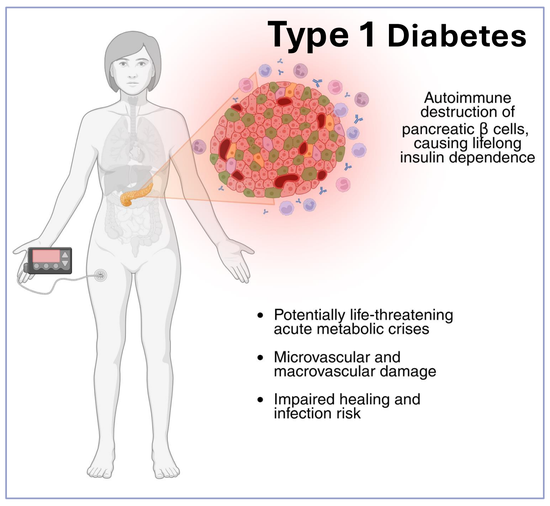
Engineering 3D pseudoislets from perinatal stem cells for regenerative approaches in Type 1 Diabetes

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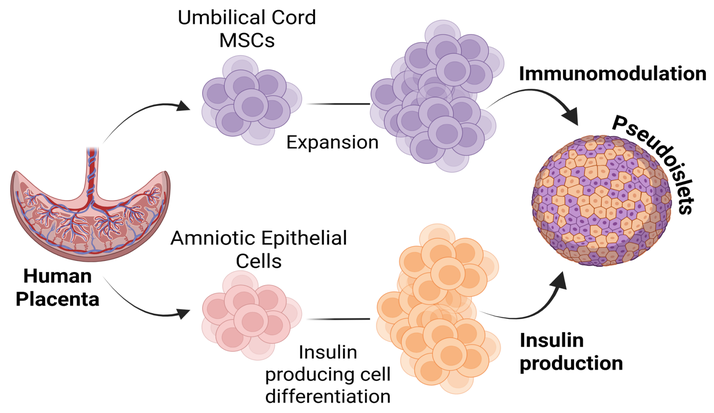
THE PROBLEM

Islet transplantation is limited by immune rejection and the need for lifelong systemic immunosuppression, which reduces graft survival and exposes patients to significant toxicity.

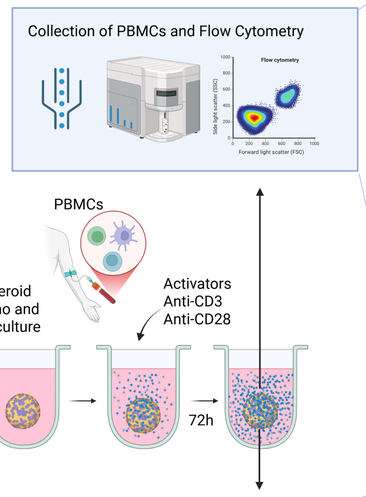
POSSIBLE SOLUTION

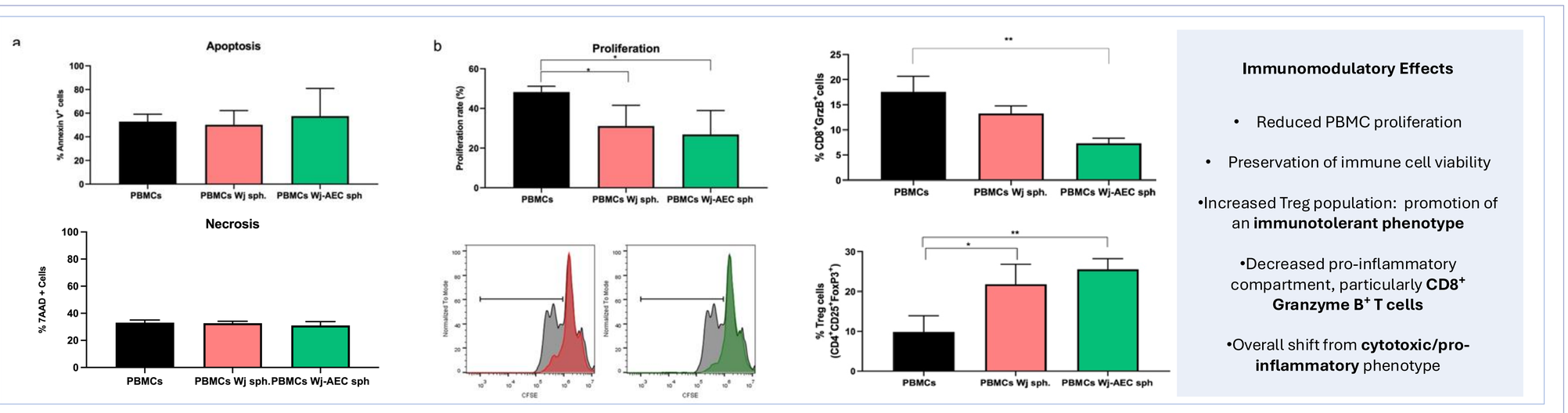
Perinatal cell-derived 3D spheroids represent a promising strategy to generate bioengineered pseudo-islets combining insulin-producing cells with intrinsic immunomodulatory properties. This dual-functional system may support graft survival by promoting a local tolerogenic microenvironment, potentially reducing the need for systemic immunosuppression.

