

## **IMMUNOTHERAPY OF ALZHEIMER'S DISEASE**

Dr. Alon Monsonego (P)

The National Institute of Biotechnology, and the Department of Microbiology and Immunology, Faculty of Health Sciences, Ben-Gurion University, Beer-Sheva 84105, Israel

Alzheimer's disease (AD) is not classically considered inflammatory or immune mediated, although the immune system may play an important role in the degenerative process. Furthermore, it has become clear that the immune system itself may have beneficial effects in nervous system diseases considered neurodegenerative. Immunotherapeutic approaches designed to induce a humoral immune response have recently been developed for the treatment of Alzheimer's disease. These studies have led to human trials that resulted in both beneficial and adverse effects. Recently, we have shown for the first time that cellular components of the immune system are significantly elevated in elderly healthy individuals and patients with AD than in middle-aged adults, which was strongly dependent on certain HLA-DR class II alleles. We then examined in a mouse model of AD whether lymphocytes can migrate to brain and affect disease pathogenicity. Our data demonstrate that accumulation of amyloid beta-peptide (Ab) in the CNS, MHC genetic background, and inflammatory signal such as IFN- $\gamma$  are required to induce specific immune responses in a mouse model of AD similar to that observed in A $\beta$ -vaccinated patients with AD. Thus, the occurrence of increased T-cell reactivity to the self antigen A $\beta$  appears to represent a dialogue between the brain and the immune system during the aging process, may itself be linked to AD susceptibility and course, and has implications for the design of A $\beta$  vaccines.