Engineering A Low Cost, Multicellular Patient-Derived Model of Pancreatic Cancer Tissue: A Path Towards Personalised Medicine

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Introduction

Pancreatic Ductal Adenocarcinoma (PDAC) is a devastating disease with a 5-year survival rate of 7%, largely due to its complex tumour microenvironment (TME) and inherent therapeutic resistance. Current gold-standard *in vitro* models, such as organoids, often require expensive growth factors for expansion and frequently deplete stromal cells, failing to fully recapitulate the intricate cellular interplay of the *in vivo* PDAC TME. In this work, building on our previous bioengineered PDAC models[1-4], we developed a cost-effective zonal co-culture model using patient-derived PDAC tissue. The model enables the maintenance of both cancer and activated stellate cells, a key stromal component, for extended periods. Such approach can help overcome limitations of currently available systems.

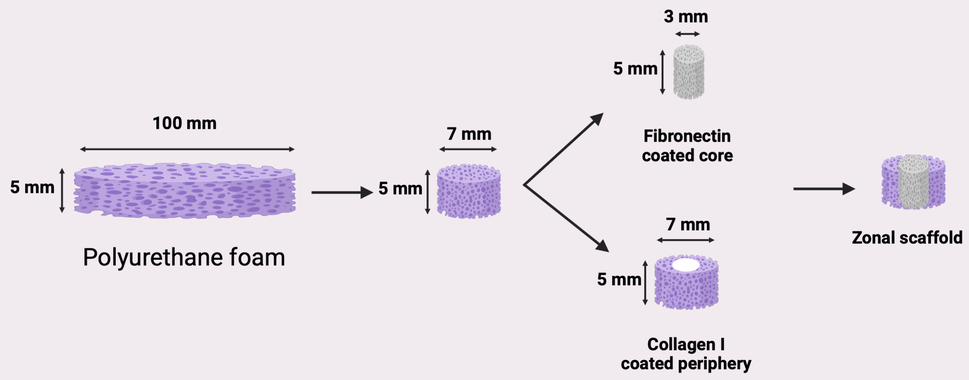
Aims & Objectives

To develop a cost-effective zonal co-culture model of PDAC using patient-derived tissue

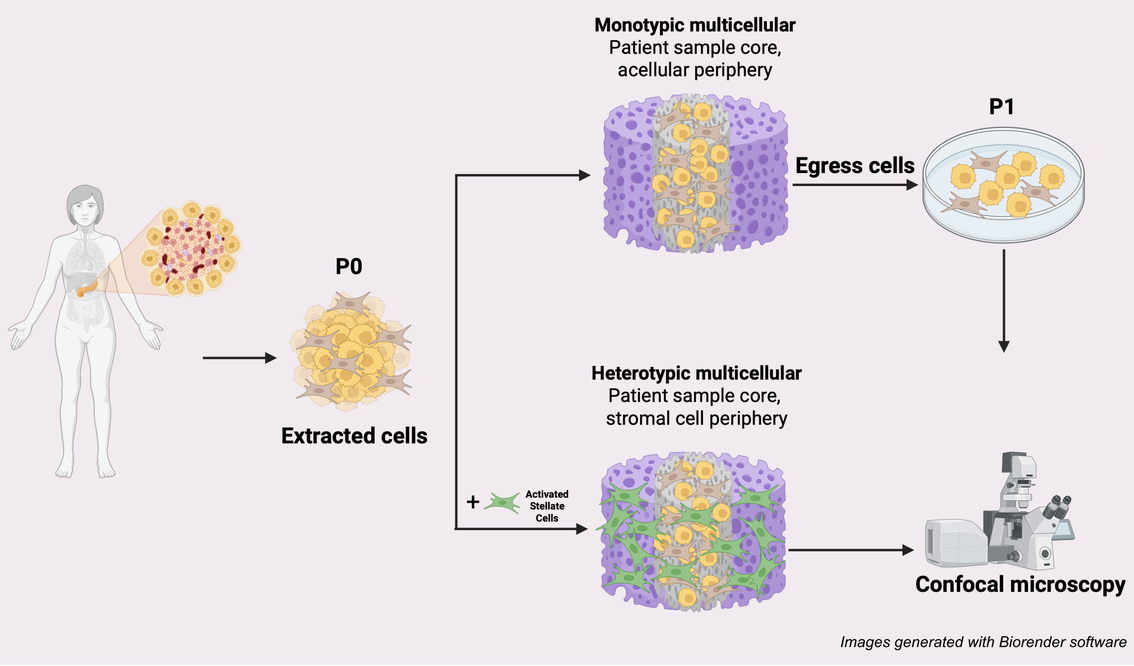
- Isolate and dissociate patient-derived PDAC tissue
- Develop zonal and multi-cellular models of PDAC
- Assess cell viability of patient samples in zonal scaffolds with or without activated stellate cells
- Assess cell topography and differentiation of patient samples within the scaffold

