In Vitro and In Vivo Efficiency Comparison of Plasmid Vectors Containing cDNA or gDNA Sequences of Human Growth Hormone (hGH) for Non-viral Gene Therapy


cnperoni@ipen.br

Biotechnology Department, National Nuclear Energy Commission (IPEN-CNEN), Cidade Universitária, São Paulo, SP, Brazil

Abstract

INTRODUCTION: Gene therapy is a promising new field of biosciences to treat monogenic and acquired diseases, as well as to improve current treatments for several systemic diseases as growth hormone deficiency. In vivo gene therapy based on the administration of naked DNA is safer than the procedures based on viral vectors. However this approach presents in general a poor gene expression, being necessary to improve the vector delivery method or to choose the best gene sequence to be utilized: genomic, complementary or optimized DNA. MATERIAL AND METHODS: Two plasmids, one containing the genomic (gDNA) and the other the complementary (cDNA) hGH sequences under the control of the CMV promoter, were utilized for transient transfection of HEK-293 and C2C12 cells and for naked DNA administration in dwarf immunodeficient (lit/scid) mice, using a muscular gene electrotransfer protocol (8 pulses of 150V/cm and 20 ms). RESULTS AND DISCUSSION: hGH in vitro expression was significantly higher for cDNA plasmid in both cell lines. After the administration of the same vectors to verify hGH effect in lit/scid mice, we observed a weight gain of 26.0% and 33.2% for the cDNA and the gDNA group, respectively, in a 49-day assay. Mean circulatory levels for the entire period were 2.95 ± 1.33ng hGH/ml for the cDNA and 1.17 ± 0.38ng/ml for the gDNA group. The mIGF-I levels for the cDNA were higher than for the gDNA group at all times, but this difference was significant only on day 49. The percentage of increase for other growth parameters (nose-to-tail, tail and femur lengths and liver weight) was higher for the cDNA than for the gDNA group. CONCLUSION: These results show that the use of cDNA in gene therapy procedures in the muscle tissue seems to be under some aspects more efficient than the use of genomic sequence.

Supported by FAPESP and CNPq

Key words: gene therapy, genomic sequence, complementary sequence, human growth hormone