MODULATION OF PANCREATIC ISLET ALLO IMMUNOGENICITY AND IMMUNOBIOLOGICAL IN VITRO AND IN VIVO CONSEQUENCES.

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Immunogenicity of isolated islets of Langerhans is predominantly dependent on antigen-presenting "passenger cells" within the graft and on graft-contaminating exocrine tissue fragments. To abolish this immunogenicity, the following was studied in collagenase-digested rat and human pancreatic islet: (a) in vitro culturing of isolated islets, (b) pretreatment with cell-group specific cytotoxic monoclonal antibodies and (c) separation of exocrine tissue fragments by the electromagnetic cell separation procedure (magnetic microspheres coupled to exocrine cell-specific lectins). It was found that each of these procedures decreases islet cell immunogenicity significantly, as shown morphologically by immunofluorescence microscopy and functionally by mixed-lymphocyte-islet-culture. Transplantation of immunogenicity-downmodulated, strongly MHC-allogeneic rat islets revealed that manipulated islet allografts are still rejected. However, additional short-term immunosuppression of the graft recipient leads to long-term allograft acceptance. From these data we conclude that immunogenicity-downmodulation, though seemingly uneffective by its own, may allow limited recipient immunosuppression to obtain long-term graft survival. This appears to be of great clinical relevance.