TWO FINANCED PhD POSITIONS

Study of dynamic cell-matrix interactions

within microfabricated 3D arrays mimicking the tumor microenvironment

(PhD position 1) Chemistry/biomaterials and cell biology

(PhD position 2) Biophysics and image analysis

Project

The mechanical, geometrical and chemical properties of the **3D fibrous extracellular matrix** play a key role in cancer initiation and progression, by controlling the movement and fate of tumor cells as well as surrounding fibroblasts or immune cells. A strong emphasis has been put recently in the community on the development of matrices with controllable fiber properties, as tools to understand cell mechanical behavior and migration. However, while numerous biomaterials have been engineered to obtain the desired properties at the multicellular scale, controlling the 3D architecture and the chemistry of fibers at a subcellular scale necessitates specific techniques like two-photon polymerization. Our team has developed over the years **a full toolbox to produce at will complex 3D geometries and fiber networks** [1,2], in hybrid polymers, hydrogels or protein materials, which also includes an innovative measurement of 3D forces exerted by cells. Now our system provides an ideal tool to understand finely the dynamic adaptation of cell individual and collective migration to the microenvironment, including migration behaviors and cell shape changes in tumors.

This project aims to characterize the **dynamic behavior** of cancer cells and surrounding cells, in relation to the fine geometry and to local mechanical and chemical properties of their 3D fiber microenvironments. Two-photon polymerization will be used to build a variety of **3D generic architectures** of fiber grids characteristic of the **tumor extracellular matrix**, like structures with gradients of stiffness, fiber density or different fiber cross-linkings. In these different architectures, the migration biases, the dynamic morphology of cells and of their nuclei and membrane protrusions (including filopodia) and the local 3D forces will be systematically analyzed, and the results integrated in a general framework in link with the local physical and chemical cues of the grid. **Cell lines** studied will be fluorescently-labeled tumor cells models of breast or renal cancer, fibroblasts or cancer-associated fibroblasts, or immune cells. **Image acquisition** will be performed by advanced optical tools, spinning disk or Lattice Light Sheet Microscopy. An important part of the project will be to develop from previous tools of the group and from the existing literature **automated image analysis** pipelines with Artificial Intelligence-based techniques, and to integrate these results in a general frame.

This project is based on the expertise of the consortium on chemistry, two-photon polymerization and cell dynamics, including image analysis and 3D force measurements. It will highly benefit from synergy with parallel collaborative projects developed in the team in various 3D architectures. The system developed, from microstructures to cell dynamic datasets and automated image analysis development, will be of general interest for the community, and will pave the way to future applications in the domain of cancer treatments, for example targeting matrix organization.

1. Ucla, P. *et al.* Dynamics of Endothelial Engagement and Filopodia Formation in Complex 3D scaffolds. *Int. J. Mol. Sci.* **23**, 2415. (2022).
2. Coscoy, S. *et al.* Microtopographies control the development of basal protrusions in epithelial sheets. *Biointerphases* **13**, 041003 (2018).

Candidate profiles

We are looking for candidates for two PhD positions wishing to work in an interdisciplinary environment, and we will consider a variety of profiles for this project. Applicants with backgrounds **either in chemistry, biomaterials, (bio)physics, image analysis or cell biology** could be a good match for the project. Depending of the profile and of the wishes of the candidates, the individual PhD projects could be focused on experimental aspects (position 1), on image analysis developments (position 2), or a combination of both. Both projects have complementary aspects, and PhD candidates will benefit from the synergy between their two subjects.

(PhD position 1) Ideally, the candidate will be in charge of developing and characterizing chemistries and architectures of 3D fiber networks, and on performing dynamic imaging of fluorescent cells on these networks.

(PhD position 2) The candidate will be in charge in developing automated image analysis pipelines with classical and AI-based techniques to detect the dynamic evolution of cell shape in function of the local characteristics of the fiber arrays and of the invasive potential of cancer cells. This position can be combined or not with an experimental aspect, depending on the wish of the candidate.

Hosting structures

This project will be carried out at **Institut Curie**, a leading French cancer center combining a multidisciplinary research center and hospital, and at **Chimie ParisTech-PSL**, a chemistry engineering school and active research center in chemistry. It will be performed in the frame of a collaborative project between **Sylvie Coscoy** (team Macromolecules and Microsystems for Biology and Medicine, Curie) and **Vincent Semetey** (team Materials, Interface and Soft Matter). The aim of the global **project** is to develop innovative approaches to build reconstituted 3D fiber architectures perfectly controlled in a geometrical, chemical and mechanical point of views, in order to study fundamental mechanisms of cell-fiber dynamic interactions. This project benefits from a **strong collaborative network** for mechanical, imaging and biology aspects. Institut Curie and Chimie ParisTech-PSL are both located in the center of Paris, in close proximity, and the project benefits from the **rich infrastructure** of both institutes (state-of-the-art imaging platform, cell culture, microfluidics and microfabrication, modeling of biophysical phenomena; chemical surface analysis equipment and wide expertise in chemistry), with **two-photon polymerization set-ups** specifically dedicated to the project.

These PhDs are financed by an ANR grant (Agence Nationale de la Recherche).

Contacts

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