MHC Class I on Pancreatic Islets from Longstanding Diabetes Patients: Persistent Hyperexpression is Restricted to Type 1 Diabetes and Does Not Correlate with Enteroviral Infection, Infiltration or Insulin Depletion

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Purpose: Major Histocompatibility Class (MHC) class I antigens present intracellular peptides to CD8 T cells and render the expressing cell susceptible to killing. Islet cells from recently diagnosed type 1 diabetes patients are known to exhibit upregulated expression of MHC class I for yet unclarified reasons. This study reports on a systematic survey of MHC class I expression patterns and potentially causal pathways in samples obtained via the network for Pancreatic Organ Donors (nPOD).

Methods: Freshly frozen pancreas samples were obtained from 39 longstanding type 1 diabetes patients, 14 non-diabetic control individuals, 5 non-diabetic, islet autoantibody positive individuals, 6 type 2 diabetes patients, 1 patient with gestational diabetes and 1 undefined case of diabetes. Sections were stained for insulin, MHC class I and CD8 by immunofluorescence. Consecutive sections from samples with pronounced MHC class I hyperexpression on islets were subjected to PCR analysis and immunofluorescence for enterovirus species and type I interferon signature genes.

Summary of Results: MHC class I hyperexpression on islets was found in four cases and was specific to type 1 diabetes. Upregulation may persist for as long as eight years after clinical onset and was observed independent of insulin sufficiency and CD8+ infiltration. Despite modulation of type I interferon signature genes, none of the samples showed evidence of chronic enteroviral infection.

Conclusions: Persistent MHC class I upregulation on pancreatic islets is a type 1 diabetes-specific phenomenon that is unlikely to be a consequence of chronic enteroviral infection.