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Mechanical guidance of collective cell migration and invasion

XAVIER TREPAT, Institute for Bioengineering of Catalonia

A broad range of biological processes such as morphogenesis, tissue regeneration, and cancer invasion depend on the collective migration of epithelial cells. Guidance of collective cell migration is commonly attributed to soluble or immobilized chemical gradients. I will present novel mechanisms of collective cellular guidance that are physical in origin rather than chemical. Firstly, I will focus on how the mechanical interaction between the tumor and its stroma guides cancer cell invasion. I will show that cancer associated fibroblasts exert a physical force on cancer cells that enables their collective invasion. In the second part of my talk I will focus on durotaxis, the ability of cells to follow gradients of extracellular matrix stiffness. Durotaxis is well established as a single cell phenomenon but whether it can direct the motion of cell collectives is unknown. I will show that durotaxis emerges in cell collectives even if isolated constituent cells are unable to durotax. Collective durotaxis applies to a broad variety of epithelial cell types and requires the action of myosin motors and the integrity of cell-cell junctions. Collective durotaxis is more efficient than any previous report of single cell durotaxis; it thus emerges as robust mechanism to direct collective cell migration in development and disease.