ISPAD Research Grant: Six-Month Progress Report

Title: Targeting the Pancreatic Barrier to Treat Type-1 Diabetes

Type 1 Diabetes (T1D) is characterized by the immune-mediated destruction of pancreatic β-cells, leading to absolute insulin deficiency. A critical, yet often overlooked, aspect of T1D pathogenesis is the role of the blood-pancreatic barrier (BPB) and the associated vascular changes in disease progression. The highly metabolically active islets rely on a specialized microvasculature that ensures optimal β-cell function through high blood flow, direct venous drainage, and a lower glucose threshold for insulin secretion. However, in T1D, the vascular network undergoes significant modifications, including a reduction in capillary density, impaired β-cell perfusion, and early endothelial dysfunction, all of which contribute to disease progression. Notably, these vascular alterations precede peri-insular lymphocyte infiltration but coincide with macrophage activation, suggesting a pivotal role of BPB dysfunction in T1D onset. Our research aims to investigate the mechanisms driving BPB dysfunction during T1D pathogenesis. Specifically, we seek to answer the fundamental question: How pancreatic cellular morphology is altered which lead to T1D pathogenesis.

Literature Review

In parallel with our experimental work, we conducted an extensive review on mitochondrial dysfunction in pancreatic β-cells and its implications for T1D. This effort culminated in a review article. We anticipate that this review will contribute to the existing body of knowledge and serve as a foundation for our future experimental findings.

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