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Ex Vivo Gene-manipulated Mature Adipocytes: Novel Gene Therapy Medicine for Sustained Protein Replacement Therapy of Variety of Intractable Diseases

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Gene therapy-based protein replacement is one of absolute needs for treatment of inherited diseases. Based on much experiences of clinical transplantation therapy in cosmetic and reconstructive surgery, adipose tissue is now recognized as a source of proliferative cells for cell-based therapy. We have developed manipulation procedure of mature adipocytes through ceiling culture with subsequent retroviral/lentiviral gene transduction. The propagated cells, designated as ceiling culture-derived proliferative adipocytes (ccdPAs), provide efficient gene transduction efficiency with stable secretion of the transduced-gene products. GMP production procedure, by which the gene-transduced ccdPAs could be expanded up to nearly 10^{12} cells from 1 g of fat tissue for three weeks after fat tissue preparation, has been developed. The platform technology has been applied for *ex vivo* gene therapy of familial lecithin:cholesterol acyltransferase (LCAT) deficiency. Clinical first in human study for treatment of familial LCAT deficiency has been approved by Ministry of Health, Labour and Welfare, followed by initiation of patient enrollment in Japan. We further continue our research and development to obtain approval as gene therapy medicine. Thus, ccdPAs would provide an excellent platform for developing a protein replacement therapy not only for LCAT deficiency but also variety of intractable diseases including hemophilia and lysosomal storage diseases.