

P036 Amyloid peptides in different assembly states and related effects on isolated and cellular proteasomes

Valentina Cecarini, Laura Bonfili, Manila Amici, Mauro Angeletti, Anna Maria Eleuteri

University of Camerino, Department of Biology M.C.A., 62032 Camerino (MC), Italy

The role of Amyloid- β ($A\beta$) protein in the pathogenesis of Alzheimer's disease (AD) has been widely investigated and amyloid aggregates are considered a major cause of neuronal dysfunction. Increasing data have identified a correlation between this protein and the proteasome, the cellular proteolytic machinery, in particular the ubiquitin-proteasome system. The 20S proteasome is the catalytic core of a complex, known as 26S proteasome, and is the main responsible for the clearance of misfolded and oxidized proteins. In this work we have investigated the effects of different assembly states of two major amyloid peptides, $A\beta$ (1-40) and $A\beta$ (1-42), on the 20S proteasome functionality and on the ubiquitin-dependent pathway of protein degradation. In particular, we have tested proteasome activities after $A\beta$ treatment on purified 20S complexes and on lysates of a human neuroblastoma cell line. Our findings show a significant decrease in proteasome activity, more evident in cell lysates than in isolated complexes, and an increased amount of ubiquitin-protein conjugates and a known proteasome substrate (p27). Furthermore, the altered proteasome functionality is not associated with a decrease in cell viability, but is linked with increased levels of protein oxidation.