Current Research Therapeutic Strategies for Alzheimer's Disease Treatment

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Alzheimer's disease (AD) currently presents one of the biggest healthcare issues in the developed countries. There is no effective treatment capable of slowing down disease progression. In recent years the main focus of research on novel pharmacotherapies was based on the amyloidogenic hypothesis of AD, which posits that the beta amyloid (A?) peptide is chiefly responsible for cognitive impairment and neuronal death. The goal of such treatments is (a) to reduce A? production through the inhibition of ? and ? secretase enzymes and (b) to promote dissolution of existing cerebral A? plaques. However, this approach has proven to be only modestly effective. Recent studies suggest an alternative strategy centred on the inhibition of the downstream A? signalling, particularly at the synapse. A? oligomers may cause aberrant N-methyl-D-aspartate receptor (NMDAR) activation postsynaptically by forming complexes with the cell-surface prion protein (PrPC). PrPC is enriched at the neuronal postsynaptic density, where it interacts with Fyn tyrosine kinase. Fyn activation occurs when A? is bound to PrPC-Fyn complex. Fyn causes tyrosine phosphorylation of the NR2B subunit of metabotropic glutamate receptor 5 (mGluR5). Fyn kinase blockers masitinib and saracatinib have proven to be efficacious in treating AD symptoms in experimental mouse models of the disease.