Diagnostic method for adult polyglucosan body disease

Technology #cu15065

Adult polyglucosan body disease (APBD) is a disease that has been associated with a mutation in the GBE1 gene, which encodes a protein responsible for glycogen branching. Symptoms include uncontrollable bladder, gait problems, sensory loss in extremities and mild cognitive difficulties. Currently, diagnosis of late-onset APBD is based on the presence of a collection of symptoms, blood tests, MRI evidence of changes in the cerebral white matter, and laboratory tests requiring a nerve biopsy. Since the disease is inherited autosomal recessively, genetic counseling can be used for early diagnosis of APBD to prevent unnecessary nerve biopsy and early management of the disease. This technology describes the second-most common mutation in GBE1 found in APBD patients. Identification of the mutation will enable pre-onset detection of APBD for early disease management.

Intronic mutation in GBE1 facilitates more accurate diagnosis of APBD

Currently, common genetic tests that aim to diagnose APBD involve exome sequencing for mutations in the GBE1 gene. Furthermore, many populations at high risk for APBD carry one type of exome mutation that does not lead to the development of APBD. The mutation identified in this technology is found in the intron of the GBE1 gene, and thus is undetectable by exome sequencing techniques. This mutation is highly correlated to the development of APBD, and will allow for more accurate diagnosis of APBD. Furthermore, this has the potential to be utilized as a target in therapeutic treatments for APBD, and may be used to diagnose other disease contexts where GBE1 is implicated.

Three antisense oligonucleotides have been designed in collaboration with ISIS Pharmaceuticals and have effectively targeted this intronic mutation in GBE1 to restore GBE activity in vitro.

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Applications:
• Early diagnosis of adult polyglucosan body disease through genetic testing
• Therapeutic treatments targeting GBE1 mutation
Advantages:

- More accurate and earlier diagnosis of APBD in genetic tests
- Can be screened in conjunction with other GBE1 mutations for comprehensive screening
- Provides more insight into development of APBD

Patent Information:

Patent Pending (WO/2016/090001)

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Related Publications:


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