## Transplanted pancreatic islets survive and reverse type I diabetic neuropathy

<u>Paola Marmiroli</u><sup>1</sup>, Roberto Bianchi<sup>2</sup>, Marina Figliuzzi<sup>3</sup>, Arianna Scuteri<sup>1</sup>, Valentina Carozzi<sup>1</sup>, Annalisa Canta<sup>1</sup>, Cristina Meregalli<sup>1</sup>, Federica Avezza<sup>1</sup>, Mariarosaria Miloso<sup>1</sup>, Giuseppe Lauria<sup>2</sup>, Andrea Remuzzi<sup>4</sup>

<sup>1</sup> Department of Neuroscience and Biomedical Technologies, University of Milan "Bicocca", Monza, Italy

<sup>2</sup> "Carlo Besta" Foundation, Milan, Italy

<sup>3</sup> "Mario Negri" Institute for Pharmacological Research, Bergamo, Italy

<sup>4</sup> Faculty of Enginery University of Bergamo, Dalmine, Italy

Type 1 diabetes is a chronic disease often leading to systemic complications, such as peripheral neuropathy, nephropathy and cardiovascular complications. Whole pancreas as well as pancreatic islets transplantation has been proposed for the cure of type 1 diabetes, allowing a more efficient and physiological metabolic control. We investigated the effects of microencapsulated and immunoisolated islet transplantation in a model of streptozotocin-induced diabetes in 3 groups of Lewis rats: healthy controls, untreated diabetic rats and diabetic rats transplanted with microencapsulated islets into the peritoneal cavity two months after diabetes induction. Our results demonstrated that following transplantation hyperglycemic rats became normoglycemic in few days and this was accompanied by a rapid raise in body weight. Meanwhile, thermal (hot plate test) and mechanical sensitivity (Randal-Selitto paw withdrawal test measured with an analgesymeter) were increased and decreased by 180 and 40-60%, respectively. In addition, the density of footpad intraepidermal nerve fibers was significantly reduced by 20% in diabetic group and islet transplantation restored normal skin innervation. Nerve conduction velocity in the tail nerve and the Na<sup>+</sup>, K<sup>+</sup>-ATPase activity in the sciatic nerve, both reduced by about 25% in diabetic rats, were also normalized by islet transplantation.

In conclusion, our data obtained in a model of type 1 diabetes, showed that transplant of microencapsulated pancreatic islets, besides controlling glycemia, arrested neuropathy worsening and was able to restore all the diabetic-induced alterations within the 2-month follow-up period after transplantation.

On the basis of these encouraging results, a new experiment with 4-month long diabetes followed-up for 4 months after allogenic transplantation has been performed and the preliminary analysis confirmed the effectiveness of the procedure also in these long-term diabetic animals. In fact, effective treatment of the peripheral nervous system damage was demonstrated at the behavioral and neurophysiological levels and the viability of the transplanted cells could be demonstrated until the end of the study at the functional and morphological levels.

We believe that these data can offer a solid basis for the future implementation of more sophisticated models of diabetes treatment based on cellular transplantation.