Pseudoislets



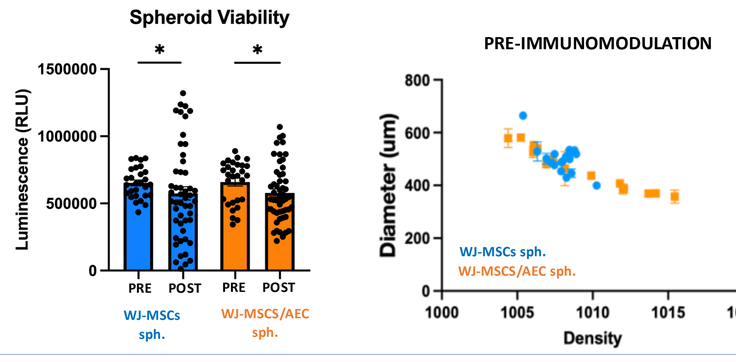
Immunomodulation





Immunomodulatory Effects

- Reduced PBMC proliferation
- Preservation of immune cell viability
- Increased Treg population: promotion of an **immunotolerant phenotype**
- Decreased pro-inflammatory compartment, particularly **CD8⁺ Granzyme B⁺ T cells**
- Overall shift from **cytotoxic/pro-inflammatory** phenotype

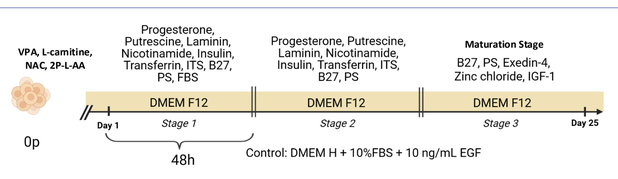


Spheroid Stability and Biophysical Properties

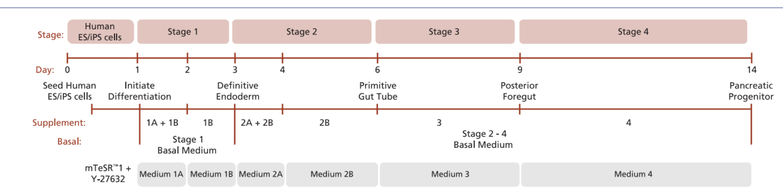
- Co-culture with **PBMCs induces a partial reduction in spheroid viability**, higher in WJ-MSC-only spheroids
- **AECs exert a protective effect**, preserving spheroid integrity under immune stress
- WJ-only spheroids transition from a highly compact structure to a more disorganized morphology following PBMC exposure

