Post-doctoral offer in Molecular and Cellular Biology

Stress et Cancer laboratory
Institut Curie, U830 Inserm, Paris, FRANCE
Dr. Fatima Mechta-Grigoriou, fatima.mechta-grigoriou@curie.fr

Title of the project : Heterogeneity and plasticity of carcinoma-associated fibroblast subsets in cancer

Context:

By combining studies from tumor samples and *in vitro* functional assays, our lab has recently identified 4 distinct sub-populations of Carcinoma-associated fibroblasts (CAF) (referred to as CAF-S1 to CAF-S4) in breast and ovarian cancers. Among these 4 CAF sub-populations, we found that CAF-S1 fibroblasts are immunosuppressive by acting through a multi-step mechanism. Indeed, CAF-S1 cells are able to attract, increase survival and promote differentiation of regulatory T lymphocytes in breast and ovarian cancers (Costa, *Cancer Cell* 2018; Givel, *Nat. Commun*, 2018). Recently, we performed single cell RNA sequencing on more than 18000 immunosuppressive CAF-S1 fibroblasts isolated from breast cancer patients and found that this subpopulation is, on its own, heterogenous and composed by distinct cellular clusters.

Project:

This project plans to understand at molecular levels the plasticity of the CAF-S1 subpopulation and CAF-S1 cellular clusters identified by single cell analysis. What are the mechanisms driving accumulation of CAF-S1 subset and CAF-S1 cellular clusters in cancer ?

The project will be divided into 3 main axes that will:
(1) determine the cells of origin of CAF-S1 clusters, such as Mesenchymal Stem Cells (MSC) and/or resident fibroblasts;
(2) define the role of tumor and immune cells on CAF-S1 heterogeneity and plasticity;
(3) decipher the involved mechanisms.

Analyses will combine studies on human samples from prospective and retrospective cohorts of patients, mouse models and functional assays using primary CAF-S1 fibroblasts cultured *in vitro* in various conditions.

Required expertise:

We are looking for a strong and highly-motivated post-doctoral candidate. Expertise in cellular biology, in particular in culture *in vitro* of primary cells in 3-dimensions, will be appreciated for developing this project. Candidate with good communication skills, and being good team player with a certain degree of autonomy will be appreciated.

Contact:

Please send candidature, including CV, a motivation letter and contact information for academic references or letters of reference to: fatima.mechta-grigoriou@curie.fr

Dr. Fatima Mechta-Grigoriou, Head of Stress and Cancer laboratory
Deputy Director “genetic and Biology of Cancer” Unit
Institut Curie, Inserm U830
26 rue d’Ulm, 75005 Paris

Main recent publications :

Gentric G., Kieffer Y., Mieulet V., Goundiam O., Bonneau C., Nemati F., Hurbain I., Raposo G., Popova T., Stern MH., Lallemand-Breitenbach V., Müller S., Cañeque T., Rodriguez R., Vincent-Salomon A., de Thé H., Rossignol R. and **Mechta-Grigoriou F.** PML-regulated mitochondrial metabolism enhances chemosensitivity in human ovarian cancers.
Cell Metabolism, 2019 Jan 8;29(1):156-173.e10.

Costa A., Kieffer Y., Scholer-Dahirel A., Pelon F., Bourachot B., Cardon M., Sirven P., Magagna I., Fuhrmann L., Bernard C., Bonneau C., Kondratova M., Kuperstein I., Zinovyev A., Givel AM, Parrini MC, Soumelis V., Vincent-Salomon A. and **Mechta-Grigoriou F.** Fibroblast heterogeneity and immunosuppressive environment in breast cancers.
Cancer Cell. 2018 Mar 12;33(3):463-479

Givel AM, Kieffer Y., Scholer-Dahirel A., Sirven P., Cardon M., Pelon F., Magagna I., Gentric G., Costa A., Bonneau C., Mieulet V., Vincent-Salomon A. and **Mechta-Grigoriou F**. miR-200-regulated CXCL12b promotes fibroblast heterogeneity and immunosuppression in ovarian cancers.
Nature Communications. 2018 Mar 13;9(1):1056.

Lefort S, Thuleau A, Kieffer Y, Sirven P, Bieche I, Marangoni E, Vincent-Salomon A, **Mechta-Grigoriou F**. CXCR4 inhibitors could benefit to HER2 but not to triple-negative breast cancer patients.
Oncogene, 2017 Mar 2;36(9):1211-1222.

Gentric G.*, Mieulet V.*. and **Mechta-Grigoriou F**. Heterogeneity in Cancer Metabolism: New Concepts in an old Field.
Antioxidant & Redox Signalling. 2017 Mar 20;26(9):462-485

Gruosso T.*, Mieulet V.*, Cardon M., Kieffer Y., Bourachot B., Vincent-Salomon A., Miller K. and **Mechta-Grigoriou F**. Chronic oxidative stress promotes H2AX protein degradation and enhances chemosensitivity in breast cancer patients. (*Co-1st)
EMBO Molecular Medicine. 2016 May 2;8(5):527-49

Batista L, Bourachot B, Mateescu B, Reyal F, **Mechta-Grigoriou F**. Regulation of miR-200c/141 expression by intergenic DNA-looping and transcriptional read-through.
Nature Communications. 2016 Jan 4;7:8959.

Gruosso T., Garnier C., Abelanet S., Kieffer Y., Lemesre V., Bellanger D., Bieche I., Marangoni E., Sastre-Garau, Mieulet V*. and **Mechta-Grigoriou F***. MAP3K8/TPL2/COT is a potential predictive marker for MEK inhibitor treatment in high-grade serous ovarian carcinomas.
Nature Communications. 2015. Oct 12;6:8583.

Lefort S*, Joffre, C*, Kieffer, Y, Givel AM, Bourachot B, Zago G, Bieche I, Dubois T, Meseure D, Vincent-Salomon A, Camonis J and **Mechta-Grigoriou F**. Inhibition of autophagy as a new means of improving chemotherapy efficiency in high-LC3B triple-negative breast cancers.
Autophagy, 2014, Dec 2;10(12):2122-42.