PhD Position in Bioprinting at Bordeaux (start: 01/09/2022, 3 years)

ART BioPrint facility (H. Oliveira)

NOVEL BIOPRINTING APPROACHES FOR THE CREATION OF ADVANCED PANCREATIC CANCER INITIATION MODELS

Context

Pancreatic cancer is a complex and progressive disease, and in-depth studies of cancer initiation, migration, and progression-associated mechanisms that can lead to the development of new therapeutic strategies, are urgently needed. This pathology involves spatiotemporal changes, cell–microenvironment and cell–cell interactions, and evolutive signal transmission in cells, which makes the fabrication of in vitro tumor models extremely challenging.

Animal models have advanced our understanding of this complex diseases, nonetheless these are complex, time consuming, expensive and ethically restrictive. In recent years, advances in biomaterials and biofabrication methods, especially bioprinting technology, have paved the way for innovative platform technologies for in vitro cancer research. Indeed, 3D bioprinting is an attractive additive manufacturing technique that allows, starting from a digital model, the deposition of biomaterials loaded with cells and biologic molecules, and the production of 3D objects with complex shapes. This makes bioprinting a tool of choice for the creation of high-throughput cancer models and enable the study of cancer ontogenesis.

In this process, the following parameters are key: A) the precision of cell deposition, including different cell types, as a mean to evaluate the heterotopic communication between different relevant cells, B) the ability to control local cell concentration and their precise 3D positioning within a matrix, enabling the creation of near-physiological models, C) the ability to replicate the same model with great precision and within a small volume, allowing the evaluation of a desired mechanism at high-throughput with strong statistical power.

Here, we will focus on the establishment of advanced 3D in vitro pancreatic cancer models to decipher the initiation mechanism of this pathology, by tackling the intrinsic and extrinsic factors leading to PDAC initiation/progression. Numerous studies have shown that the tumor microenvironment shapes and influences the neoplasm progression:

1) The extracellular matrix composition (i.e. collagen, hyaluronic acid, laminin abundance) modulates cell proliferation and migration, leading to PDAC development.

2) A predominant fraction of the PDAC stroma are pancreatic stellate cells (PSCs) that assume an active myofibroblast-like phenotype in the tumor microenvironment. Dynamic interactions of these cells with other tumor components shape the extracellular matrix (ECM) and influence the neoplasm progression.

3) Within the pre-cancerous niche, the creation of an hypoxic environment (a hallmark for PDAC) has shown to support the EMT (epithelial to mesenchymal transition) of pancreatic epithelial to malignant neoplastic cells. Interestingly, EMT occurs very early in PDAC onset, further stressing the importance of this process in this pathology.

Here, we want to establish biofabrication procedures to create in vitro tridimensional complex models

that can replicate the in vivo precancerous niche and be used as tools to decrypt the complex interplay between cancer initiation cells and their niche.
These novel in vitro tools should increase our understanding of the main oncogenic signal dynamics in pancreatic cancerogenesis and allow us to propose novel diagnosis and interception therapeutic leads .
This project is fully financed by the ANR (Project BioPrint_PaCiniMo, JCJC 2021 Oliveira,H). A strong collaboration is already established with Julie GUILLERMET-GUIBERT (CRCT, Toulouse), strengthening the know-how in pancreatic cancer.

The Lab

The Laboratory for the Bioengineering of Tissues (BioTis U1026) is located in Bordeaux (France) and its research spans from the fundamental aspects of cell-cell and cell-matrix interactions, all the way to the development of translational models and their clinical applications in vascular, orthopedic, oral and maxillofacial surgery. There is also an strong expertise on biofabrication and bioprinting approaches (particularly at the ART Bioprint, https://artbioprint.fr).

Profile and skills required

The PhD candidate will work in a multidisciplinary research environment (BioTis) where medicine, cellular biology and engineering are combined to improve the development of biomedical engineering approaches.
We are looking for a talented, curious, enthusiastic, and motivated life scientist for a three-year PhD position. As a PhD candidate, you are committed to conduct independent and original scientific research, to report on this research in international publications and conferences, and to assist in the supervision of research projects for both bachelor and master students.
Committed to a mission, willing to learn and to solve problems, and not afraid to take decisions. Ability to take initiative, be organized, self-directed, able to assume responsibility. Good interpersonal skills, ability to work in a team and network.

Previous experience with cell culture, bioprinting, tissue engineering and biomaterials is a plus.

Qualifications

Candidates should have a MSc degree with expertise/background in materials science/ engineering and interface with biology. We would particularly welcome applications from candidates with background in engineering materials, chemical engineering and biofabrication. Previous experience in cell biology, cancer biology and/or tissue engineering are welcomed.

The PhD candidate is expected to have an excellent academic record and should be able to work in a multidisciplinary environment in close cooperation with other experts. Excellent communication skills and a good expertise of English (oral and written) are also required.

Start Date and duration:

3 year-contract (full-time) starting September 2022

Information and Application

Questions regarding this position can be directed to: Dr Hugo Oliveira

email: hugo.de-oliveira@inserm.fr

Applications, including a CV, a statement of your interest must be attached to your application form. Also, if possible, the names and contact of two references should be included.

Recent Bibliography

H Oliveira, C Médina, G. Labrunie, et al. “Cell-Assembled extracellular Matrix (CAM): a human biopaper for the biofabrication of prevascularized tissues able to connect to the host circulation in vivo.”, 2022 Biofabrication 14 015005.

N Dusserre, ML Stachowicz, …, F Paris, H Oliveira, “Microvalve bioprinting as a biofabrication tool to decipher tumor and endothelial cell crosstalk: application to a simplified glioblastoma model”, Bioprinting, Volume 24, December 2021, e00178

H Oliveira, C Médina, ML Stachowicz, BP dos Santos, L Chagot, et al. “Extracellular matrix (ECM)-derived bioinks designed to foster vasculogenesis and neurite outgrowth: Characterization and bioprinting”, Bioprinting, Volume 22, 2021;

M Cuvellier, F Ezan, H Oliveira, S Rose, JC Fricain, S Langouët, et al. “3D culture of HepaRG cells in GelMa and its application to bioprinting of a multicellular hepatic model”, Biomaterials, 269, 120611 7, 2021;

Hakobyan D, Medina C, Dusserre N, Stachowicz M-L, Handschin C, Fricain J-C, Guillermet-Guibert J, Oliveira H. Laser-assisted 3D bioprinting of exocrine pancreas spheroid models for cancer initiation study. Biofabrication. 2020, Apr 16;12(3):035001.