Integrin: Mechanical and Biochemical Control of Cell Processes

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Abstract:

The cytoskeleton, integrin-mediated adhesion, and substrate stiffness control a common set of cell functions required for development and homeostasis that are often deranged in cancer. The connection between these mechanical elements and chemical signaling processes is not known. A combination of force detachment and chemical cross-linking methods were used to analyze the control of adhesive bonds. Unlike the control of soluble ligand binding as seen for cells circulating in the blood, the limited diffusion involved in forming of adhesive bonds switches the control of binding from a binding rate-limited to a diffusion-limited process. The control of bond number becomes controlled mechanically through the off-rate. This mechanics is controlled through the action of myosin II and the stiffness of the extracellular matrix substrate. Force combines with extracellular matrix stiffness to generate tension that triggers the integrin switch. This switch directly controls the a5b1-fibronectin bond strength through engaging the synergy domain in fibronectin and is required to generate signals through phosphorylation of focal adhesion kinase. In the context of tissues, this integrin switch controls the mechanical connection between cytoskeleton and extracellular matrix and hence regulates the level of adhesive bonds,adhesion-dependent motility and adhesion-dependent signaling pathways.

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