

Repurposing Guaiacol for the Treatment of Adult Polyglucosan Body Disease (APBD)

"Our research group at Columbia University Medical Center (New York, NY USA) is working on the genetic disorders of energy metabolism. We have experience in mitochondrial and glycogen storage diseases that affect energetics of the cell and nervous system. Our research and findings increased information necessary to bring patients and researchers together. Due to our and patient's efforts Adult polyglucosan body disease research foundation (APBDRF) was established in 2005 to inform the patients, scientists, and raise the awareness about this disease called APBD.

APBDRF has funded researchers to find a cure for this rare disease and educate APBD patients and family members. Disease is caused by deleterious mutation or mutations in a gene coding the enzyme called glycogen branching enzyme (GBE). A single gene defect yet causes a disease with complex symptoms making this disease very difficult to bear and manage. We cannot bypass the enzyme defect by a substrate therapy because GBE do not have a simple substrate. When GBE is deficient, glycogen that is the only glucose storage molecule, forms an unusual shape making it difficult for our cells to use it. Therefore this abnormal glycogen known as polyglucosan accumulates in the cell and start to interfere with the normal function. Neurons and their axons where there are a very high metabolic demand and very little space to accommodate a molecule like polyglucosan.

We concentrate our efforts to prevent the synthesis of this large molecule. We knew that we could not bypass its activity by another substrate or eliminate the reaction that it catalyzes involving many other enzymes important for our life. Therefore we designed a high throughput assay system visualizing polyglucosan bodies. We treated this cell system blindly with thousands of molecules one at a time. Because we can visualize and measure polyglucosan, we have found few molecules that decrease the polyglucosan in the cell. Guaiacol is one of those molecules that has almost no serious side effect and easy to produce.

In this coming NORD Summit, I am honored to present our initial findings for rare disease community. We will very much appreciate the support we may have from the industry and directions to reach anyone we can help affected from this debilitating disease."

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