Core–Shell Hydrogel Based on Supercritical CO_2-Decellularized Pancreatic ECM for Functional β-Cell Encapsulation and Immune Protection

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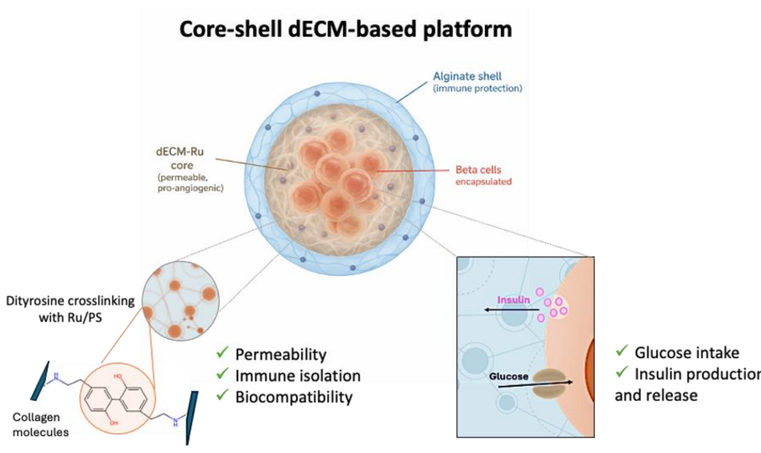
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Introduction

Type 1 Diabetes Mellitus (T1DM) affects over 9 million individuals worldwide and results from autoimmune destruction of insulin-producing pancreatic β-cells. While exogenous insulin remains the standard treatment, it often leads to suboptimal glycemic control due to dosing challenges [1]. Pancreatic islet transplantation offers a potential cure by restoring endogenous insulin production, but its success is limited by immune rejection and poor graft vascularization [2]. To address these challenges, we developed a permeable, pro-angiogenic, immune-isolating core–shell hydrogel that mimics the native pancreatic microenvironment [3]. The system consists of a porcine pancreatic dECM core containing β-cells, surrounded by an alginate shell that enables nutrient diffusion while providing immunoprotection. Given that pancreatic regions differ in islet density, vascularization, and ECM composition [4], this study compares dECM hydrogels derived from the body and head/tail to evaluate their effects on β-cell viability and potential graft performance.

Objectives

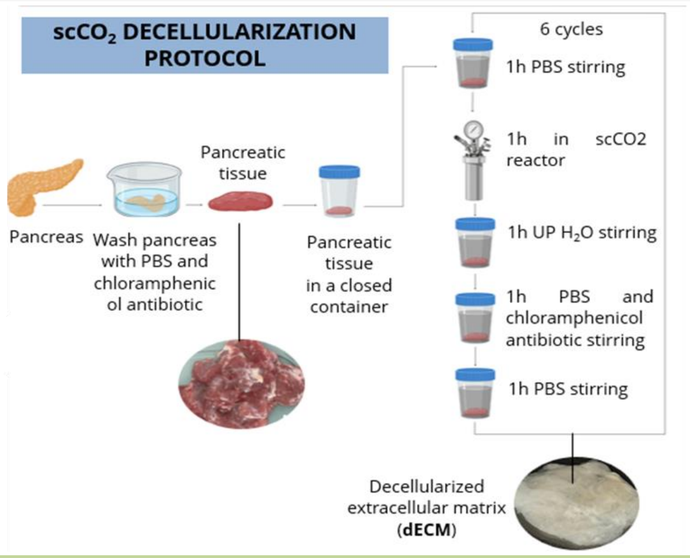


Development of a:

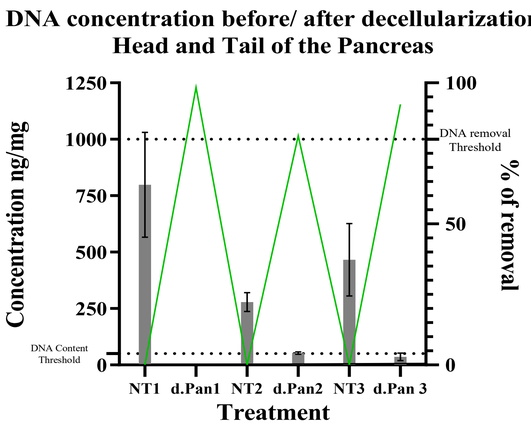
- **permeable**
- **pro-angiogenic**
- **immune-isolation**

