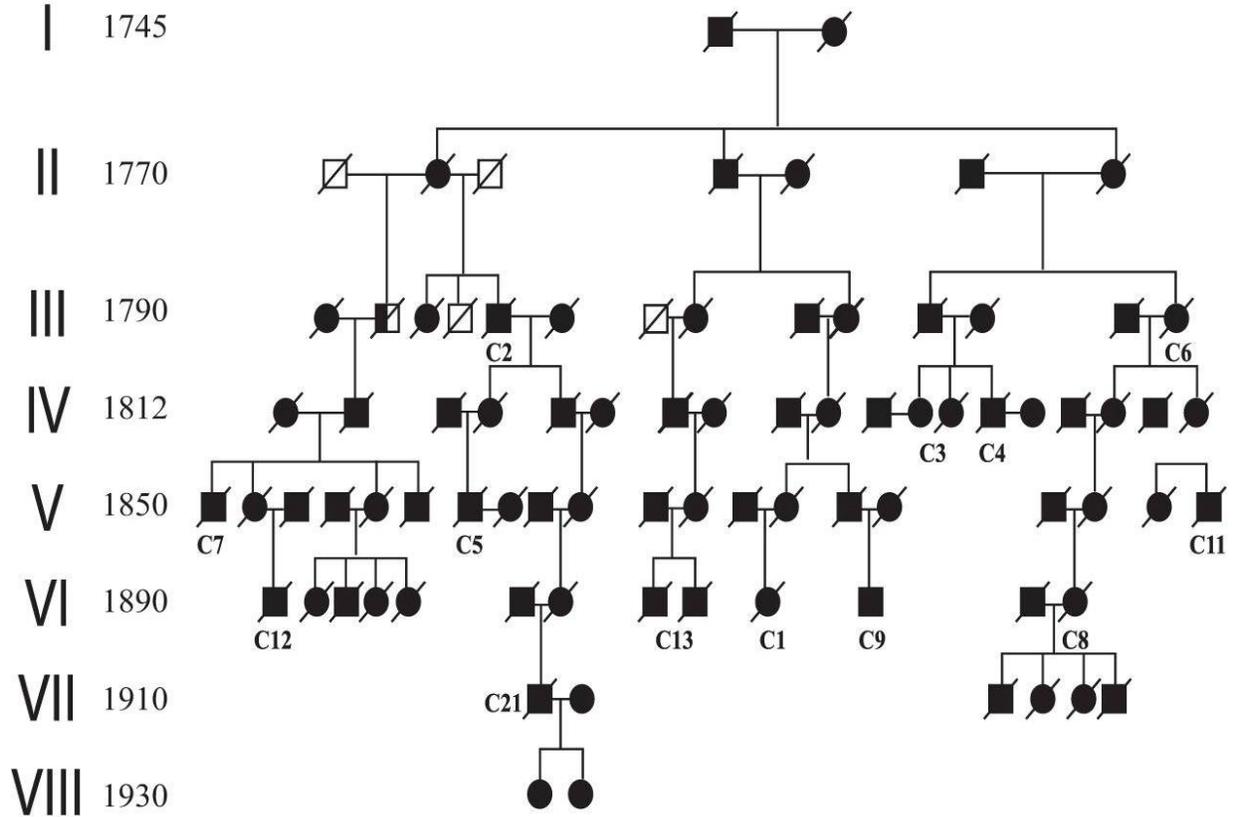




# Origin of a Gene Mutation Causing Early-Onset Alzheimer's Disease



**Caption:** Pedigree of an extended family in Antioquia, Colombia, showing a mutation in the *PSEN1* gene, which causes early-onset familial Alzheimer's disease. Black circles (female) and squares (male) indicate individuals afflicted with the disease. Half-shaded shapes indicate individuals with an uncertain disease status. White shapes indicate unaffected individuals. Shapes with a line through them indicate that the family member is deceased. Roman numerals mark each generation and the approximate year that the generation began. This pedigree combines 13 subpedigrees (each labeled with a C plus a number) that all share a common ancestor.

## BACKGROUND INFORMATION

Alzheimer's disease is characterized by the accumulation of amyloid plaques and tangles as well as the loss of connections between nerve cells and the death of nerve cells in the brain. There are two types of Alzheimer's disease, early-onset and late-onset. The early-onset type affects people age 30 to 60 and represents less than 5% of all people with Alzheimer's. Most early-onset cases are genetic and are caused by a mutation in one of three genes: presenilin-1 (*PSEN1*), presenilin-2 (*PSEN2*), or amyloid precursor protein (*APP*). Researchers studied a large extended family in Antioquia, Columbia, that has a high prevalence of early-onset familial Alzheimer's disease due to a mutation in the *PSEN1* gene. They performed whole-genome sequencing on living individuals in this family, which allowed them to confirm that all affected members of this family carried the same mutation. By using historical records and interviewing living family members, they determined which deceased family members had developed early-onset Alzheimer's disease and constructed a pedigree of 13 families with shared ancestry.