GLYCOGEN STORAGE DISEASE TYPE III
MODELING USING HUMAN INDUCED PLURIPOTENT STEM CELLS

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Glycogen storage disease type III (GSDIII) is a rare genetic disease caused by mutations in *AGL* gene encoding glycogen debranching enzyme (GDE). The deficiency of this enzyme involved in glycogen degradation leads to pathological glycogen accumulation in muscle and liver. These metabolic changes result in severe hypoglycemia and hepatomegaly during patient's childhood followed by a progressive and generalized myopathy during adulthood. To date, no curative treatment is available for GSDIII patients, and current symptomatic treatments are mostly based on strict diet regimens to avoid recurrent hypoglycemia. Here, we combined the self-renewal and differentiation capabilities of human induced pluripotent stem cells (hiPSCs) with cutting edge CRISPR/Cas9 gene editing technology to establish a stable *AGL* knockout cell line and explore glycogen metabolism in GSDIII using Glycogen-Glo™ Assay. Following skeletal muscle cells differentiation of the edited and control hiPSC lines, our study reports that the insertion of a nonsense mutation in *AGL* results in the loss of GDE expression and glycogen accumulation under glucose starvation conditions. This study introduces the first *in vitro* skeletal muscle cell model of GSDIII derived from hiPSCs and establishes a platform with Glycogen-Glo™ Assay to assess the therapeutical potential of pharmacological inducers of glycogen degradation or the efficacy of gene replacement therapies.