Successful Transplantation from Pig Embryos to Mice

June 20 2006

Millions of diabetics face a lifetime of daily injections to replace the insulin their bodies fail to produce, as well as a host of risks that includes blindness, amputation, kidney failure, and heart disease. For many, particularly those afflicted with juvenile diabetes, transplants of the pancreatic tissue in which insulin is produced might alleviate these problems. Unfortunately, there are not nearly enough organ donors available for transplantation.

Insulin-producing pancreas tissues from animals could potentially provide a nearly unlimited supply for transplantation. But until now, attempts to transplant such animal tissues into non-human primates have evoked a fierce immune response. However, embryonic tissues, such as those from pigs (in which the insulin-producing cells are similar to those of humans), might not be rejected as strongly. New research by Prof. Yair Reisner of the Weizmann Institute's Immunology Department has brought the possibility of transplants from pig embryos one step closer. The results of the study appeared in the June issue of *PLoS Medicine*.

In previous work, Reisner and his team had shown that each embryonic organ has its own 'time window' during which the chances for successful transplantation are optimal. Prior to this window, the early tissue's cells, which are still largely undifferentiated, can give rise to tumors. Past the window, however, they may be too well-developed: The host identifies these cells as foreign, causing the body to reject them. By transplanting tissues from pig embryos into mice lacking proper immune systems, they determined that the best time frame for pancreatic tissue was about a

third of the way through gestation (from 42 to 56 days).

In the new study, Reisner's team wanted to see if such tissues could function in the body. They first implanted embryonic pancreatic tissue from pigs into mice that lacked an immune system of their own, but had human immune cells injected into them. From this experiment they learned that tissues taken at 42 days (within the time frame they had previously determined) exhibited a markedly reduced immune response.

Next, the team tried the experiment on mice with fully functioning immune systems, but destroyed the insulin-producing cells in their pancreases before proceeding with the transplant. With the aid of relatively mild immune suppression protocols, the implanted tissues were fully functional over time, producing insulin and maintaining the mice's blood sugar at normal levels.

"The results of this study," says Reisner, "warrant further, pre-clinical research on primate models."

Prof. Yair Reisner's research is supported by the J & R Center for Scientific Research; the Belle S. and Irving E. Meller Center for the Biology of Aging; the Gabrielle Rich Center for Transplantation Biology Research; the Abisch Frenkel Foundation for the Promotion of Life Sciences; the Loreen Arbus Foundation; the Crown Endowment Fund for Immunological Research; the Ligue Nationale Francaise Contre le Cancer; the Mario Negri Institute for Pharmacological Research – Weizmann Institute of Science Exchange Program; the Charles and David Wolfson Charitable Trust; Renee Companez, Australia; Mr. and Mrs. Barry Reznik, Brooklyn, NY; and Tissera, Inc., Herzliya, Israel.

Source: Weizmann Institute of Science