

## **PANCREATIC ISLET TRANSPLANTATION INTO THE BONE MARROW OF THE RAT**

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**Antecedents:** Transplantation of endocrine pancreatic tissue can cure diabetes. Pancreatic islet transplantation in humans has been performed with increasing success. However, loss of islet mass remains one obstacle in achieving insulin independence and long-term graft survival. The liver, as a receptor site, contributes to the loss of islet grafts secondary to immunological and non-immunological factors, besides having important technical complications and limitations. Bone marrow offers an extrahepatic, easily accessible and widely distributed receptor site which lacks the limitations and the physiologically adverse environment seen in the liver. In addition, the bone marrow has been postulated as a site for Treg reservoir and extrathymic Treg differentiation, which may induce hyporesponsiveness to tissue antigens. We tested the hypothesis that the bone marrow may be used as a receptor site for pancreatic islet grafts.

**Materials and Methods:** We performed pancreatic islet transplants into the bone marrow of rats: isografts (Lewis to Lewis N= 12), allografts (WF to SD N=5) and xenografts (Fish to Rat n=5). Recipients were sequentially sacrificed up to 21 days after transplant, and histopathology and immunohistochemistry were performed.

**Results:** There was complete engraftment of isografts and allografts up to 21 days after transplantation, with insulin and glucagon production, no signs of rejection and negative apoptosis markers. In contrast, xenografts were rejected in similar fashion as observed when transplanted in the renal capsule.

**Conclusions:** There are indications that the bone marrow may provide a better alternative than the liver as a receptor site. In addition, bone marrow may have immunological advantages, which seem to be specific, as xenografts were rejected.