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## Apoptosis as an effective means of inducing tolerance to pancreatic islets for the treatment of type 1 diabetes

Type 1 diabetes (T1D) is an autoimmune disease initiated and perpetuated by T cells targeting various autoantigens expressed by insulin producing beta cells, thereby setting off a serious of immunological reactions that result in the destruction of beta cells, insulin deficiency, and hyperglycemia. Insulin treatment as standard of care is often ineffective in preventing recurrent hyperglycemic episodes with subsequent development of micro and macroangiopathic lesions and the development and progression of chronic complications. Pancreatic islet transplantation has proven effective in improving metabolic control/ quality of life and preventing severe hypoglycemia in patients with T1D. Immune rejection, however, severely limits broad application of islet transplantation, irrespective of chronic use of immunosuppression and its sequelae. Therefore, novel approaches that control rejection in the absence of chronic immunosuppression will have significant impact on the field of islet transplantation. T-cells are the primary culprit of islet graft rejection. As such, control of T cell responses has the potential to induce tolerance and treatment of T1D. T cells upregulate Fas receptor and become sensitive to Fas/FasL-mediated killing. Therefore, Fas-mediated apoptosis has great potential to serve as an effective means of inducing transplantation tolerance. Using a novel form of FasL protein with improved apoptotic activity, we have demonstrated the utility of this concept for the induction of tolerance to allogeneic as well as xenogeneic pancreatic islets in preclinical rodent experimental models.

## **Biography**

Haval Shirwan is Dr. Michael and Joan Hamilton Endowed Chair in Autoimmune Disease, Professor of Microbiology and Immunology, Director of Molecular Immunomodulation Program at the Institute for Cellular Therapeutics. He conducted his Graduate studies at the University of California in Santa Barbara, CA, and Postdoctoral studies at California Institute of Technology in Pasadena, CA. He joined the University of Louisville in 1998 after holding academic appointments at various academic institutions in the United States. His research focuses on the modulation of immune system for the treatment of immune-based diseases with particular focus on type 1 diabetes, transplantation, and development of prophylactic and therapeutic vaccines against cancer and infectious diseases. He is an inventor on over a dozen of worldwide patents, widely published, organized and lectured at numerous national/international conferences, served on study sections for various federal and non-profit funding agencies, and is on the Editorial Board of a dozen of scientific journals. He is member of several national and International societies and recipient of various awards.

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