SORBONNE UNIVERSITÉ

Interfaces pour le vivant

Title of the research project: **Contrôle optogénétique de la migration collective maligne**
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Doctoral School : ED564

Subject description :

Understanding how metastases form remains a key step in our ability to better cure cancer, as they are responsible for 90% of cancer-related death. As opposed to the commonly assumed model relying on an epithelial-to-mesenchymal transition, Fanny Jaulin's lab recently discovered a new mode of tumor dissemination: spherical clusters of cancer epithelial cells collectively propagate, displaying an unexpected outward apical pole. These clusters use actomyosin contractility to migrate, a process reminiscent of single-cell amoeboid migration and never reported before for collectives.

We propose to study this new mode of malignant collective invasion thanks to the optogenetic tools developed in Mathieu Coppey's lab. These tools allow a spatiotemporal control of Rho-GTPase activities with light to control cell migration and contractility.

The project will be organized in 3 objectives:

Development of an in vitro model to study the migration of cell clusters: using both cancer cell clusters from patient and cell lines, the student will image 3D spherical clusters and track their migration in 3D physiological hydrogels.

Induction of collective migration by optogenetic control of Rho-GTPases: using patterns of light, a given fraction of cells from the cluster will be activated. Thanks to the control of RhoA/Rac1 balance, we expect to be able to induce the two modes of collective migration: adhesion-based and amoeboid-like.

Optogenetic control of upstream TGF-β signaling to switch the mode of migration: known for promoting metastases, TGF-β is also potentially selective for the mode of migration. Using an optogenetic system allowing a precise control of its activity, we expect to control the mode of migration with only one input that will let us switch the mode of migration.

Our aim is to show that cancer cell clusters can migrate using two distinct processes and that there is a plasticity between these modes of migration controlled by the level of TGF-β signaling.