This Week in ST

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DEVELOPMENT:
Geometry of Cell Proliferation

Localized differences in cell proliferation can help sculpt tissues during morphogenesis, leading to the complex structures found in mature tissues. In some cases, however, changes in tissue structure occur before changes in cell proliferation (see Ingber). To investigate the possibility that spatial organization could itself provide a feedback mechanism that helps regulate cell proliferation, Nelson *et al.* cultured bovine pulmonary artery endothelial cells on a substrate consisting of small fibronectin-coated islands surrounded by nonadhesive regions. Examination of proliferation patterns on islands of different sizes and shapes--or of cells grown on undulating surfaces--revealed characteristic patterns of cell proliferation that depended on the overall geometry. Computational modeling indicated that cell proliferation was greatest in predicted regions of high mechanical stress, a correlation that was confirmed by culturing cells over a micromechanical force sensor array that allowed traction forces to be measured directly. Pharmacological inhibition of Rho kinase, myosin light chain kinase, or nonmuscle myosin II ATPase (to decrease tension generated through the cytoskeleton), or disruption of cadherin-mediated intercellular adhesions with a dominant-negative mutant, attenuated gradients of cell proliferation, whereas expression of a constitutively active RhoA mutant enhanced them. Thus, the authors conclude that tissue geometry, through effects on mechanical stress, plays a role in regulating cell proliferation and tissue growth.

C. M. Nelson, R. P. Jean, J. L. Tan, W. F. Liu, N. J. Sniadecki, A. A. Spector, C. S. Chen, Emergent patterns of growth controlled by multicellular form and mechanics. *Proc. Natl. Acad. Sci. U.S.A.* **102**, 11594-11599 (2005). [Abstract] [Full Text]

D. E. Ingber, Mechanical control of tissue growth: Function follows form. *Proc. Natl. Acad. Sci. U.S.A.* **102**, 11571-11572 (2005). [Full Text]

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- Francis J. Alenghat and Donald E. Ingber (12 February 2002)
  Mechanotransduction: All Signals Point to Cytoskeleton, Matrix, and Integrins
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