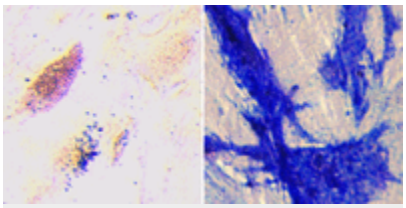
Published online 3 May 2004 as 10.1083/jcb1653rr5.

The Journal of Cell Biology

Research Roundup

Fat and bone



MSCs become fat cells (red) if RhoA is inactive (left) or osteoblasts (blue) if RhoA is active (right).

Chen/Elsevier

Too many fat cells make us round. But on a molecular level, roundness makes fat cells, based on results from Rowena McBeath, Christopher Chen, and colleagues (Johns Hopkins University, Baltimore, MD).

Fat cells derive from mesenchymal stem cells (MSCs), which are also the precursors of bone-depositing osteoblasts. Chen's group shows that the shape of an MSC determines which of these two cell types it will become.

MSCs that were spread out on a matrix formed osteoblasts, but round cells with only a small matrix-attached surface became fat cells. Changing the cell's surroundings after commitment did not alter the outcome, so the decision must be made at commitment, before differentiation.

Shape is detected via myosin-generated tension in the actin cytoskeleton. Levels of the RhoA GTPase effector ROCK, which activates myosin, were higher in spread than in round cells. Activating or inhibiting RhoA alone was even able to substitute for growth factors that induce osteoblasts or fat cells, respectively. It is not clear how shape is communicated, but perhaps spreading-induced lipid raft reorganization activates more RhoA.

Tension might be sensed at focal adhesions to determine which differentiation pathways are turned on. "Distortion [during morphogenesis] may initiate an adaptive response from cells to become a tissue that would deal with these stresses," says Chen. "The pushes and pulls that cause changes in shape may be used as a signal to decide what the cells are supposed to become." It is also possible that there is more matrix where bone will be made, but this link has not been demonstrated. ■

Reference:

McBeath, R., et al. 2004. *Dev. Cell.* 6:483-495. [Abstract]

Nicole LeBrasseur

lebrasn@rockefeller.edu