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ORIGINAL ARTICLES

A Cell-Based Approach for Diabetes Treatment Using Engineered Non-β Cells

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Abstract

Background:

Implantation of insulin-secreting cells has the potential to provide tight glycemic regulation in diabetic subjects. Implantation of cadaveric human islets in immunosuppressed human patients is currently applied at a very small scale. To overcome the limitations of tissue availability and recipient immunosuppression, encapsulation of nonautologous cells and use of potentially autologous nonislet cells, the latter engineered for insulin secretion, are being pursued. This article reports on recent findings with the implantation of tissue constructs containing enteroendocrine cells stably expressing recombinant insulin in diabetic mice. The concept of a dual recombinant hepatic and enteroendocrine cell system, which may better approximate the secretory response of islets, is discussed.

Methods:

Mouse GLUTag-INS cells engineered to secrete human insulin were developed and incorporated in tissue constructs as reported previously. Constructs were implanted intraperitoneally in diabetic mice, and blood glucose levels, animal weights, and plasma insulin levels were measured at various time points.

Results:

GLUTag-INS-containing tissue constructs secreted insulin preimplantation and postexplantation, and human insulin was detected in the plasma of diabetic mice. However, normoglycemia was not restored.

Conclusions:

A variety of cell types and of encapsulation methods to enhance immune acceptance of insulin-secreting grafts are being pursued. Recombinant enteroendocrine cells show promise, but it is likely that they need to be combined with recombinant hepatic cells to achieve glycemic normalization.

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Abbreviations: (IDD) insulin-dependent diabetes, (GLP-1 and -2) glucagon-like peptide-1 and -2, (mRNA) messenger ribonucleic acid, (PC) prohormone convertase, (RIA) radioimmunoassay, (SIS) small intestinal submucosa, (STZ) streptozotocin

Keywords: β-cell surrogates, enteroendocrine cells, GLUTag, hepatocytes, insulin secretion dynamics, tissue engineering

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