＜シンポジウム 02―1＞アカデミア発の創薬・治療研究

Aβ42Gene Vaccine for Prevention and Treatment of Alzheimer's Disease

Roger N. Rosenberg, M.D.

（臨床神経 2010;50:838）
Key words：Alzheimer's disease, Amyloid, DNA Abeta42 vaccine, Immunotherapy, Anti-Abeta42antibody

Alzheimer's disease (AD) pathogenesis has been associated with the accumulation, aggregation and deposition of amyloid beta (Aβ) peptides in the brain. Aβ immunotherapy provides great potential to treat or prevent AD. A clinical trial with Aβ42 peptide vaccination in AD patients caused meningo-encephalitis in 6% of the participants which was likely due to a Th1 immune response, and was stopped. In this study, we have compared in detail the immune response in wild-type mice after vaccination with Aβ42 trimer DNA delivered by gene gun and i.p. injection of Aβ42 peptide in combination with the adjuvant Quil A. Antibody titers, epitope mapping and isotype profiles of the Aβ42 specific antibodies were followed throughout the immunization procedure. Results were as follows: (1) Aβ42 trimer DNA vaccination using the Gal4/UAS expression system resulted in high Aβ42 specific antibody titers. (2) Epitope mapping showed that both antigens, DNA and peptide, elicited a response towards the known B cell epitope, Aβ1-15 (3) The isotype profile of the antibodies differed markedly; a predominant IgG1 antibody response was found in the DNA vaccinated mice indicating a Th2 type of immune response. The peptide immunized mice showed a mixed Th1/Th2 immune response with IgG1 and IgG2a antibodies in similar amounts. The characteristic Th2 type of response after Aβ42 DNA vaccination reduces the likelihood of inflammatory activities of the immune system towards the self peptide Aβ42 in brain. Therefore, this vaccination protocol has a high probability to be effective and safe for a treatment therapy in AD.

University of Texas Southwestern Medical Center at Dallas〔5323 Harry Hines Boulevard, Dallas, Texas 75390, USA〕
（Received: 21 May 2010）