Recent advancements have been made in Alzheimer's research that focus on the role of the APOE4 gene and its link to the development of the disease. It has previously been known that inheriting one copy of the variant increases the risk of developing Alzheimer's and inheriting two copies of the gene greatly increases the risk. The APOE gene exists in three forms, APOE2, APOE3, and APOE4; however, the APOE4 can be quite harmful compared to the other two variants. The APOE4 gene plays an important role in the development of Alzheimer's, as it increases the accumulation of amyloid plaques in the brain, one of the main hallmarks of Alzheimer's. A new study described in this article found that individuals with two copies of the APOE4 gene have almost all developed Alzheimer's. Researchers say that having two copies of this gene should be determined as a cause of Alzheimer's, not just a risk factor. The study also indicated that individuals with two copies of the APOE4 gene started to develop symptoms younger than most individuals who did not have the gene variant. Individuals with the gene started to show signs of the biological markers for Alzheimer's at age 55, and at 65, started to show signs of cognitive decline. According to the article, about 2-3% of the population have two copies of the APOE4 gene with 15-20% of these individuals having Alzheimer's dementia. Individuals with one copy of the APOE4 gene make up about 15-25% of the general population with 50% of these individuals being Alzheimer's dementia patients. Of the three APOE gene variants, APOE3 is the most common though it seems to have little to no effect on the development of Alzheimer's, although about 75% of the population has one copy of the APOE3 gene. In a journal published by Nature Medicine supporting information in this article stated that the APOE gene is the strongest genetic risk factor for developing Alzheimer's disease with APOE4 homozygotes having a 60% chance of developing Alzheimer's compared to noncarriers or heterozygotes. Similarly, a journal published by the National Institutes of Health also stated that individuals homozygous for the APOE4 gene have been found to have an increased risk of developing Alzheimer's by the age of 85. The journal published in NIH went on to say that though the APOE4 homozygotes only account for about 2% of the population, they account for 15% of Alzheimer's disease cases, further supporting information expressed in this article.

Some researchers feel that identifying Alzheimer's as a genetic condition could significantly improve treatment options to reduce amyloid plaque. Similarly, other experts feel that identifying Alzheimer's patients as having a distinct genetic form of the disease would increase interest in developing drugs and increase the urgency for finding ways to prevent cognitive decline in individuals with the gene who have not yet shown symptoms. This being said, other experts feel that genetic ancestry plays a huge part in the development of Alzheimer's as white individuals have a higher likelihood of developing the disease compared to African Americans. According to the article, white individuals with two copies of the APOE4 gene had a 13 times higher risk of developing the disease than white individuals with two copies of the APOE3 gene. African Americans with both copies of the APOE4 gene had 6.5 times the risk of developing Alzheimer's with two copies of the APOE3 gene. Experts against this new research have argued that it is unusual for diseases to follow a semi dominance pattern with two copies of the gene causing the disease but only one copy of the gene increasing the risk. Doctors have also advised to stray away from genetic testing to see if people have the APOE4 variant until there are treatments or trials available for people with two copies of the APOE4 gene as it can "only cause grief at this point." Though, researchers continue to study the contributions of the APOE4 gene and its implications in Alzheimer's disease, focusing on its effects on amyloid plaque buildup, to help aid in finding drugs and treatments to potentially help the individuals both diagnosed and undiagnosed with Alzheimer's.

Works Cited

- Belluck, P. (2024, May 6). Study Suggests Genetics as a Cause, Not Just a Risk, for Some Alzheimer's. *The New York Times*. https://www.nytimes.com/2024/05/06/health/alzheimers-cause-gene-apoe4.html
- Fortea, J. et al. APOE4 homozygosity represents a distinct genetic form of Alzheimer's disease. *Nat Med* 30, 1284–1291; <u>https://www.nature.com/articles/s41591-024-02931-w</u> (2024).
- 3. Study defines major genetic form of Alzheimer's disease. *National Institutes of Health* (*NIH*);

https://www.nih.gov/news-events/nih-research-matters/study-defines-major-genetic-form -alzheimer-s-disease (2024).