Adeno-Associated Virus Mediated Delivery of Genes to Pancreatic Beta-Cells for Improved Efficacy of Transplantation

DESCRIPTION
This is a method for protecting pancreatic beta-cells from the detrimental effects of immune-mediated damage. Protection is achieved by transducing beta-cells with an adeno-associated virus (AAV) that is engineered to encode cytoprotective genes. The transduced beta-cells are thereby made suitable for transplantation and are resistant to rejection.

Inclusion of certain genes—manganese superoxide dismutase, thioredoxin, interleukin-12 antagonist p40(2), glutathione peroxidase, catalase, 15-lipoxygenase, interleukin-10, leptin, and interleukin-4—in AAV has been shown to reduce immune-mediated cell toxicity against the transduced cells. Additionally, incorporation of antisense RNA and ribozymes into AAV have been shown to reduce expression of inducible nitric oxide synthase, poly-ADP-ribose polymerase, cyclooxygenase 2 or 12-lipoxygenase, which can decrease cytotoxicity of beta-cells following transplantation.

KEY ASPECTS
• Protects pancreatic beta-cells from immune-mediated injury and rejection following transplantation
• AAV is a proven safe and effective gene vector in mammalian systems
• Several AAV vectors are FDA-approved for use in humans
• Customized AAV vectors can incorporate wide array of genes, antisense RNA and ribozyme constructs

INTELLECTUAL PROPERTY

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