Biological Design Dissertation Defense

Hyrogels approaches to deliver and protect cell grafts

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Abstract

Type 1 diabetes (T1D) and endometriosis are chronic conditions with an enormous clinical burden, where limitations in controlling the cellular microenvironment hinder effective therapy and disease modeling. This work focuses on using engineered biomaterial-based delivery approaches to protect therapeutic cells and develop physiologically relevant disease models.

In T1D, autoimmune-mediated beta cell destruction necessitates lifelong exogenous insulin therapy. Stem cell therapies have the potential in reversing T1D but require immunosuppression due to graft rejection. To address this challenge, we used a hydrogel injection molding-based macroencapsulation spiral geometry with a high surface area to volume ratio to encapsulate stem cell-derived beta cell clusters (sBC). This design supports cell viability, while isolating grafts from host immune cells. Encapsulated sBC shows longevity and function in vitro and in vivo. Using a humanized immune model, we demonstrate that macroencapsulation protects sBC from direct T cell-mediated rejection.

Endometriosis affects >10% women globally and is associated with chronic, disabling pelvic pain and infertility, however, diagnosis remains invasive and delayed. We developed a PEG-based hydrogel delivery system and endometriotic cell lines to study lesion formation and establish a human endometriosis lesion model, enabling evaluation of targeting strategies. We identified PAEP an IL20-RA as potential targets from scRNA datasets, however, the gene and protein level validation showed inconsistencies in their expression across cell line and patient samples.

Together, these findings demonstrate that engineering the cellular microenvironment using hydrogels enables immunoprotection by limiting direct antigen recognition and improved experimental model for complex disease.

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