

CONFORMATIONALLY ALTERED p53: A POTENTIAL PREDICTIVE MARKER FROM MCI TO ALZHEIMER'S DISEASE?

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Background: According to the current clinical criteria, definite Alzheimer's disease (AD) can only be diagnosed following neuropathological examination of brain samples, obtained by biopsy or autopsy. Furthermore, when evaluating the intermediate state between normal aging and established AD, known as mild cognitive impairment (MCI), not all MCI patients progress to AD and hence there is a need of a reliable prediction tool able to identify which patients with MCI will progress to AD. The current inability of clinical criteria to accurately identify this at-risk group underscores the importance of developing biomarkers able to potentially supplement the clinical approaches. Recently a role for conformationally altered p53 as a novel candidate biomarker for early onset AD has been described. The aim of our work is to investigate the usefulness of this method especially for younger patients, thus supporting its putative application for subjects with MCI and earlier in the clinical course of AD.

Methods: We used a flow-cytometric approach to investigate the different expression of conformationally altered p53 among MCI, AD and non-AD subjects on peripheral blood cells.

Results: We found that peripheral blood cells from MCI specifically expressed increased levels of unfolded p53 compared to age-matched controls. We found that the expression of conformationally altered p53 is age dependent. For our preliminary data analysis we have arbitrarily worked out the related cut-points by linear regression, taking as reference linear fit of controls, thus dividing the subjects in specific age interval segments. Young (≤ 70 years) MCI patients show levels of conformationally altered p53 comparable to those measured in AD patients, but significantly different from subjects of control group.

Conclusions: The highest levels of conformationally altered p53 have been observed in amnesic MCI patients, which represent an early stage of AD, thus supporting the promise of this protein measurement to accurately identify this at-risk group.