Introduction

- Type 1 Diabetes (T1D) is an autoimmune disease affecting over 8 million people worldwide. During disease progression, autoimmune attack leads to the demise of the insulin-producing beta cells of the pancreatic islet.
- It was recently uncovered that T1D is associated with early onset autoimmune maturation that precedes the adaptive autoimmune response.
- The link between islet maturation and vulnerability to innate autoimmune attack is unclear; does an immature phenotype protect beta cells from autoimmune attack, or does autoimmune attack induce a de-differentiated phenotype?
- Direction of causality can be determined by treating a pancreatic islet organoid model system with a cytokine cocktail that models autoimmune attack at varying stages of organdi maturity.

Objective: Optimize a cytokine cocktail for use on a pancreatic islet organoid model system.

Background

I. Pancreatic islet organoid model system: differentiation & entainment

II. T1D disease progression

III. Adaptive vs. Innate Autoimmunity

Conclusions & Future Directions

- 3D Min6 cells are unresponsive to the IFNα + II-1β and IFNγ + II-1β cytokine cocktails in terms of cell death, but do respond with increased ER stress. An optimal cytokine cocktail cannot yet be determined. Future optimization experiments will include the IFNα + IFNγ + II-1β cytokine cocktail as a positive control for interferon signaling. Future experiments will use Poly I:C transfection to account for intracellular receptors.
- Once an optimized cocktail is determined, future experiments will involve treatment of entrained islet organoids to model vulnerability to immune attack at varying stages of maturity.

References

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