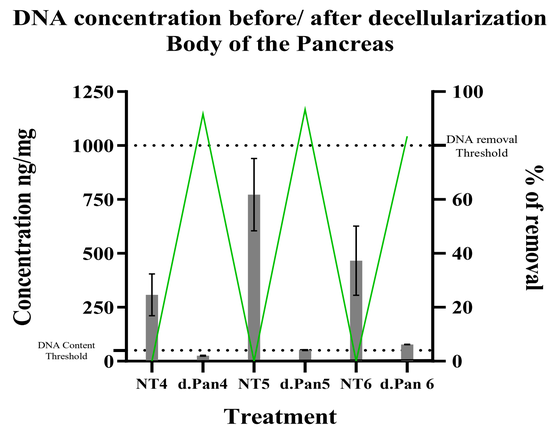
hydrogel using decellularized pancreatic extracellular matrix (dECM) crosslinked with Ruthenium surrounded by an alginate core for the growth of beta cells.

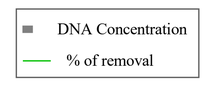
Methods and Results



DNA QUANTIFICATION

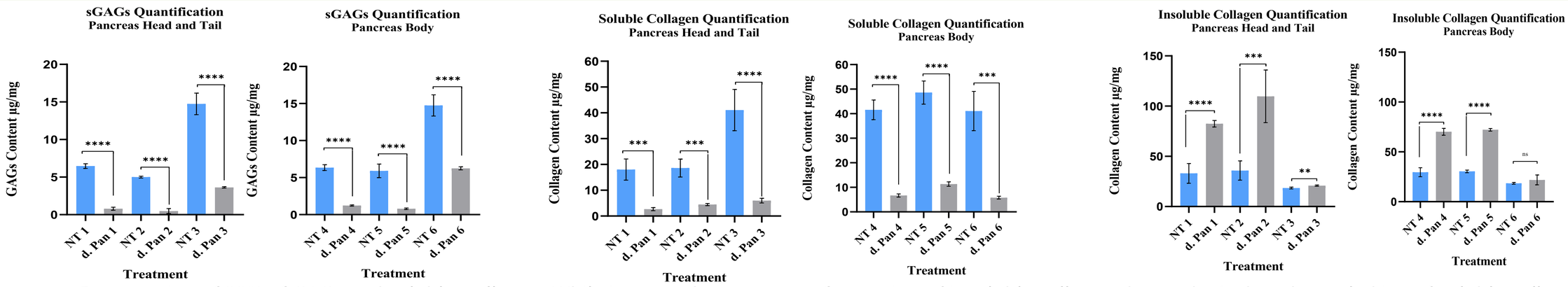






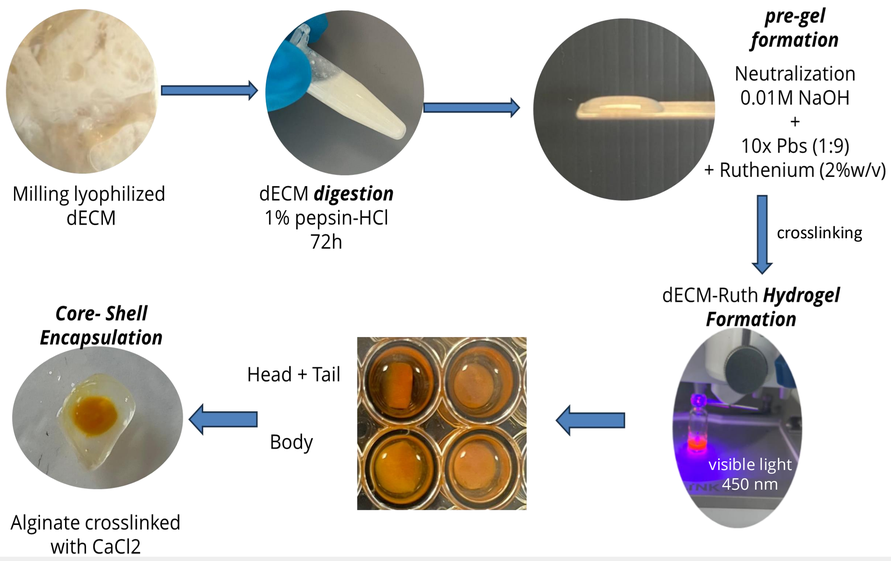
Reduced DNA content in porcine pancreatic tissue after five cycles of decellularization, resulting in a DNA concentrations **below 50 ng/mg**, indicating removal of nucleic material above 80%.

