DNA immunization against amyloid beta 42 has high potential as safe therapy for Alzheimer's disease as it diminishes antigen-specific Th1 and Th17 cell proliferation.

Abstract:

The pathogenesis of Alzheimer's disease (AD) has been strongly associated with the accumulation of amyloid beta (Aβ) peptides in brain, and immunotherapy targeting Aβ provides potential for AD prevention. A clinical trial in which AD patients were immunized with Aβ42 peptide was stopped when 6% of participants showed meningoencephalitis, apparently due to an inflammatory Th1 immune response. Previously, we and other have shown that Aβ42 DNA vaccination via gene gun generates a Th2 cellular immune response, which was shown by analyses of the respective antibody isotype profiles. We also determined that in vitro T cell proliferation in response to Aβ42 peptide re-stimulation was absent in DNA Aβ42 trimer-immunized mice when compared to Aβ42 peptide-immunized mice. To further characterize this observation prospectively and longitudinally, we analyzed the immune response in wild-type mice after vaccination with Aβ42 trimer DNA and Aβ42 peptide with Quil A adjuvant. Wild-type mice were immunized with short-term (1-3× vaccinations) or long-term (6× vaccinations) immunization strategies. Antibody titers and isotype profiles of the Aβ42 specific antibodies, as well as cytokine profiles and cell proliferation studies from this longitudinal study were determined. Sufficient antibody titers to effectively
reduce Aβ42, but an absent T cell proliferative response and no IFNγ or IL-17 secretion after Aβ42 DNA trimer immunization minimizes the risk of inflammatory activities of the immune system towards the self antigen Aβ42 in brain. Therefore, Aβ42 DNA trimer immunization has a high probability to be effective and safe to treat patients with early AD.