

## **The molecular basis of Alzheimer's disease: New therapeutic targets**

B. Kokkas, G. Kitsios, M. Tsolaki

Department of Pharmacology and 3rd Neurology Clinic,  
Medical School, Aristotle University of Thessaloniki

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Increased biosynthesis of  $\beta$ -amyloid and its deposition in the brain and brain vessels is the major problem leading to the development of Alzheimer's disease (AD). The real cause of this disease is not known but a continuous research uncovers new information and offers new targets for a pharmacological intervention at a molecular level. A major approach to the treatment of AD has involved attempts to augment the cholinergic function of the brain tissue and especially in the hippocampus and cortex where the degeneration of the cholinergic neurons is one of the earliest findings. Strategies aiming to replace or mimic acetylcholine were tested and second generation of acetylcholinesterase inhibitors are now in current use. Estrogens that have a protective effect against  $\beta$ -amyloid induced vascular dysfunction combine with antioxidant properties may contribute to the therapeutic strategies. Agents influencing the adrenergic and the glutaminergic systems are under research or clinical trials as auxiliary agents in the whole treatment of the AD. One future approach involves the study of the pharmacological modulation of amyloid precursor protein metabolism in which the goal is to reduce the formation of the potential neurotoxic peptide. The deposition of this  $\beta$ -amyloid in brain and vessels is the major pathological feature of AD and this deposition is accompanied by neuronal death with signs of apoptosis. Factors influencing apoptosis like caspases and Bcl-2 protein family are among the molecular targets for the synthesis of antiapoptotic agents. Many other compounds targeting other aspects of the disease are in clinical trials. These include non-steroid anti-inflammatory drugs, antioxidants, statins and inhibitors of tau protein hyperphosphorylation, among others.

**Key words:** *Alzheimer's disease, pathogenetic mechanisms, pharmacological interventions.*

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M. Tsolaki, Desperai 3, 54621 Thessaloniki, Greece

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