APOE4 refers to a specific allele of the apolipoprotein E (APOE) gene, known as ε4 allele. The APOE gene encodes a protein called apolipoprotein E, which plays a crucial role in lipid metabolism and transport in the body, particularly in the brain. There are three common alleles of the APOE gene: ε2, ε3, and ε4.

APOE4 is associated with an increased risk of developing certain diseases, particularly Alzheimer's disease (AD). Individuals who inherit one copy of the APOE4 allele have an increased risk of developing late-onset Alzheimer's disease, while those who inherit two copies (one from each parent) have an even higher risk. APOE4 is the strongest known genetic risk factor for late-onset AD.

In addition to Alzheimer's disease, APOE4 has also been associated with an increased risk of other neurological conditions, such as cognitive decline, dementia with Lewy bodies, and cerebral amyloid angiopathy. Furthermore, APOE4 has been implicated in cardiovascular disease and may influence the risk of other health conditions, including diabetes and stroke.

It's important to note that while APOE4 is a significant risk factor for certain diseases, not everyone who carries the allele will develop these conditions. Environmental factors, lifestyle factors, and other genetic factors likely interact with APOE4 to modulate disease risk. Additionally, other alleles of the APOE gene, such as APOE2 and APOE3, may have protective effects against certain diseases.

Genetic testing for APOE4 may be performed in clinical settings, particularly in cases where there is a family history of Alzheimer's disease or other related conditions. However, it's essential to consider the implications of genetic testing and to interpret results in the context of other risk factors and individual circumstances. Additionally, genetic counseling may be recommended for individuals considering APOE testing.

APOE4 is widely recognized as a genetic risk factor for Alzheimer's disease (AD), implicated in 60-80% of all AD cases. Recent research suggests that microglia carrying the APOE4 genotype display abnormal lipid metabolism and accumulate lipid droplets, which may exacerbate the pathology of AD. Microglia play a critical role in immune surveillance within the central nervous system and are responsible for removing harmful particles and preserving neuronal function. The APOE4 genotype causes abnormal lipid metabolism in microglia, resulting in excessive accumulation of lipid droplets. This accumulation not only impairs the phagocytic and clearance capabilities of microglia but also disrupts their interactions with neurons, resulting in disorganization and neurodegenerative alterations at the neuronal network level. In addition, the presence of APOE4 modifies the metabolic landscape of microglia, particularly affecting purinergic signaling and lipid metabolism, thereby exacerbating the pathological processes of AD. In conclusion, the accumulation of lipid droplets and abnormal lipid metabolism may be critical mechanisms in the progression of AD in microglia carrying the APOE4 genotype [1)]

1)
Hu X, Ma YN, Xia Y. Association between abnormal lipid metabolism and Alzheimer's disease: New research has revealed significant findings on the APOE4 genotype in microglia. Biosci Trends. 2024 Apr 17. doi: 10.5582/bst.2024.01092. Epub ahead of print. PMID: 38631884.