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MEETING ABSTRACTS

RECIPES TO DESIGN SPECIFIC LIGANDS OF HUMAN BUTYRYLCHOLINESTERASE

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Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) hydrolyze the neurotransmitter acetylcholine and function thereby as regulators of cholinergic neurotransmission. Recently, interest has greatly increased in BChE. Firstly, BChE is a good broad spectrum bioscavenger of nerve agent and its efficiency could be significantly increased by the mean of specific reactivators. Secondly, BChE activity in the brain increases with the progression of Alzheimer's disease, thus classifying BChE as a promising drug target in the advanced phase of the disease. AChE and BChE display specificities for substrates and ligands that only partially overlap. This disparity is largely due to differences in the number of aromatic residues lining the active site gorge, which leads to large differences in the shape of the gorge and potentially to distinct interactions with an individual ligand. Considerable structural information is available for the binding of a wide diversity of ligands to AChE. In contrast, structural data on the binding of reversible ligands to BChE was lacking. In the recent years, we solved the X-ray structures of multiple BChE-ligand complexes. Here we will present BChE structures with various ligands, some recently synthesized, to highlight the structural elements leading to their BChE affinity and specificity. These structural data will help to design specific reversible ligands that behave as inhibitors or reactivators.