Abstract

Title: Quantitative Predictions of biomechanical drivers of cell delamination in stratified epithelia (skin epidermis) using a dynamic 3D vertex model

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During embryonic development, the skin epidermis gradually transitions from a single layer of stem cells to a stratified, multi-layered tissue. This process involves the coordinated differentiation and upward movement of basal cells, known as delamination. It is not clear what mechanisms control this differentiation and delamination, allowing cells to move upward across the sharp basal-suprabasal boundary to regulate stratified tissue self-renewal and homeostasis. Although some delamination events are coupled to cell division, we first focus on the simpler case where delamination occurs in the absence of cell division, and develop a biomechanical model to investigate several experimentally driven hypotheses for what drives delamination in those cases: i) changes in the adhesion of basal cells to extra cellular matrix in the basement membrane, ii) local fluidization of surrounding tissue due to fluctuations or nearby cell divisions, or iii) cell autonomous changes to cell-cell adhesion and cortical tension. Experimental data from the developing mammalian epithelium in the Niessen and *Wickström* labs have identified specific changes to the transcriptome of cells committed to delamination. Many of these changes are associated with cell-cell and cell-substrate adhesion pathways. We incorporate them in the computational models as changes to the model parameters describing heterotypic and homotypic cell-cell interfacial tensions and adhesion to substrate. We make quantitative predictions for cell shape, delamination probabilities, and delamination rates that we compare directly to experiments, in both control and perturbed systems, to determine how different mechanisms are driving delamination.