

Appendix S1.

METHODS FOR GENE MUTATION ANALYSIS

To identify mutations in the genes encoding γ -secretase subunits in this Japanese family with HS, we conducted a mutation analysis for *PSENI*, *PSENEEN*, and *NCSTN* genes.

Genomic DNA was extracted, using the QIAamp DNA Blood Maxi Kit (Qiagen, Germantown, MD, USA), for PCR amplification of the *PSENI*, *PSENEEN* and *NCSTN* genes. PCR was performed using the exon flanking intronic primers, and the PCR products were purified for sequencing analysis by Greiner Bio-One Japan (Tokyo, Japan). For detailed analysis of the PCR fragment with mutation, electrophoregrams were obtained using the ABI PRISM 3130 genetic analyser (Applied Biosystems, Foster City, CA, USA).