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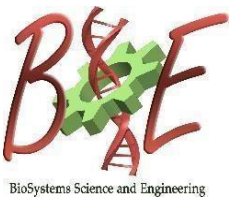

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Mechanical interactions dictate wound repair and tumorigenesis in epithelial tissues

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ABSTRACT:

Epithelial tissues act as physical barriers that line and protect our organs from infections, as well as aid in the absorption of nutrients from the food. Cells within the epithelial tissues perform these tasks while maintaining a jammed homeostatic state. In addition, any aberrant cells are constantly recognized by surrounding cells and are removed from the tissue using cell-competition. Furthermore, in an event of a wound, the otherwise jammed epithelial cells become unjammed and heal the wound by collective cell migration. Studies in the past decades have identified several molecular signalling pathways, which cells use to maintain homeostasis, to compete with their neighbours, and to migrate. However, since cells within the epithelia constantly exert active mechanical forces on each other, a comprehensive understanding on any of these physiological phenomena should also include a biophysical angle. In this presentation, I will discuss the role of physical interactions between cells in regulating the physiology and pathology of epithelial tissues using instances from 1) wound repair and 2) tumorigenesis. In the first part, I will address the problem of how leader cells emerge and how they coordinate collective cell migration during wound healing. I will show that leader cell formation is a non-cell autonomous phenomena, which is determined by cooperative mechanical interactions between cells. Our studies suggest that mechanical resilience of epithelial tissues, obtained by a certain extent of cell-jamming at homeostasis, allow for the long range spatial coordination observed during wound repair. In the second part, I will discuss my ongoing project, wherein we are trying to understand how cell-competition may drive tumorigenesis in Squamous Cell Carcinoma (SCC). We show that, when p53 is mildly elevated in the coculture of p53 mutant cells and wild type cells, the former outcompete the latter using mechanical compaction. I will also discuss the underlying molecular pathway behind this mechanical cell competition and talk about how cancer cells in SCC (p53 mutants) may be exploiting cell competition to grow at the expense of the host cells. Towards the end, I will talk about my future scientific goal of combining cell-biology with biophysics to obtain a comprehensive understanding of Epithelial defence against cancer.