Gene Therapy in Alzheimer's Disease: Novel Therapies and Ethical Aspects of Somatic Gene Editing

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Mission: To develop a disease modifying therapy (DMT) for late onset Alzheimer's disease (LOAD) targeting APOE ε4 that will decrease disease toxicity by limiting the amount of protein produced

Investigate the ethical and social implications of developing DMT for LOAD ⇨ **Identify a phenotypic difference between APOE alleles within different cell types to to substantiate a targeted treatment plan** ⇨ **Develop allele-specific viral vector technology to downregulate APOE on targeted cells**

Background

What is Alzheimer's Disease (AD)?

- A progressive neurodegenerative disease that causes memory loss and cognitive decline

Why Study It?

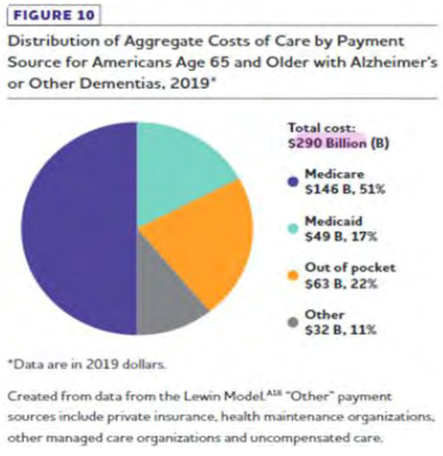
- AD affects 5.8 million people in the U.S. and is projected to affect 14 million by 2050
- Previous clinical trials targeting amyloid plaques, a common hallmark, have failed
- Causative factors and the mechanism behind its onset and progression remain unknown; no cure currently exists

Why APOE?

- APOE ε4 has been identified as the strongest and most reproducible genetic risk factor for LOAD

What is a DMT?

- seeks to stop or slow the progression of the disease by making alterations to the pathological steps that lead to the AD



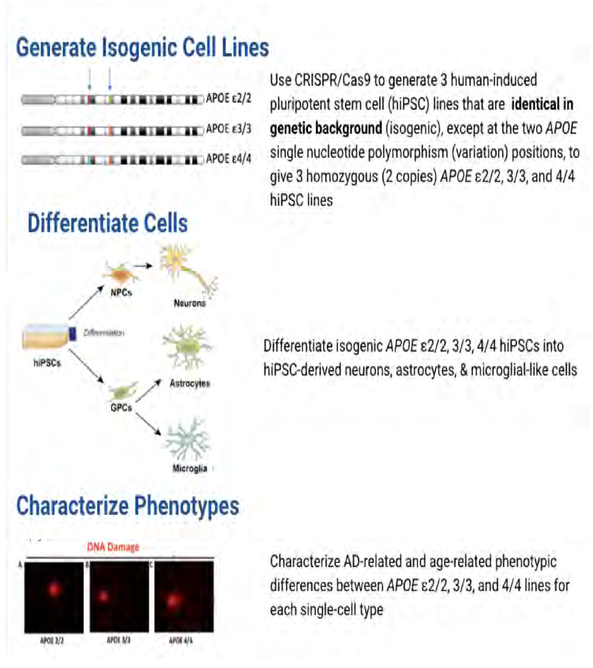
Healthcare cost for dementia patient $350,174

DMT, what then?

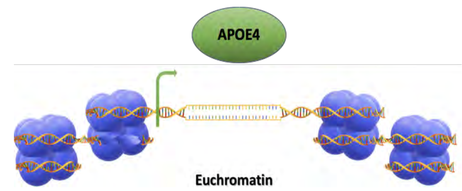
- New therapies emphasize the need to examine legal and social issues of an AD DMT (pricing, cost, treatment)

Understanding the role of APOE ε4 in AD

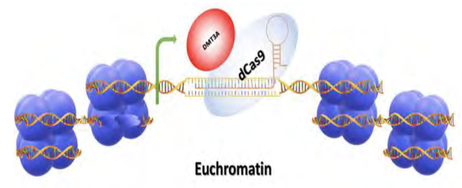
- How do we measure for differences between APOE ε4 (the risk allele) and APOE ε2and ε3 in AD pathology?



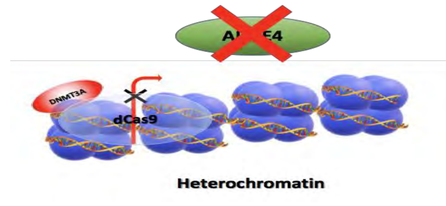
How do we stop protein production?



DNA ready to be converted into proteins is typically open and ready for co-factors to bind



DNMT3A attaches to the DNA, guided to the site by another protein (dCas9)



DNMT3A adds chemical tags to the DNA, causing it to bunch up so that cofactors can no longer bind to begin production