Tata Institute of Fundamental Research
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Seminar

Investigating Golgi remodelling in epithelial wound healing and development

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Epithelial cells exhibit a tightly regulated cellular and intracellular asymmetry known as apico-basal polarity, critical for their barrier function. However, epithelial migration during physiological conditions like wound healing, morphogenesis, and metastasis induces a reorganization of the epithelial asymmetry. During the reorganization, the shift in the Golgi position from an apical to the basal surface is a critical event. Yet, a mechanistic understanding of the Golgi position change and the subsequent direction of Golgi reorientation with respect to migration remains elusive. Using epithelial monolayer migration, we show that Migration Induced Golgi Apparatus Remodelling (MIGAR) occurs through a transient dispersion of Golgi into the nuclear equatorial plane. The equatorial Golgi dispersion is carried out by Arp2/3 derived actin-rings remodelling of the Golgi organization, mediated through the Golgi localised MENA-GRASP65 complex. Physiologically, the equatorial Golgi dispersion is required for persistent and directional cell migration. To understand how the direction of Golgi reorientation is selected, we systematically examined several geometrical and biophysical factors that may influence Golgi reorientation. The evaluation of these factors using a custom-built Graph Neural Network based model indicated that Golgi orientation is influenced majorly by the local force experienced by the cells.

The role of Golgi organization in directional migration led us to ask if intracellular Golgi localization could also be important in more complex physiological collective environments. To this end, we focused on intestinal organoid development to capture the homeostatic turnover of intestinal epithelial cells. In the developing organoids, we found a perinuclear Golgi localization in cells of the hinge region. The hinge cells are critical for crypt-villi compartmentalization and, proper spacing and patterning of villi. The perinuclear Golgi localization may be involved in sustaining the cell-shape alteration associated with the unique localization of the hinge cells in intestinal architecture. Put together, our work underlines the importance of Golgi remodelling in regulating directional cell migration, and, suggests a similar role in other complex collective environments.

Wednesday, Feb 8th 2023

02:30 PM (Tea / Coffee 02.15 PM)

Auditorium, TIFR-H