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Senior Science Editor  
Journal of Visualized Experiments

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Dear Dr. Singh,

My colleagues and I are submitting to '*Journal of Visualized Experiments*', a manuscript entitled "Gene transfer for insulin-deficient diabetes using helper-dependent adenoviral vector". We respectfully request that the paper be considered for publication in *JoVE*.

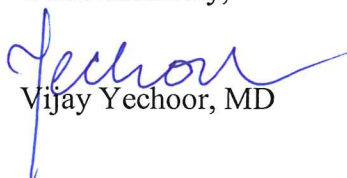
Gene transfer is a powerful technique that allows the selective expression of genetic material that could be used to increase or decrease expression of endogenous proteins or transfer extraneous proteins to target specific cells or pathways. The common vectors used, the first-generation adenovirus, is effective but only for a short period of a few weeks in rodent models. This is because the vector also codes for virus-derived proteins that trigger an immune response leading to the removal of vector-infected cells. The helper-dependent adenoviral (HDAd) vectors are a modification of this, wherein this vector has no viral coding element allowing an efficient long-lasting in vivo transfer of genes. Indeed, only one injection is sufficient to induce a lifelong expression of the transferred gene in mice. However, the generation of these HDAd vectors is complex involving multiple steps and requires good quality control to obtain optimal virus quality and quantity for in vivo gene transfer experiments.

In this manuscript we describe the detailed protocols for generating these effective gene transfer HDAd vectors and apply them in treating insulin deficient diabetes. We have shown before that gene transfer of Neurogenin3 and Betacellulin genes to the liver of diabetic mice leads to an efficient expression of these genes and subsequent generation of 'neo-islets' in the liver that produce insulin and cure diabetes in these mice. We also detail the methods for generating diabetic mouse models and assessing the reversal of diabetes.

We believe that these protocols will be of significant interest to many investigators and laboratories in multiple disciplines, including gene therapy, cell biology, molecular biology, immunology, islet and stem cell biology and regenerative medicine.

Thank you,

Yours sincerely,

  
Vijay Yechoor, MD