Fibrin glue increases the cell survival and the transduced gene product secretion of the ceiling culture-derived adipocytes transplanted in mice.

Authors: Aoyagi Y., Kuroda M., Asada S., Bujo H., Tanaka S., Konno S., Tanio M., Ishii I., Aso M., Saito Y.

Publication Date: 2011

Abstract:

The development of clinically applicable scaffolds is important for the application of cell transplantation in various human diseases. The aims of this study are to evaluate fibrin glue in a novel protein replacement therapy using proliferative adipocytes and to develop a mouse model system to monitor the delivery of the transgene product into the blood and the fate of the transduced cells after transplantation. Proliferative adipocytes from mouse adipose tissue were transduced by a retroviral vector harboring the human lecithin-cholesterol acyltransferase (lcat) gene, and were subcutaneously transplanted into mice combined with fibrin glue. The lcat gene transduction efficiency and the subsequent secretion of the product in mouse adipocytes were enhanced using a protamine concentration of 500 mug/ml. Adipogenesis induction did not significantly affect the lcat gene-transduced cell survival after transplantation. Immunohistochemistry showed the ectopic enzyme production to persist for 28 days in the subcutaneously transplanted gene-transduced adipocytes. The increased viability of transplanted cells with fibrin glue was accompanied with the decrease in apoptotic cell death. The im-munodetectable serum LCAT levels in mice implanted with the fibrin glue were comparable with those observed in mice implanted with Matrigel, indicating that the transplanted lcat gene-transduced adipocytes survived and functioned in the transplanted spaces with fibrin glue as well as with Matrigel for 28 days. Thus, this in vivo system using fibrin is expected to serve as a good model to further improve the transplanted cell/scaffold conditions for

the stable and durable cell-based replacement of defective proteins in patients with LCAT deficiency.