LYMPHOCYTES AS PUTATIVE PERIPHERAL BIOMARKERS FOR AD

M. Memo
Department of Biomedical Sciences and Biotechnologies, University of Brescia, Brescia, Italy

Alzheimer's disease (AD) is the most common form of dementia among elderly people that gradually destroys brain cells and leads to progressive decline in mental function. AD is difficult to diagnose, especially in the early course of the disease. The confirmatory diagnosis of AD is possible only post mortem and is based on the recognition and quantification of senile plaques and neurofibrillary tangles, which are the pathognomonic markers of the disease.

To date, on the basis of the current diagnostic criteria, AD can not be diagnosed until dementia appears, thus the detection of early disease-related biomarkers is crucial to facilitate the development of new diagnostic tools and drug therapies. Candidate biochemical markers for AD may be molecules able to represent some of the cerebral pathogenetic processes typical of AD or representing altered metabolic or cellular processes as shown by several studies performed either on brain or on peripheral tissues from affected patients. In this regard, to date, three cerebrospinal fluid (CSF) biomarkers have been found to show the highest diagnostic potential: total-tau, phospho-tau and Abeta 1-42.

In the search of putative markers useful for an early detection of the disease, an intriguing correlation between p53 and AD has been recently demonstrated Lanni et al., Mol Psych 2008). In particular, it has been demonstrated that peripheral blood cells from sporadic AD patients specifically express an anomalous and detectable conformational state of p53 (mutant p53) that allows to differentiate them from peripheral blood cells of age-matched non-AD subjects.
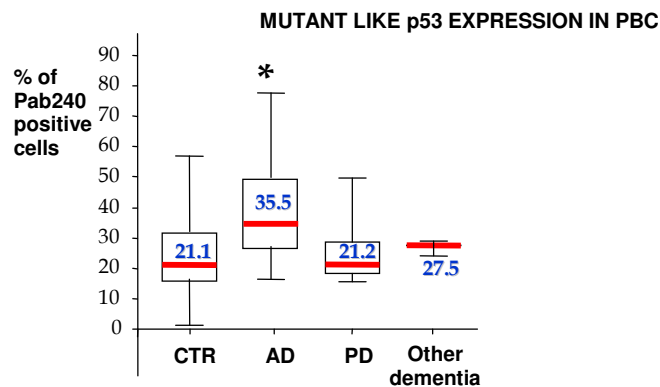
In this regard, peripheral changes of the immune system have been reported including lymphocytes function and subset distribution (Richartz-Salzburger et al., J Psych Res 2007). Moreover, biological analysis of 18 plasma signalling proteins, including mainly cytokines and chemokines, points to systemic dysregulation of immune response in AD (Ray et al., 2007).

We hypothesize that the pathological processes leading to AD would cause characteristic changes circulating peripheral cells, generating a detectable disease-specific cell phenotypes. In this contest, lymphocytes appear to be the most interesting cells to be analyzed. The relevance of this hypothesis is twice. From one side, the presence of peripheral markers of AD may represent novel putative diagnostic tool to improve a clinical diagnosis of AD. From the other, AD should be considered as a systemic disease.