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## Pancreatic islets engineered with a chimeric PD-L1 protein overcome rejection in allogeneic recipients

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Allogeneic islet transplantation is an important therapeutic approach for the treatment of type 1 diabetes (T1D). However, graft rejection initiated and perpetuated by pathogenic T effector (Teff) cells presents a major barrier. One approach that has proven successful for promoting graft tolerance is shifting the T cell balance away from the induction of pathogenic Teff cells and towards the generation of protective T regulatory (Treg) cells. PD-1/PD-L1 immune checkpoint pathway plays an important role in the Teff and Treg balance with demonstrated clinical efficacy in cancer immunotherapy. We generated a chimeric PD-L1 molecule that can be transiently displayed on the surface of pancreatic islets. *In vitro*, PD-L1 enhanced TGF-beta-induced conversion of Teff into Treg cells and effectively suppressed the proliferation of Teff cells in response to alloantigen stimulation. *In vivo*, PD-L1-engineered BALB/c islet grafts under a short window of rapamycin treatment achieved sustained long-term graft survival and function. These results provide strong proof-of-efficacy and feasibility for using PD-L1 protein as an immunomodulator to promote allogeneic islet graft survival in the absence of continued immunosuppression.

### 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 Post-doctoral 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 of over a dozen of worldwide patents, Founder and CEO/CSO of FasCure Therapeutics, LLC, 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 number of scientific journals. He is member of several national and international societies and recipient of various awards.

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