Growth Parameter Increase and Anti-hGH, Anti-mGH Antibody Determination in *lit/lit* Mice After a Single Injection of Naked DNA Followed by Electroporation

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ABSTRACT

INTRODUCTION: Plasmid-based gene therapy has recently proven to be particularly effective, especially when followed by electroporation, with potential application to the treatment of different systemic diseases. An alternative method for growth hormone deficiency (GHD) treatment has been developed by using gene therapy associated to electroporation. MATERIAL AND METHODS: A previously used plasmid containing the genomic sequence of human growth hormone (hGH) or a new construction based on an homologous system containing the genomic sequence of mouse growth hormone (mGH), were injected via intramuscular in immunocompetent mice following a protocol of gene electrotransfer (8 pulses of 150V/cm and 20 ms). Mice were weighed during a 94-day assay and growth parameters (nose-to-tail, tail and femur lengths) were measured at the end of the assay by a digital pachymeter. DISCUSSION AND RESULTS: After 94 days, the weight increase for mGH-treated mice was 34.3%, while nose-to-tail, tail and femur lengths parameters, directly measuring longitudinal growth, increased 9.5, 5.9 and 24.3%, respectively, when compared to the initial values. The progressive growth arrest of the hGH-treated mice was not unexpected, considering the obvious immunogenic reaction of the immunocompetent animals against human GH. The results confirmed anti-hGH antibody titers ranging from 1:50 to 1:3200, while no significant binding was observed in the sera of mGH-treated mice. CONCLUSION: We are now performing the anti-mGH antibody determination, to confirm that immunocompetent mice do not present a reaction against the homologous GH hormone secreted in their circulation. We believe, thanks to this homologous treatment approach, to be able to move further close to a valid preclinical testing model for GHD gene therapy.

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