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Protein- and DNA-based epitope vaccines for Alzheimer's disease

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The Aβ is believed to play an important role in the onset and progression of AD. Many strategies currently proposed as therapies for AD aimed at reducing the level of Aβ in the brain or blocking the assembly of the peptide into pathological forms. One potentially powerful strategy for reducing the level of Aβ in the brain is immunotherapy, where Aβ-specific antibody facilitates the clearance of Aβ. First immunotherapy clinical trial in AD patients utilized AN-1792 vaccine containing the B and T cell "self epitopes" of $A\beta_{42}$ was halted, when approximately 6% of the vaccinated participants developed aseptic. Published data suggested that that the aseptic meningoencephalitis may have been caused by a T cell-mediated autoimmune response rather than by anti-Aβ antibodies. Importantly, extensive Aβ removal was observed in patients with the biggest antibody. Unfortunately, about ~80% of immunized subjects had no or relatively low plasma anti-Aβ antibody titers indicating that stronger immunogenic antigen is needed for effective immunotherapy. Thus, almost 10 years ago we hypothesized that safe and effective AD vaccine should possess immunodominant self-B cell epitope and non-self T helper cell epitope to avoid autoreactive immunity. Accordingly, we generated and tested in mice, rabbits and monkeys peptide/protein- or DNA-based epitope vaccines composed of multiple copies of small Aβ self-epitope fused with the strong non-self T helper cell epitope/s. These data will be presented along with information on currently active clinical trials with therapeutic vaccines based on N-terminal Ab peptides fused with various foreign immunogens and carriers.

Biography

Dr. Agadjanyan is the Vice-President, Head of the Immunology Department, Professor at the IMM, and a Visiting Professor at UCI MiND, California, USA. He received his professional education in Moscow, i.e. both a Ph.D. and Doctor of Science (D.Sc. the highest degree in Europe). He has authored several book chapters and more than hundred scholarly articles in vaccine research and immunology that have been published in top, peer-reviewed journals around the world. Dr. Agadjanyan's current research interest is the development of vaccines against Alzheimer's disease, Parkinson's disease, viruses, and cancers.