

Adult-onset Polyglucosan Body disease (APBD) is a recessively inherited form of glycogen storage disease, associated with reduction in glycogen branching enzyme activity (GBE) to 10-20% of normal. Symptoms generally develop in the fourth or fifth decade with bladder dysfunction, gait disturbance, sensory and motor neuropathy, weakness, and fatigue. Mild attention and memory deficits may occur with brain white abnormalities noted on neuroimaging. By their early 60's patients require a walker and are subsequently wheelchair dependent. The actual prevalence of the disease is probably much greater than reported due to misdiagnoses such as multiple sclerosis, Charcot-Marie-Tooth disease, ALS and spinal muscular atrophy (Schwartz L, et al. Am J Rare Dis: Diagn Ther. 2020;3(1):004-008.)

The APBD Research Foundation was established in 2005 to foster research in APBD and to provide patient and family support. Under their auspices, much has been learned about the genetic bases for tissue storage of polyglucosan bodies. Animal models have been established for the two major mutations in the GBE1 gene, and repurposed drugs have been examined for their ability to enhance glycogen branching activity. Substrate synthesis inhibition has been examined to reduce endogenous polyglucosan body formation.

A single grant of \$99,025 or two grants of \$49,513* will be awarded depending on the merits of the applications received. The primary focus for this grant opportunity is:

- Identification of measurable biomarkers to quantify the amount of insoluble glycogen developing serially in tissues.

Investigations related to the below will also be considered:

- The development of novel neuroimaging techniques for establishing correlations between disease symptomatology and pathology
- Identification of therapeutic targets that will prevent polyglucogon body storage or facilitate its removal from vital organs such as the brain and peripheral nervous system.

Grantees are expected to have access to senior mentors who can provide guidance and if needed, additional resources to accomplish the proposed work. Close collaboration with other scientists and clinicians knowledgeable about APBD is strongly encouraged. Proposals should include a sharing of data statement, and make use of available patient specimens such as cultured skin fibroblasts and animal models. It is hoped that the data generated by this funding mechanism will enable investigators to successfully compete for larger multi-year grants to carry forward their research and translate their results to improvement in the clinical care of patients.

*Please submit a proposal for the total amount of \$99,025. The ODC may choose to fund two awards at \$49,513 each, at which point we will request a revised work plan and budget.