Methodology

Zonal scaffold generation and functionalisation



Patient sample experimental design



Results

1. Patient-derived tumour tissue is composed of cancer and stromal cells

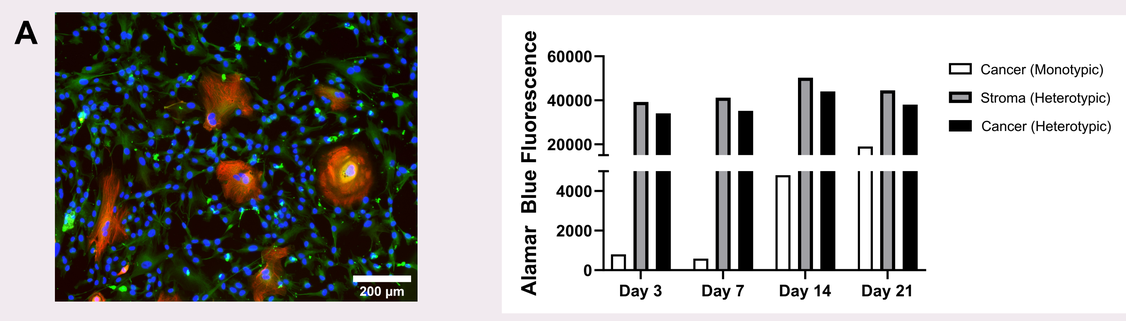


Figure 1. Tumour tissue composition and metabolic activity in different 3D configurations.
A. Representative fluorescent image of egress tumour tissue cells stained with pan-cytokeratin (red), α-SMA (green) and DAPI (blue). **B.** Metabolic activity measured by alamarBlue of monotypic and heterotypic multicellular models monitored over 3 weeks of culture.

