Presenilin 1

Mutations in the Presenilin 1 (PSEN1) gene are the most common cause of autosomal dominant familial Alzheimer's disease.

Presenilin 1 is a protein that is encoded by the PSEN1 gene in humans. It is a transmembrane protein found primarily in the endoplasmic reticulum and Golgi apparatus of cells.

Presenilin 1 plays a critical role in the processing of amyloid precursor protein (APP) and the formation of beta-amyloid, a protein that accumulates in the brains of individuals with Alzheimer's disease. Specifically, presenilin 1 is a component of the gamma-secretase complex, which cleaves APP to produce beta-amyloid. Mutations in the PSEN1 gene have been found to be a cause of early-onset familial Alzheimer's disease.

Presenilin 1 also has other functions, including the regulation of calcium homeostasis and the processing of other transmembrane proteins. It is involved in several signaling pathways and is important for the proper development and function of the nervous system.

Research into presenilin 1 is ongoing, with the aim of understanding its role in disease and developing therapies for Alzheimer's and other neurological disorders.

O'Connor et al. report the clinical, imaging, and postmortem findings of kindred carrying a novel duplication mutation (Ile168dup) in the PSEN1 gene. We interpret the pathogenicity of this novel variant and discuss the additional neurological features (pyramidal dysfunction, myoclonus, and seizures) that accompanied cognitive decline. This report broadens the clinical phenotype of PSEN1 insertion mutations while also highlighting the importance of considering duplication, insertion, and deletion mutations in cases of young-onset dementia [1)].

1)
O'Connor A, Abel E, Fraser MR, Ryan NS, Jiménez DA, Koriath C, Chávez-Gutiérrez L, Ansorge O, Mummery CJ, Lashley T, Rossor MN, Polke JM, Mead S, Fox NC. A novel presenilin 1 duplication mutation (Ile168dup) causing Alzheimer's disease associated with myoclonus, seizures and pyramidal features. Neurobiol Aging. 2021 Feb 5:S0197-4580(21)00046-4. doi: 10.1016/j.neurobiolaging.2021.01.032. Epub ahead of print. PMID: 33648786.