Substrate stiffness differentially alters cell proliferation and apoptosis during tissue morphogenesis

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A key challenge in cell and tissue morphogenesis is to learn how the evolving tissue pattern is guided and maintained by a suitable balance between cell proliferation and apoptosis. Considering these two processes strongly coupled with cell's interaction with the extracellular matrix (ECM), adhesion dependent active mechanosensing of local stiffness is crucial. Adhered cells both create and sense tension in the extracellular matrix and change the environment to favorable condition in which they can survive. In this project, we aim to understand how various tissue patterns are generated when proliferation and apoptosis of cells are altered by varying the physical and mechanical properties of the ECM. Using an *in silico* elastic network in two dimensions, we simulate the composite *cell-ECM* structures with varying structural and mechanical integrity of ECM and review characteristic features of the tissue upon successive cell proliferation and apoptosis. Our data suggests that, in general, a uniformly rigid ECM facilitates proliferation, while apoptosis is predominant on a compliant ECM; more precisely, cell's viability is a function of the local stress. Cells in a tissue, simultaneously undergoing proliferation and apoptosis rapidly grow in locally stressed regions forming spike like structures on a rigid substrate. On the other hand, regions lacking stress become devoid of cells; a feature commonly observed during tumorigenesis. Additionally, we find that recovery of a scratch wound is delayed for cells harbored on a compliant or (and) in a highly collagen depleted ECM. Our model predictions concur with available experimental results.