Supervisor(s):
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Host laboratory:
BGE bge-lab.fr/

Host group/team:
Biomics

Title of the M2 research internship:

Study of pancreatic ductal adenocarcinoma initiation using a 3D in vitro model for biomarker discovery

Project summary:

The pancreas is a multifaceted organ responsible for regulating blood glucose and aiding in digestion. Its functions are divided between the Langerhans islets, which regulate blood glucose levels by secreting insulin and glucagon, and acinar structures, which produce digestive enzymes for transport to the duodenum through ductal structures lined by epithelial cells. Despite their functional differences, these components are closely located anatomically.

Pancreatic cancer can arise in different parts of this organ, pancreatic ductal adenocarcinoma (PDAC) accounting for the vast majority of cases. It carries a grim prognosis, with a low 5-year survival rate of 9%, lower than most cancers. The difficulty lies in its late diagnosis, often when the disease is already incurable due to the absence of early symptoms.

Diabetes mellitus, characterized by abnormal blood sugar levels, exhibits a complex relationship with PDAC, as evidenced by epidemiological studies. However, the underlying cellular and molecular mechanisms remain unclear.

Our focus is on developing a 3D in vitro model of PDAC that captures the anatomical complexity of the pancreas. Specifically, we aim to create a model incorporating epithelial duct structures within a hydrogel matrix mimicking pancreatic endocrine function. By studying cellular interactions between these components, we seek to unravel the connection between diabetes mellitus and pancreatic cancer, hypothesizing that diabetes may predispose individuals to pancreatic cancer development. Various methods will be employed to induce neoplastic transformation in this model, with the ultimate goal of identifying new biomarkers and testing potential therapeutic agents. 3D cell culture and microfluidic perfusion will be used, as well as classical molecular biology (RTqPCR, ELISA, ...) and cutting edge imaging (light sheet microscopy, immunostaining,...).

The student's involvement in the project will be based on the advancements made prior to the start of the internship.

This internship is part of a funded project already underway in the laboratory. The student recruited will be jointly supervised by a second-year PhD student (Pierre Caullet) and her supervisor (Flora Clément). This subject may lead to a thesis.

Keywords:
pancreatic cancer initiation, diabetes mellitus, pancreas-on-chip

Relevant publications of the team:

1/Papoz A, Clément F, Laporte C, Tubbs E, Gidrol X, Pitaval A. Les Langerhanoïdes, des organoïdes d'îlots pancréatiques [Generating pancreatic islets organoids: Langerhanoids]. Med Sci (Paris). 2022 Jan;38(1):52-58. French. doi: 10.1051/medsci/2021244. Epub 2022 Jan 21. PMID: 35060887.

2/Quintard C, Tubbs E, Jonsson G, Jiao J, Wang J, Werschler N, Laporte C, Pitaval A, Bah TS, Pomeranz G, Bissardon C, Kaal J, Leopoldi A, Long DA, Blandin P, Achard JL, Battail C, Hagelkruys A, Navarro F, Fouillet Y, Penninger JM, Gidrol X. A microfluidic platform integrating functional vascularized organoids-on-chip. Nat Commun. 2024 Feb 16;15(1):1452. doi: 10.1038/s41467-024-45710-4. PMID: 38365780; PMCID: PMC10873332.

3/Quintard C, Tubbs E, Achard JL, Navarro F, Gidrol X, Fouillet Y. Microfluidic device integrating a network of hyper-elastic valves for automated glucose stimulation and insulin secretion collection from a single pancreatic islet. Biosens Bioelectron. 2022 Apr 15;202:113967. doi: 10.1016/j.bios.2022.113967. Epub 2022 Jan 5. PMID: 35065480.

4/Laperrousaz B, Porte S, Gerbaud S, Härmä V, Kermarrec F, Hourtane V, Bottausci F, Gidrol X, Picollet-D'hahan N. Direct transfection of clonal organoids in Matrigel microbeads: a promising approach toward organoid-based genetic screens. Nucleic Acids Res. 2018 Jul 6;46(12):e70. doi: 10.1093/nar/gky030. PMID: 29394376; PMCID: PMC6158603.