

Internship Proposal

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Project Title:

How epithelial tissues collectively coordinate their movement?

Level:

Master Student

Project Summary:

Most of the cancer types arise from epithelial tissues. Epithelial tissues function as mechanically coupled barriers. In cancer, alterations at cell-cell and cell-matrix interfaces do not simply weaken adhesion, but fundamentally rewire how forces are transmitted across the tissue. This mechanical reorganization enables epithelial collectives to deform and migrate, facilitating collective cancer invasion. At larger scales, tissue behavior can influence neighboring tissues motion through heterotypic tissue boundaries interaction. However, there is limited understanding of the underlying mechanisms and whether forces at boundaries between tissues contribute to organ formation and cancer.

The *Drosophila* egg chamber is an ideal model to study how interactions between tissues influence collective epithelial rotation, an emergent mode of collective behavior that contributes to tissue morphogenesis and organ shaping. The student will learn high-resolution imaging, tissue-specific genetic manipulation, and perturbations of protein functions using light (optogenetics) to study the molecular principles that control collective cell migration and their implications in organ formation and cancer progression.

Work to be developed by the student:

The student will combine advanced optogenetic and genetic (e.g. CRISPR-based GFP-tagged lines; tissue-specific RNAi) with high-resolution imaging to characterize the impact of inter-tissue mechanical coupling at the tissue boundaries in epithelial collective cell migration, through a number of specific tasks such as:

- 1) We will use quantitative imaging analysis to determine if the impact of mechanical perturbation in the germline is correlated with defective cell migration.



2) By perturbing contractility at the germline-epithelium interface, we will determine if mechanical perturbation has an impact on the organization of focal and cell adhesions as well on components of the cytoskeleton implicated in epithelial rotation.

References:

1. Friedl P, et al., 2009. Collective cell migration in morphogenesis, regeneration, and cancer.
2. Espina JA, et al., 2022. Durotaxis: the mechanical control of directed cell migration.
3. Barlan K, et al., 2017. Fat2 and Lar Define a Basally Localized Planar Signaling System Controlling collective Cell migration.
4. Haigo SL, et al., 2011. Global tissue revolutions in a morphogenetic movement controlling elongation.
5. Coban B, et al., 2021. Metastasis: crosstalk between tissue mechanics and tumor cell plasticity.