

## Utilizing Variant Transcripts of PSEN2 for Diagnosis and Treatment of Tauopathies

**The solution is an alternatively spliced exon in PSEN2 that leads to an aberrant protein product, providing a potential target for therapeutic intervention for sporadic Alzheimer's Disease.**

### What is the Problem?

Alzheimer's Disease (AD), the most common neurodegenerative disease, is categorized into two main types: early-onset familial and sporadic AD. Early-onset AD is often characterized by pathogenic mutations in APP, PSEN1 and PSEN2. However, over 90% of individuals with AD have sporadic AD and do not have a mutation in one of these three genes. As a result, there is a need to identify potential therapeutic targets for the diagnosis and treatment of sporadic AD.

### What is the Solution?

The solution is an alternatively spliced exon in PSEN2 that leads to an aberrant protein product, providing a potential target for therapeutic intervention for sporadic AD. Using next-generation long-read RNA isoform sequencing, the alternatively spliced exon in PSEN2 was found to be significantly enriched in patients with sporadic AD compared to healthy patients. As this is specific to sporadic AD, the aberrant PSEN2 exon can be targeted using antisense oligonucleotides for both diagnosis and treatment applications. Therapies can be developed to either prevent inclusion of this alternative exon in mature PSEN2 mRNA or remove transcripts bearing this alternative exon, thus preventing abnormal accumulation of the aberrant protein produced from the alternative PSEN2 exon.

### What is the Competitive Advantage?

The competitive advantage of this technology lies in its ability to provide a sporadic AD-specific therapeutic target. The solution demonstrates that variant transcripts of PSEN2 can be used to diagnose and treat sporadic AD as well as other tauopathies. As the global AD market was valued at \$4.1 billion in 2022 with an expected CAGR of 20%, there is a significant opportunity for this technology to advance AD diagnostic and therapeutic approaches.

### References

1. Course, M.M., Gudsnuik, K., Keene, C.D., Bird, T.D., Jayadev, S., Valdmanis, P.N.(2023), <https://academic.oup.com/brain/article/146/2/507/6660735>, <https://academic.oup.com/brain>, 146, 507-518

### Technology ID

BDP 8801

### Category

Therapeutics/CNS  
Selection of Available  
Technologies  
Diagnostic

### Authors

Paul Valdmanis

### Learn more