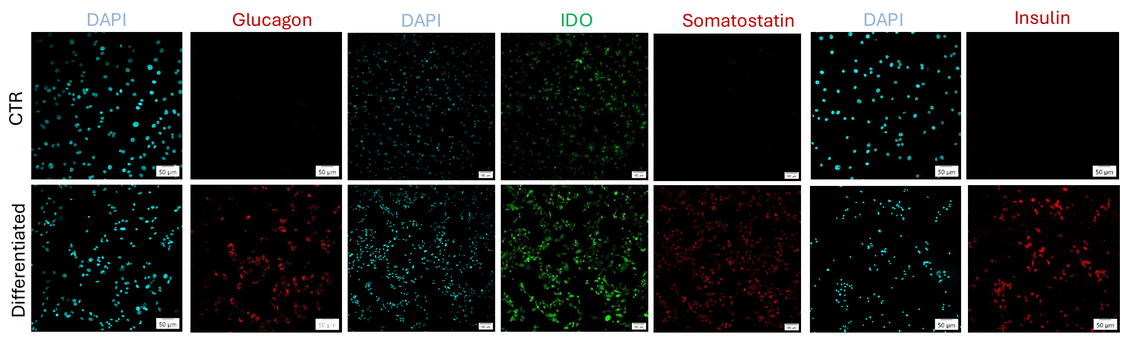
Insulin Producing Cells

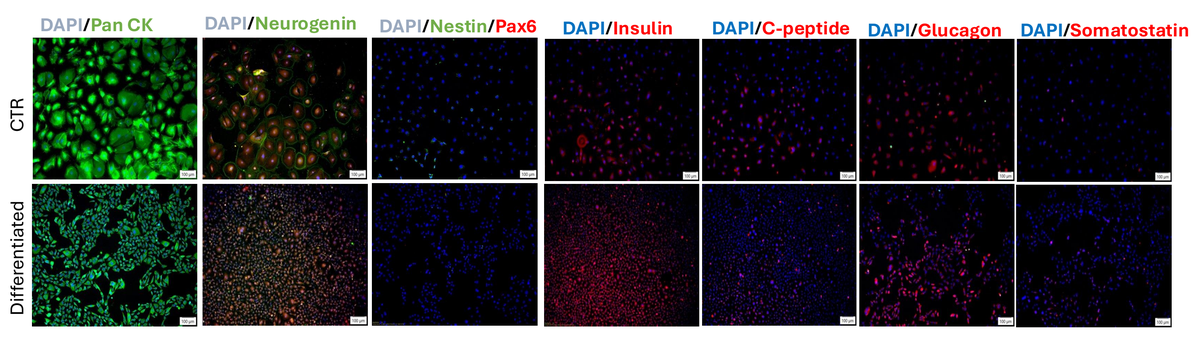
Lab-developed

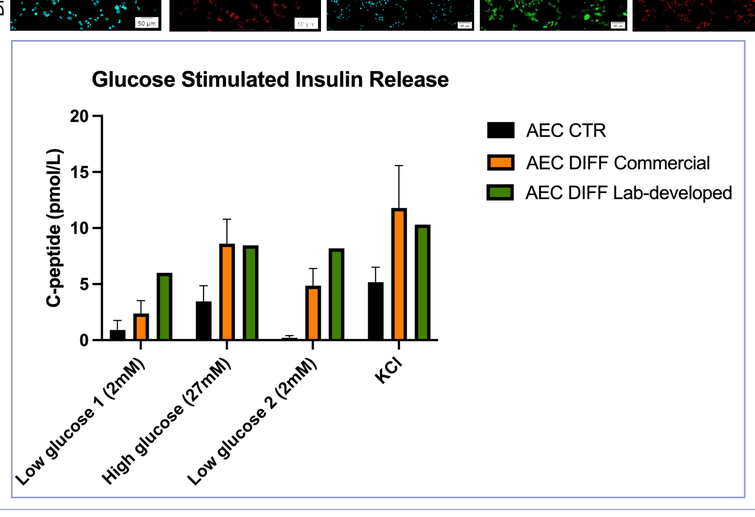


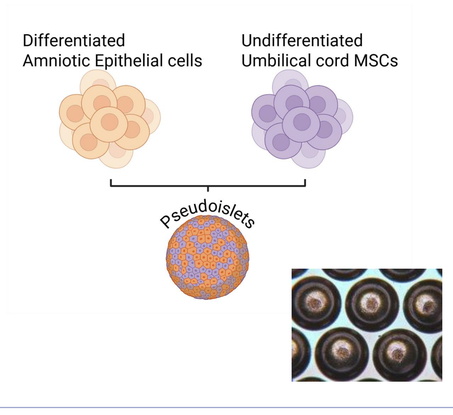
Commercial

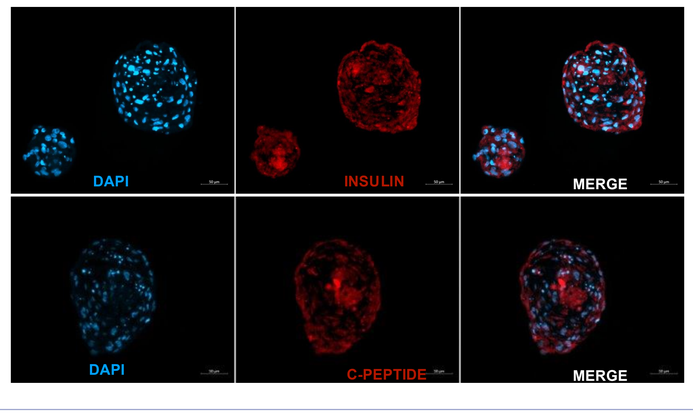












Insulin Producing Cell differentiation

- GSIR analysis revealed comparable performance between lab-developed and commercial differentiation protocols
- Insulin secretion levels remain **suboptimal**, highlighting the need for further optimization strategies
- Pseudo-islets retain **differentiation marker expression after assembly**, supporting stability of the functional phenotype

Conclusions and Perspectives

These findings demonstrate that **perinatal stem cells can be harnessed to engineer functional pseudo-islets with insulin-producing capacity**. Importantly, these constructs **exhibit intrinsic immunomodulatory properties**, promoting a tolerogenic immune profile while preserving cell viability. The integration of epithelial and mesenchymal components enhances both functional performance and structural resilience under immune stress. Altogether**, this platform represents a promising strategy for the development of advanced 3D bioengineered constructs for Type 1 Diabetes.**

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