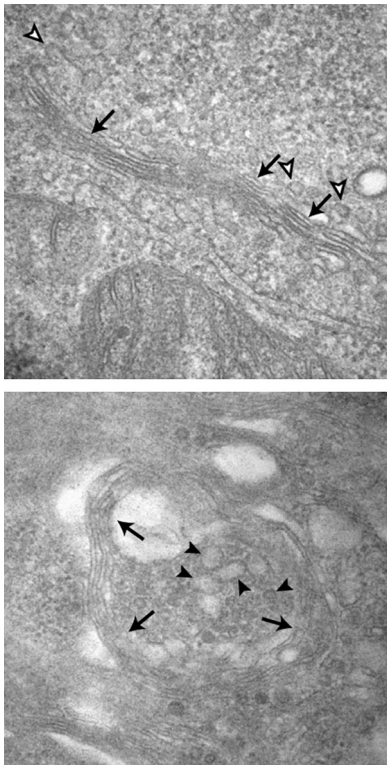
Mitosis involves more than parceling out chromosomes. A daughter cell also inherits part of the Golgi apparatus and ER from its parent cell. Nakajima et al. reveal that a protein once thought to dictate when a cell enters mitosis helps ensure that these organelles get passed on.

Conventional wisdom about the protein Myt1 held that it works with another protein called Wee1 to delay mitosis. Evidence for that view includes the fact that the proteins phosphorylate and inhibit Cdc2, a take-charge molecule that instigates mitosis when it enters the nucleus from the cytoplasm. Moreover, previous studies of yeast and human cells showed that overexpression of Myt1 prevents mitosis.

Nakajima et al. found otherwise when they used RNAi to cut Myt1 and Wee1 levels in human cells. Although cells low on Wee1 hurried into mitosis, the loss of Myt1 had little effect on mitotic timing. But Myt1 did perform a key job, the researchers discovered. During prometaphase, the Golgi apparatus fractures into thousands of tiny vesicles, some of which travel into the daughter cell and reassemble into a new Golgi apparatus. The breakup occured in cells missing Myt1, but the reunion did not. Instead of its normal folded ribbon shape, the Golgi apparatus in postmitotic, Myt1-lacking cells consisted of clustered vesicles and short or elongated tubes. Whether these defects hamper the Golgi is not clear.

Myt1 might also get the ER back into shape at the end of mitosis. Although researchers don't know all the changes that the ER undergoes during mitosis, the network appeared abnormal in Myt1-depleted cells that had just divided, Nakajima et al. found. The tubes were thicker than usual, and the cisternae that are normally scattered around the cell concentrated at its edge. Myt1 targets the B1 and B2 cyclins, which team up with Cdc2. The researchers conclude that by blocking these Cdc2/cyclin combinations, Myt1 allows the Golgi apparatus and ER to reform as mitosis concludes. JCB

Nakajima, H., et al. 2008. *J. Cell Biol.* 181:89–103.



The Golgi apparatus's layered look (top) is lost without Myt1 is (bottom).