2. Tumour cells migrate to zonal scaffold periphery

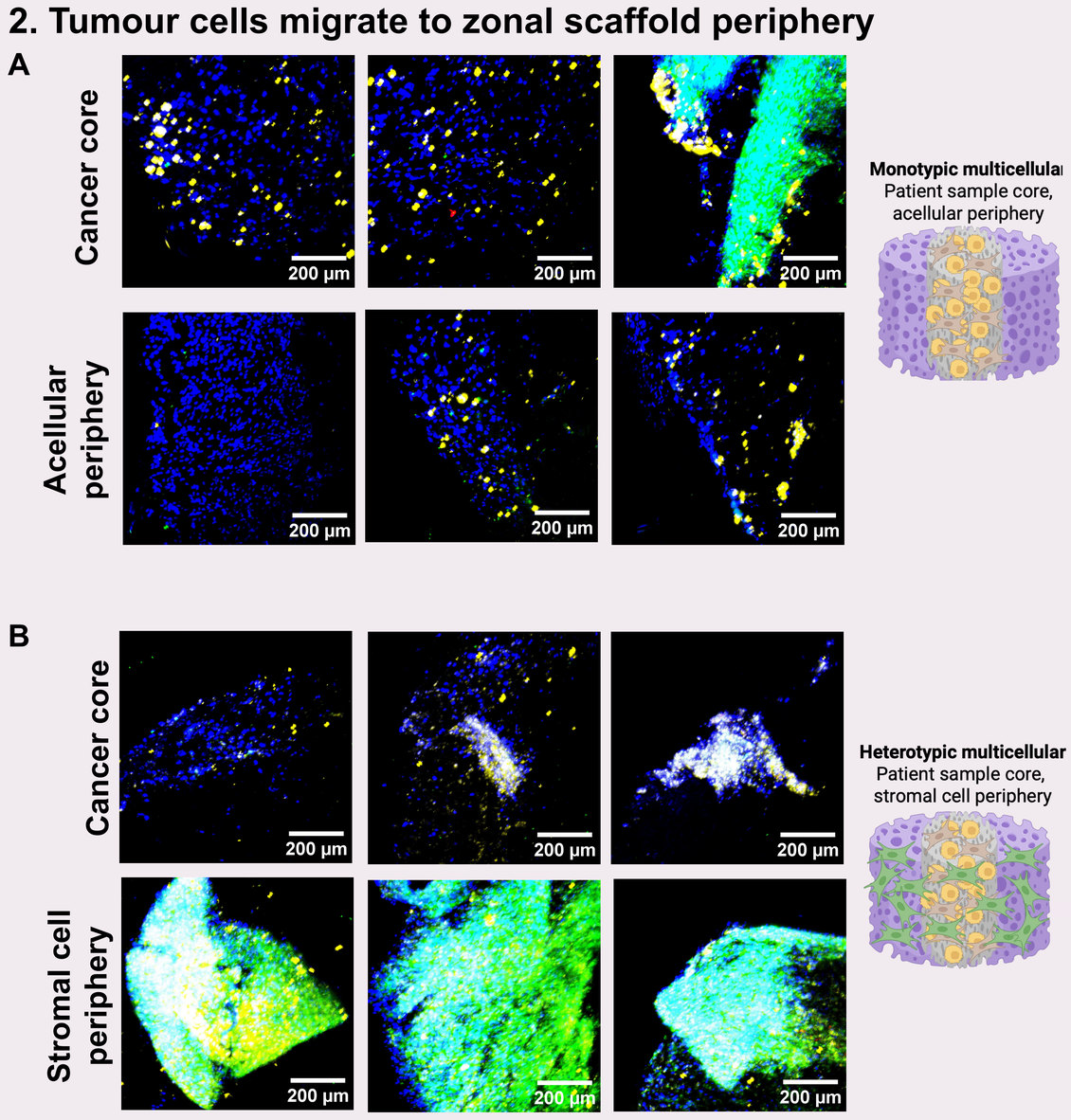


Figure 2. Cell topography and marker expression in monotypic and heterotypic multicellular models. A. Representative fluorescent images of extracted PDAC tissue seeded in the zonal scaffold creating a monotypic multicellular model**.** Cancer cells (yellow) are detected in the acellular periphery. **B.** Representative fluorescent images of extracted PDAC tissue seeded in the core and activated stellate cells (green) seeded in the periphery. Cancer cells (yellow) co-localise with stromal cells in the periphery of the zonal scaffold.

Conclusions

This optimized platform provides a robust, low-cost solution for long-term culture of patient-derived tissue samples, preserving the essential cancer-stromal cross-talk. The model's capability to support a balanced, complex cellular environment without multiple expensive growth factors establishes it as a powerful tool to elucidate TME cross-talk and accelerate studies in personalized PDAC therapy.

References

(1) Gupta, et al. Frontiers in Bioengineering & Biotechnology. 2020; 8 (290)
(2) Gupta et al., Advanced Biology 2024; 8 (7)
(3) Gupta, et al. RSC Advances.2019; 9 (71)
(4) Kataki et al. ASC Applied Material & Interfaces (https://doi.org/10.1021/acsami.5c02296)

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