DECM CHARACTERIZATION



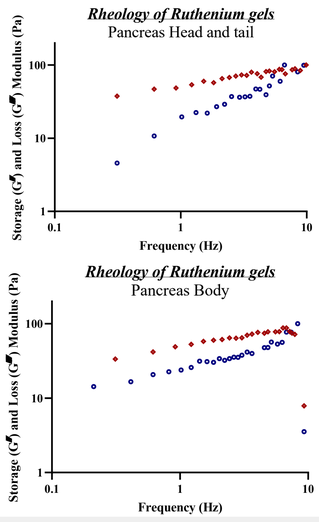
Preservation of 20% of GAGs and soluble collagen. While increased percentage of retention of insoluble collagen due to the induced crosslinking of soluble collagen during the decellularization with $scCO_2$.

dECM DIGESTION AND CORE-SHELL HYDROGEL



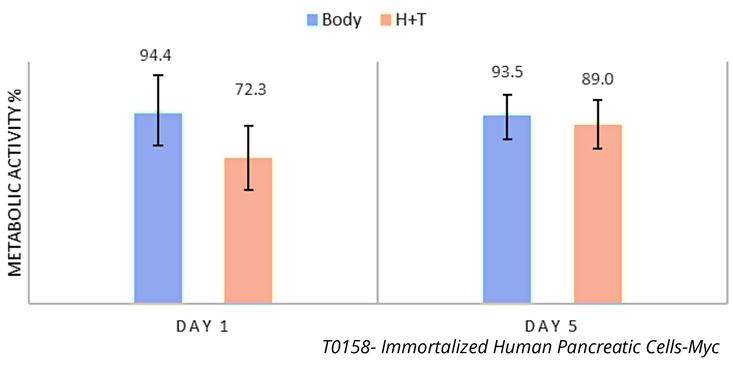
HYDROGEL CHARACTERIZATION AND CYTOCOMPATIBILITY

Rheology of dECM-Core



Higher G' indicates gel like characteristics for our core dECM-Ru crosslinked hydrogel.

dECM-based core-shell hydrogel cytocompatibility



T0158- Immortalized Human Pancreatic Cells-Myc

- No cytotoxicity observed.
- Anatomic areas studied present similar metabolic activities along the timeline tested.

Conclusions

This study validated a supercritical CO_2 decellularization protocol as a robust and effective method for pancreatic dECM preparation, achieving reliable DNA removal across organ variability. Decellularization reduced GAGs and soluble collagen while increasing insoluble collagen, results also highlighted regional differences within the pancreas. A core-shell hydrogel for B cell spheroids seeding was developed. The core, ruthenium-based hydrogels showed desired crosslinking but low stability after 7 days which will need to be improved. The core-shell construct showed no signs of cytotoxicity and allowed cell seeding before alginate crosslinking. Preliminary cell studies showed similar metabolic activity along the timepoints tested. Future work will focus on optimizing stiffness, reducing residual of crosslinkers in hydrogels, and expanding cellular assays. Overall, these findings establish pancreatic dECM hydrogels as promising scaffolds for β-cell replacement therapies in diabetes

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