Antisense oligonucleotide therapy for APBD

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Adult polyglucosan body disease (APBD) is an adult-onset variant of glycogen storage disease type IV that manifests as a neuromuscular disease. APBD is recessively inherited due to mutations in the glycogen branching enzyme gene and is characterized by the presence of poorly-branched, precipitated glycogen aggregates, called polyglucosan bodies. Genetic intervention in the APBD mouse model identified glycogen synthase (Gys1), the main enzyme responsible for glycogen chain synthesis, to be an effective therapeutic target for APBD. Antisense oligonucleotides (ASOs) provide a clinically-translatable approach to induce targeted protein knockdown and we therefore aim to test the therapeutic efficacy of Gys1-targeted ASOs in the APBD mouse model. Mice were administered ASOs at one and two months of age via intracerebroventricular injection, prior to their sacrifice at three months of age. Preliminary results show a significant reduction in Gys1 mRNA and protein, and a trend towards polyglucosan body reduction. Tissue analysis and further *in vivo* experimentation is ongoing and the potential of Gys1-targeted ASOs as a therapy for APBD patients remains promising.