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Electro-gene transfer as a possible therapeutic approach for a rare metabolic disease

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Extended Abstract

Glycogen Debranching Enzyme (GDE) is a large cytosolic protein involved (together with glycogen phosphorylase) in glycogen breakdown. Mutations along the *Agl* gene (encoding for the human GDE), that cause loss of enzymatic activity, are associated with a rare metabolic disorder, Glycogen Storage Disease type III (GSDIII). In GSDIII patients, abnormal glycogen accumulates in skeletal/cardiac muscle and liver. The most frequent form of GSDIII (type IIIa) is considered a muscular dystrophy: muscle disorders, may become evident in adults with progressive weakness and distal muscle deterioration, with some patients requiring the use of a wheelchair for mobility.

No cure is currently available for GSDIII and patient management is based on dietary treatments. In recent times, adeno-associated virus (AAV)-based gene therapy has generated proof-of-concept in GSDIII pre-clinical models. However, the current limitations of AAV-mediated gene transfer represent challenges for successful gene therapy in GSDIII [1].

We developed a synthetic cDNA, encoding for a functional human GDE [2]. The gene was inserted into a mammalian expression vector and used to develop protocols for *in vitro* and *in vivo* electro-transfection. We will show results of introduction of the gene in GDE-defective human fibroblasts and preliminary results on electroporation of mice muscles with the long-term goal of contributing to an alternative/complementary non-viral gene therapy approach for GSDIII.

References

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