Complete Analysis of the Presenilin 1 Gene in Early Onset Alzheimer’s Disease


In 1992, scientists discovered a linkage to early onset familial Alzheimer’s disease (FAD) on chromosome 14q24.3. Several large collaborative groups of scientists formed in an attempt to discover the gene associated with FAD at this locus. After several years, in 1995, mutations in the gene called S182, now known as presenilin-1 (PS-1), were found to be associated with FAD in five families.

In this paper, our group (The Alzheimer’s Disease Collaborative Group) continued our work on the genomic structure of the PS-1 gene and described a set of 10 intronic primer pairs that were used to sequence all 10 exons of the gene. The group also discovered and described two novel mutations in PS-1. These PS-1 intronic primers have served as a toolbox for many investigators who wished to sequence the exons of the PS-1 gene to find mutations in their own families. To date, investigators have located over 70 mutations associated with FAD using these primers.

In addition, the group discussed the distribution of all of the then-known mutations in PS-1 that lead to FAD. Clustering of missense mutations was seen at the seven suspected transmembrane regions of the PS-1 protein, especially at the borders of the large hydrophilic loop between transmembrane regions 6 and 7. We considered the implications of this clustering of mutations to the possible dysfunction of this protein and the etiology of AD.