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MEETING ABSTRACTS

THE OTHER SIDE OF AChE: ALLOSTERIC SITES AND MODULATORS

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The best-known function of acetylcholinesterase (AChE) is the hydrolysis of the neurotransmitter acetylcholine, however we are increasingly aware of the multifunctionality of this enzyme [1]. The non-hydrolytic functions of AChE are driven by allosteric sites as the peripheral allosteric site (PAS) responsible for amyloidosis in Alzheimer's disease through interaction with β-amyloid peptide.

We would like to show our work about the identification and characterization of new allosteric sites in AChE, using computational tools. This study has allowed us to identify allosteric inhibitors by virtual screening using our in-house MBC chemical library [2] guided by structure-based and fragment hotspot strategies. The identified compounds were also screened for in vitro inhibition of AChE and three of them were observed to be active. Further experimental (kinetic) and computational (molecular dynamics) studies have been performed to verify the allosteric activity. Thus, new compounds have been developed as allosteric modulators that may be valuable pharmacological tools in the study of non-cholinergic functions of AChE.

Keywords: allosteric sites; Alzheimer's disease; molecular dynamics; allosteric inhibitor

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