

MEETING ABSTRACTS

RESTORING MITOCHONDRIA (DYS)FUNCTION AND ACETYLCHOLINE LEVELS AS A PROSPECTIVE THERAPEUTIC STRATEGY FOR ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a progressive and degenerative neurological disorder resulting in memory loss and cognitive decline. The severity of AD dementia was found to correlate with the extent of the cholinergic loss and acetylcholine (ACh) depletion.

In brain synapses ACh can be hydrolyzed by two cholinesterases (ChEs), acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), which were found in neurons and glial cells as well as in AD neuritic plaques and tangles. AChE is the prevalent enzyme in the healthy brain, while BChE is considered to play a minor role in the regulation of synaptic ACh levels. However, in AD advanced stages, AChE activity is decreased while BChE activity is unchanged or even increased, making both ChEs stimulating targets for the treatment of AD. Current AD therapy is based on AChE inhibitors, although they have very modest clinical effects in treating the symptoms of the disease and are unable to halt disease progression.

Oxidative stress (OS) and mitochondrial dysfunction are also considered critical factors in AD pathogenesis. As a result, targeting mitochondrial oxidative stress (OS) in the prodromal phase of AD to slow or prevent the neurodegenerative process and restore neuronal function is thus viewed as a valid therapeutic approach.

As part of our drug discovery program focused in oxidative stress-related diseases, and following a multi-target strategy, new mitochondriotropic antioxidants based on natural scaffolds acting as dual and bifunctional cholinesterase inhibitors have been developed. The results will be reported in this communication.

Keywords: Alzheimer disease; mitochondriotropic antioxidant; cholinesterase inhibitor

Acknowledgement

This work was funded by FEDER funds through the Operational Programme Competitiveness Factors-COMPETE and national funds by FCT – Foundation for Science and Technology under research grants (QUI/UI0081/2013, NORTE-01-0145-FEDER-000028 and PTDC/DTP-FTO/2433/2014)

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