ADAM10 IN PLATELETS OF ALZHEIMER DISEASE PATIENTS: A NOVEL TARGET FOR THERAPY?

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ADAM10, a member of the disintegrin and metalloproteases family, is a candidate to cleave the Amyloid Precursor Protein (APP) at the alpha-secretase site. Measuring ADAM10 protein levels in WB experiments in platelets of C subjects (n=26) and AD patients (n=33), a significantly decreased level of ADAM10 in AD was found (AD vs C: $p<0.0001$). This is paralleled by both an altered ratio of APP forms (130/106-110 kDa) and a reduction of alpha-APPs secretion in platelets of AD patients. Here we asked whether a treatment with an Acetylcholinesteraseinhibitor (AchEI) like Donepezil (D) could positively influence these biochemical parameters observed in platelets. D treatment (30 days, T30) determined a two-fold increase of the APP ratio in AD patients; even a Mini Mental State Evaluation showed a significant improvement from T0 to T30. To evaluate ADAM10 levels, we recruited 30 AD patients and collected platelets at T0, after 30 and 60 days of treatment: a significant increase of ADAM10 immunoreactivity during the course of the treatment was observed. Similar results were obtained exposing differentiated SH-SY5Y neuroblastoma cells to D: the cells released remarkably more alpha-APPs into the medium and showed increased ADAM10 level in the membrane compartment. The alpha-secretase and the amyloidogenic beta-secretase pathway were shown to be mutually exclusive, therefore the regulation of these two pathways can chbe critically relevant for the pathogenesis of Alzheimer disease. In this view, an increase in level and activity of ADAM10, caused by D treatment, might represent a crucial event in AD therapy.

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