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Abstract: Immunotherapy has the potential to provide a possible treatment therapy to prevent or delay Alzheimer disease. In a clinical trial (AN1792) in which patients received this immunotherapy and received active A?1-42 peptide immunizations, treatment was stopped when 6% of patients showed signs of meningoencephalitis. Follow up on these patients led to the conclusion that the antibody response was beneficial in removing A?1-42 from brain but an accompanying inflammatory Th1 T cell response was harmful. As a safe alternative treatment targeting the same self protein, A?1-42, in brain, we and others are working on a DNA A?1-42 immunization protocol as the immune response to DNA immunizations differs in many aspects from immunizations with peptide antigens. Because the immune response to DNA vaccination has different kinetics and has a significantly lower antibody production, we evaluated two different prime boost regimens, A?1-42 DNA prime/A?1-42 peptide boost and A?1-42 peptide prime/A?1-42 DNA boost for their effectiveness in antibody production and possible side effects due to inflammatory T cell responses. While both boost regimes significantly enhanced the specific antibody production with comparable antibody concentrations, the absence of the A?1-42 T cell response (no
proliferation and no cytokine production) is consistent with our previous findings using this DNA A?1-42 trimer immunization and greatly enhances the safety aspect for possible clinical use.