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Characterizing biomarkers for early diagnosis of pancreatic cancer

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The pancreas, essential for both endocrine and exocrine functions, is associated with serious conditions such as diabetes mellitus (DM) and pancreatic cancer (PC). PC is one of the most lethal tumors, largely due to late-stage diagnoses[1]. Individuals with DM, particularly those with new-onset diabetes, face an elevated risk of PC, yet the molecular mechanisms remain unclear[2].

Our hypothesis posits that a diabetic microenvironment facilitates the initiation of PC[3]. The project aims to develop an amphiphilic pancreas-on-chip for investigating the links between DM and PC. This chip comprises a chamber with a duct lined by exocrine cells, surrounded by islets of Langerhans in hydrogel (A). 3D cultured islets and various hydrogels enable perfusion for extended studies (B-D). Monitoring involves multi-OMICS approaches (secretome analysis, proteomics, transcriptomics), and 3D imaging.

We have already established two distinct devices (D and E), and our preliminary results demonstrate effective modeling of endocrine function using various islets of Langerhans models (F-J).

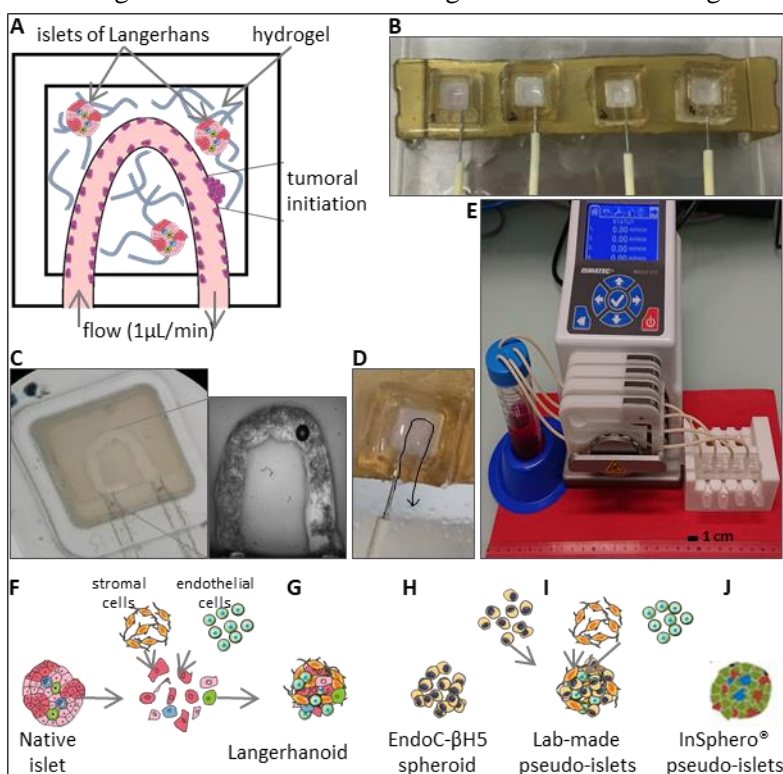


Figure 1 Amphiphilic pancreas-on-chip. **A:** Schematic view of the device: a channel is generated through the use of a sacrificial 3D printed ink. It is then surrounded by hydrogel containing islets of Langerhans. After sacrificial ink removal, the channel is lined by exocrine cells. The tumoral initiation will be visualized thanks to 3D imaging including Light Sheet Fluorescence Microscopy available in the lab (3D reconstructed samples have already been performed). **B:** 4 devices paralleled in the incubator. **C:** one device with a zoom on a channel lined by exocrine cells. **D:** perfusion flow from the entrance needle to the exit hole. **E:** new version of 4 chambers included in one device, with peristaltic pump and a collection box. This new version follows the ISO compatibility norms of medical devices. Different types of islet of Langerhans models available in the lab: **F:** native islet from deceased donor, **G:** Langerhanoids made from the reaggregation of native islet dissociation supplemented in stromal and endothelial cells[4], **H:** spheroid of EndoC-βH5 cells, **I:** pseudo-islet made from the aggregation of EndoC-βH5 cells supplemented in stromal and endothelial cells, **J:** commercially available InSphero® pseudo-islet.

The objectives encompass refining the device and modeling the diabetic microenvironment by using (i) a decellularized matrix obtained from adipose tissue of both healthy and diabetic patients, (ii) diabetic islets, (iii) diabetic adipose stem cells, and exploring neoplastic transformation for early diagnostic biomarkers.

Anticipated outcomes involve gaining novel molecular insights into the links between DM and PC, as well as identifying early PC biomarkers which are desperately needed. The microphysiological device developed will make a substantial contribution to comprehending tumor initiation PC. Furthermore, it has the potential to extend beyond pancreas, serving as a valuable tool for studying disorders in other glands.

References

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