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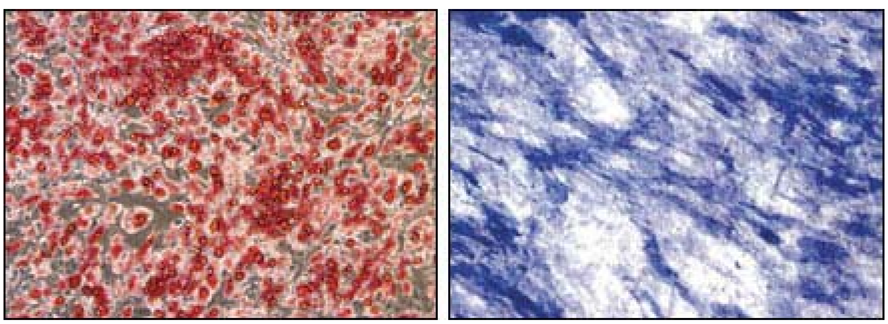
The Shape of Cells to Come

Spend enough time curled up on the couch in your youth, and you may end up as roundish blob for the rest of your life. So it is with some stem cells: The shape they assume when they're immature charts their fate, new research finds. The result might help researchers better understand some diseases and help bioengineers design better tissues.



Impressionable. Connective tissue stem cells turn into fat (red) or bone (blue) depending on their starting shape.
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Many tissues, including fat and bone, arise from a particular variety of stem cell. Researchers have been trying to understand how this precursor stem cell decides its fate. Although scientists knew that the precursor cells changed shape as they developed into adult cells, it wasn't clear whether shape determined the cells' fate.

To get a better grasp on the problem, bioengineer Christopher Chen and colleagues at the Johns Hopkins University School of Medicine in Baltimore played with the shape of growing stem cells. They lined the bottom of petri dishes with sticky proteins. In one dish, the researchers arranged the protein in tiny islands that forced each stem cell to ball up. Long, roomy patches in another dish allowed each precursor cell to spread out. Cells on the small islands grew into fat cells, filled with fatty lipids. The stretched cells turned into bone-making cells called osteoblasts, Chen's team reports in the April issue of *Developmental Cell.*

They also identified a key signaling molecule, an enzyme called Rho that stimulates stem cells to turn bone-like. Chen's team found that rounded cells had less active Rho than stretched cells, suggesting that cell shape determines cell fate by turning Rho on or off. But how does it do that? The team wondered if tension within the cell and its membrane, which gives shape to cells, affects Rho. So they disrupted cell tension by dabbing immature cultures with a chemical that dismantles the support beams inside; sans chemical, the cultures developed mostly into bone cells, but the treated cultures turned into fat cells.

"There are certainly some medical applications to this result," says biochemist Jeff Settleman of Harvard Medical School in Boston. For example, he says, the findings could help explain why exercise, which puts tension on muscles and bone, reverses the decline in bone-building seen in patients with osteoporosis. Bioengineers should also take note, he says: They may need to consider what forces to apply to cultured stem cells to coax them into the desired type of cell.

--MARY BECKMAN

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