Electrotransfer of Naked hGH cDNA in Muscle of lit/scid Mouse is More Efficient than Genomic DNA

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One of the greatest challenges of in vivo gene therapy using naked DNA is to achieve considerable expression levels of the protein of interest, as well as a prolonged in vivo secretion. Recently the use of techniques such electrotransfer, ultrasound, and improvement of plasmid design, has provided interesting results and enabled the use of naked DNA in gene therapy animal models and clinical trials. In this work electrotransfer was used to enhance the efficiency of plasmid delivery with two different constructs using the commercial pcDNA 3.1(+/-) plasmid in which complementary (cDNA) or genomic (gDNA) sequences of human growth hormone (hGH) were introduced. Both constructs (50 µg) were administered into the quadriceps muscle of *lit/scid* mice, followed by electrotransfer, using eight 50 V pulses of 20 ms and 0.5 s of interval. After one and three days, blood was collected from the retro-orbital cavity and hGH levels in the sera were determined by radioimmunoassay. The following levels of serum hGH were obtained for gDNA: 0.9 ng/mL (first day) and 1.5 ng/mL (third day), while for hGH cDNA the levels were: 3.6 ng/mL (first day) and 4.0 ng/mL (third day). The use of cDNA constructs thus showed a higher in vivo expression level than for genomic constructs. This result emphasizes the importance of choosing a construct as an important factor to enhance the performance of naked DNA strategy. Further experiments, based on different plasmid designs, can contribute to the development of models for in vivo gene therapy.

Keywords: electrotransfer, plasmid design, gene therapy.

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