Journal of Diabetes Science and Technology
Volume 2, Issue 5, September 2008

SYMPOSIUM

Thrombosis and Inflammation in Intraportal Islet Transplantation: A Review of Pathophysiology and Emerging Therapeutics

John T. Wilson, B.S.[1] and Elliot L. Chaikof, M.D., Ph.D.[1-3]

Abstract

With the inception of the Edmonton Protocol, intraportal islet transplantation (IPIT) has re-emerged as a promising cell-based therapy for type 1 diabetes. However, current clinical islet transplantation remains limited, in part, by the need to transplant islets from 2–4 donor organs, often through several separate infusions, to reverse diabetes in a single patient. Results from clinical islet transplantation and experimental animal models now indicate that the majority of transplanted islets are destroyed in the immediate post-transplant period, a process largely facilitated by deleterious inflammatory responses triggered by islet-derived procoagulant and proinflammatory mediators. Herein, mechanisms that underlie the pathophysiology of thrombosis and inflammation in IPIT are reviewed, and emerging approaches to improve islet engraftment through attenuation of inflammatory responses are discussed.

J Diabetes Sci Technol 2008;2(5):746-759

Author Affiliations: [1]Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia; [2]School of Chemical and Biomolecular Engineering, Georgia Institute of Technology, Atlanta, Georgia; and [3]Department of Surgery, Emory University School of Medicine, Atlanta, Georgia

Abbreviations: (APC) activated protein C, (EC) endothelial cell, (FasL) Fas ligand, (IEQ) islet equivalents, (IFN) interferon, (IL) interleukin, (iNOS) inducible nitric oxide synthase, (IPIT) intraportal islet transplantation, (MCP-1) monocyte chemoattractant protein-1, (NO) nitric oxide, (PEG) poly(ethylene glycol), (TAT) thrombin-antithrombin complex, (TF) tissue factor, (TM) thrombomodulin

Keywords: anticoagulant, anti-inflammatory, cell surface modification, conformal coating, instantaneous blood-mediated inflammatory reaction, intraportal islet transplantation, islet encapsulation, poly(ethylene glycol), type 1 diabetes mellitus

Corresponding Author: Elliot L. Chaikof, M.D., Ph.D., Emory University, 101 Woodruff Circle, Rm 5105, Atlanta, GA 30322; email address echaiko@emory.edu