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Transplanting fragments of diabetic pancreas into activated omentum gives rise to new insulin producing cells

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Abstract

To determine if pancreatic progenitor cells can be induced to form insulin producing cells in vivo, we auto-transplanted fragments of streptozotocin-induced diabetic pancreas into omentum pre-injected with a foreign material. As shown previously, omentum pre-activated in this manner becomes rich in growth factors and progenitor cells. After auto-transplanting diabetic pancreas in the activated omentum, new insulin secreting cells appeared in the omentum in niches surrounding the foreign particles—a site previously shown to harbor progenitor cells. Extracts of these omenta contained measurable insulin. Four of eight diabetic animals treated in this manner became normoglycemic. This shows that new insulin producing cells can be regenerated from diabetic pancreas by auto-transplanting pancreatic fragments into the activated omentum, an environment rich in growth factors and progenitor cells.

Keywords: β-Cells; Diabetes; Pancreas; Omentum; Progenitors; Growth factors; Streptozotocin; Insulin; Pdx-1; Auto-transplantation

In the treatment of type I diabetes, whole organ pancreas transplantation offers the best hope of cure but is limited by a shortage of human donors [1]. Transplanting viable islets in the portal vein as an alternative has been plagued by implant failure due to poor vascularization and immunosuppressive drug toxicity [2]. A new and exciting approach would be to regenerate β-cells in vivo from their progenitors present in the pancreatic ductal tissue, as shown in culture conditions [3–5]. Such regeneration of β-cells from existing diabetic pancreas has already been achieved by immunologically blocking the continuous autoimmune destruction of islets [6–9]. These experiments confirm the feasibility of regenerating β-cells in vivo, but this immunological approach may not be immediately applicable in humans.

Here, we attempt to regenerate β-cells in vivo from streptozotocin (STZ) diabetic pancreas by auto-transplanting pancreatic fragments into the omentum. The omentum has well-recognized healing properties after it is deliberately brought in close proximity with injured tissues (omental transposition) [10–13]. The omentum, after contact with injured tissues, brings about repair by supplying the injured tissue with angiogenic, growth and chemotactic factors [14–16]. Such factors, in our preliminary studies, could be further augmented when the omentum was activated by placing inert foreign materials in it [17]. We hypothesized that in this activated state the omentum could present a stimulating environment for allowing resting adult β-cell progenitors to differentiate and grow to maturity.

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