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Inhibition of glycogen biosynthesis via mTORC1 suppression as an adjunct therapy for Pompe disease

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Abstract

Pompe disease, also known as glycogen storage disease (GSD) type II, is caused by deficiency of lysosomal acid α-glucosidase (GAA). The resulting glycogen accumulation causes a spectrum of disease severity ranging from a rapidly progressive course that is typically fatal by 1–2 years of age to a more slowly progressive course that causes significant morbidity and early mortality in children and adults. Recombinant human GAA (rhGAA) improves clinical outcomes with variable results. Adjunct therapy that increases the effectiveness of rhGAA may benefit some Pompe patients. Co-administration of the mTORC1 inhibitor rapamycin with rhGAA in a GAA knockout mouse reduced muscle glycogen content more than rhGAA or rapamycin alone. These results suggest mTORC1 inhibition may benefit GSDs that involve glycogen accumulation in muscle.

Keywords: mTOR; Pompe disease; Glycogen storage disease; Glycogen synthase; Rapamycin; Enzyme replacement therapy

Article Outline

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