Analysis of the Effects of Active Immunization with Aβ1-42 Peptide of APPPS1 Transgenic Mice at Three and Nine Months of Age

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The brain chemistry of individuals with Alzheimer disease (AD) begins to change years before cognitive symptoms appear, making preclinical stages crucial for intervention. Identifying biomarkers is integral for diagnosis and prognosis during this time, as clinical signs and symptoms are unapparent; the two most highly validated biomarkers, amyloid-β (Aβ1-42) and tau, are associated with the two hallmark pathologies of AD, amyloid plaques and tau tangles, respectively. Studies suggest amyloid plaque formation is a key driver for AD, so potential treatments that prevent amyloid pathology during preclinical stages are important to investigate.

A transgenic mouse model was used to mimic these types of treatments. These mice overexpress human AD-causing mutations in amyloid precursor protein and Presenilin-1 (APP/PS1), and develop aggressive amyloid plaques around six weeks of age. APP/PS1 mice were immunized monthly with human Aβ1-42 peptide (or PBS as a sham treatment) to elicit an immune response creating anti-Aβ1-42 antibodies that, in other mouse models, reduced amyloid plaque load significantly. Blood was drawn to obtain anti-Aβ1-42 titers to evaluate the immune response of the mice, and half of the brain was homogenized to measure Aβ1-40 and Aβ1-42 concentrations using ELISA; the other half was sectioned and immunostained for Aβ to quantify amyloid plaque load. CSF was collected for future evaluation of potential downstream effects of immunization.

Aβ1-40 and Aβ1-42 concentrations in brain tissue and amyloid plaque load were not statistically different between immunized and sham-treated groups, indicating the immunization was ineffective in altering amyloidogenesis. The immunization resulted in very low anti-Aβ1-42 titers, meaning a weak immune response was mounted. This could be because the immunizations started at four weeks of age, before the immune system is fully developed. Further work is needed in other models that develop amyloid plaques later to test anti-Aβ treatment effects in a setting mimicking preclinical trials.