Development of RNA Vaccines Targeting Alzheimer's Disease Using Single-Cell RNA Sequencing and Proteomic Analysis

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Alzheimer's disease (AD) is the most common neurodegenerative disease affecting more than 33 million people globally. Although several protein hallmarks associated with AD have been identified, such as extracellular amyloid plaque deposition formed by Aß peptide, and intracellular neurofibrillary tangles resulted from the accumulation of hyperphosphorylated tau, we still lack clarity regarding the pathogenesis mechanism behind AD progression. Like COVID-19, there are very few confirmed disease-modifying treatments that reverse or stop the progression of AD, making prevention an efficient strategy. I investigated the potential of the two known protein hallmarks to be vaccine targets. While Aß is not an effective target, I designed a tau-based RNA vaccine. Additionally, this study uncovered a promising novel target, S100A11. By 2050, AD is estimated to cost more than $1 trillion within the US, one-twentieth of the US's GDP. The proposal of this vaccine and a new target not only uncovers a potential strategy to prevent AD's development but also provides insights into the early development of AD and the interactions between the immune system and the nervous system throughout AD's disease progression. This study also reveals new, potential pharmaceutical targets, inspiring the development of new AD treatments and prevention measures, which save millions of lives from AD and significantly improve their quality of life.

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