## Ain: To obtain a biophysical understanding on how ageing contributes to cancer.

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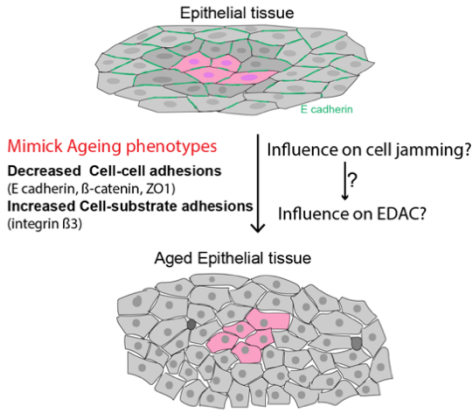
**The problem:** Aging is considered as a pro-tumorigenic state and constitutes the single most important risk factor for cancer development[1, 2]. The causative relationship between ageing and cancer is majorly considered to be the accumulation of oncogenic mutations over long period of time[2]. However, an alternative, but not mutually exclusive hypothesis is possible i.e., deregulated cellular adhesions during aging modify the physical characteristics of epithelia such that epithelial defence against cancer (EDAC)* is impaired. We will explore how ageing influence the physical characteristics of epithelia, and how it subsequently impacts epithelial defence against cancer.

*Epithelial defence against cancer (EDAC)* is a mechanism by which epithelial cells recognise and remove any aberrant neighbours and hence prevent tumor formation.*

**Project Detail:** Ageing decrease cell-cell adhesions[3] and increase cell-substrate adhesions [4]. We will attempt to mimic ageing phenotypes by genetically modifying cell-adhesion molecules. We will then investigate the mechanics of this 'age mimicking epithelia' in comparison to the normal epithelia. To do this, microscopic images will be fed into a theoretical jamming framework in order to compute physical features of cells such as cell shape, cell-density, cooperativity, dynamic heterogeneity etc. [5, 6]. Once we establish how cell-jamming is affected by imposing ageing phenotypes on cells, we will investigate how this influence their behaviour when oncogenic neighbours are introduced.




**Impact of the problem:** On the long term, an understanding on Epithelial defence against cancer will be used to generate novel anticancer therapies harnessing the protective barrier of host epithelial cells against cancer[7]. This approach would complement the current approach to therapy, which focusses solely on apoptosis to kill the tumour cells[8] and have long lasting side effects on the patient

**Prerequisite:** This project is at the interface between mathematical biology and cell biology and require basic programming skills. Proficiency in Python is beneficial. A background in Cell biology or bioengineering is beneficial but students from physics or mathematics background are also welcome if they are keen on learning applied cell biology techniques.

**Technical skills acquired in this project:** Cell culture, Gene knockout and over expression using premade plasmids, Microscopy (Confocal and inverted fluorescence microscopy), Cell segmentation and tracking on python and Image analysis tools such as ImageJ and CellPose.

**Literature**: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