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Team: Light-based observation and control of cellular organization

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Collaboration: Team Collective Invasion, Fanny Jaulin, Institut Gustave Roussy

Title: Emergence of collective cell migration

Cancer is a leading cause of death worldwide, mainly due to metastases which are responsible for 90% of the deaths. Metastases form when some cancer cells escape from the primary tumor to migrate in the organism, and create new colonies in other parts of the body. Recently, using explants from patients, Fanny Jaulin's team from Gustave Roussy Institute showed that these metastases could form collectively: instead of migrating individually, groups of around fifty cells collaborate to go across tissues[(1)].

Combining our expertise with Matthieu Piel and Raphael Voituriez's lab, we demonstrated that these groups of tumor cells use a second mode of collective migration that was never described before, which we named collective amoeboid migration. In non-adherent microfluidic channels, groups of cells propel themselves thanks to a global gradient of contractility and random cell fluctuations[(2)].

We now want to understand how cells organize themselves to initiate migration, create and maintain a collective polarity. Who is deciding? How? With chemical, electrical or mechanical signals?

To tackle these questions, the student will study this collective migration in a minimal system, with clusters containing 2 to 10 cells where migratory properties already emerge. He will question the way polarity is initiated in microfluidic microchannels, and look at the possible gain of functions of this collective system. He will use fluorescent markers of the cytoskelet, optogenetic techniques[(3)], fluorescent microscopy as well as different types of microfluidic chips to confine cells at different heights.

Techniques: Cell culture, microfluidic, microscopy, optogenetics, image analysis (Python or Matlab)

Skills required: motivation to learn and make experiments. Basic notions in biology and programming.

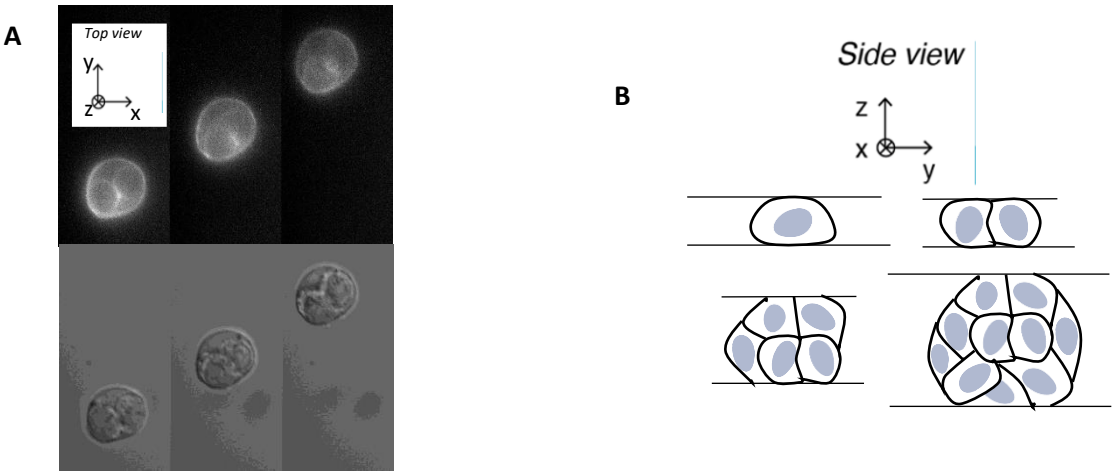

Figure : (A) Migration of a group of 5 cells in a confined environment (labeled with actin in the upper image, and in transmission on the bottom) (B) Sketch of different confinements for one, two, 5 or 10 cells.

(1) Zajac O, Raingeaud J, Libanje F, Lefebvre C, Sabino D, Martins I, Roy P, Benatar C, Canet-Jourdan C, Azorin P, Polrot M, Gonin P, Benbarche S, Souquere S, Pierron G, Nowak D, Bigot L, Ducreux M, Malka D, Lobry C, Scoazec JY, Eveno C, Pocard M, Perfettini JL, Elias D, Dartigues P, Goéré D, Jaulin F. Tumour spheres with inverted polarity drive the formation of peritoneal metastases in patients with hypermethylated colorectal carcinomas. Nat Cell Biol. 2018

(2) Pagès D.-L., Dornier E., De Seze J., Wang L., Luan R., Cartry J., Canet-Jourdan C., Raingeaud J., Voituriez R., Coppey M., Piel M., Jaulin F.. Cell clusters adopt a collective amoeboid mode of migration in confined non-adhesive environments. bioRxiv 2020

(3) Valon L., Etoc F., Remorino A., Pietro F., Morin X., Dahan M., Coppey M.. Predictive Spatiotemporal Manipulation of Signaling Perturbations Using Optogenetics. Biophysical Journal 2015.