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Real-time Visualization of Tissue Dynamics during Embryonic Development and Malignant Transformation

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Tissues undergo dramatic changes in organization during embryonic development, as well as during cancer progression and invasion. Recent advances in microscopy now allow us to visualize and track directly the dynamic movements of tissues, their constituent cells, and cellular substructures. This behavior can now be visualized not only in regular tissue culture on flat surfaces ('2D' environments), but also in a variety of 3D environments that may provide physiological cues relevant to understanding dynamics within living organisms. Acquisition of imaging data using various microscopy modalities will provide rich opportunities for determining the roles of physical factors and for computational modeling of complex processes in living tissues. Direct visualization of real-time motility is providing insight into biology spanning multiple spatio-temporal scales. Many cells in our body are known to be in contact with connective tissue and other forms of extracellular matrix. They do so through microscopic cellular adhesions that bind to matrix proteins. In particular, fluorescence microscopy has revealed that cells dynamically probe and bend the matrix at the sites of cell adhesions, and that 3D matrix architecture, stiffness, and elasticity can each regulate migration of the cells. Conversely, cells remodel their local matrix as organs form or tumors invade. Cancer cells can invade tissues using microscopic protrusions that degrade the surrounding matrix; in this case, the local matrix protein concentration is more important for inducing the micro-invasive protrusions than stiffness. On the length scales of tissues, transiently high rates of individual cell movement appear to help establish organ architecture. In fact, isolated cells can self-organize to form tissue structures. In all of these cases, in-depth real-time visualization will ultimately provide the extensive data needed for computer modeling and for testing hypotheses in which physical forces interact closely with cell signaling to form organs or promote tumor invasion.