

P005 β -Secretase (BACE1) Expression in Primary Cultures of Rat Cortical Astrocytes.

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The brains of patients suffering from Alzheimer's disease (AD) are characterized by the presence of amyloid plaques, composed mainly of 39-42 amino acid amyloid β peptides (A β Ps). These A β Ps are produced from amyloid precursor protein following sequential cleavage by β - then γ -secretase. The location of this secretase system is largely neuronal and there is still controversy about its location in non-neuronal cells. We have previously shown A β P expression in primary cultures of rat astrocytes inferring that β -secretase is both present and active in these cells. Rat astrocytes demonstrated clear immunostaining with antibodies raised against BACE1 and Western blots of astrocyte extracts, probed with the same antibody, showed clear bands at ~65 and ~70kD corresponding to immature (partially glycosylated) and mature BACE1. Treatment of the cells with the proteasome inhibitors MG132 or lactacystin, caused a large increase in the 70kD band demonstrating that, as has recently been shown in a neuronal cell line, endogenous BACE1 in astrocytes is continuously degraded by the ubiquitin-proteasome pathway. The existence of functional BACE1 in astrocytes may have important consequences in the development of neurodegeneration in AD by acting as an alternative source of A β Ps rather than clearing them from the brain.