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MEETING ABSTRACTS

CRYSTAL STRUCTURES OF HUMAN CHOLINESTERASES IN COMPLEX WITH SUPRAMOLECULAR LIGANDS

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Human acetylcholinesterase (hAChE) and butyrylcholinesterase (hBChE) are related enzymes. hAChE plays a key role in neurotransmission and is the target of organophosphorus nerve agents. hBChE is good a natural stoichiometric scavenger of nerve agents, preventing their diffusion to the central and peripheral nervous system where they inhibit hAChE.

hAChE and hBChE display different specificities for substrates and ligands due to differences in the number of aromatic residues lining the active site gorge. These aromatic residues are essential for the binding of quaternary and aromatic ligands.

Some molecules containing quaternary and/or aromatic moieties form supramolecular structures by chelating Zinc. The nature of these molecules suggested that they could have affinity for the aromatic residues in the active site gorge of human cholinesterases. It was confirmed by determining their inhibition properties. A key question was whether these supramolecular ligands bind to human cholinesterases as their Zn-complex or monomeric form? The X-ray structures of two supramolecular complexes binding to the gorge of the hAChE and the hBChE reported herein showed that either cases are possible. These structural data on two new types of ligand can be used to design original cholinesterases inhibitors or reactivators.

Keywords: Acetylcholinesterase; butyrylcholinesterase; inhibitors; metallosupramolecular complexes