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MEETING ABSTRACTS

3D STRUCTURE OF NATURAL TETRAMERIC FORM OF HUMAN BUTYRYLCHOLINESTERASE OBTAINED BY CRYO-ELECTRON MICROSCOPY

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Human butyrylcholinesterase (BChE) is a stoichiometric bioscavenger of toxic organophosphates. It can be used as an antidote to protect acetylcholinesterase, and is a protein of choice for development of detoxification biocatalysts for clinical applications. Despite the number of different monomeric structures of recombinant human BChE obtained to date, all attempts to obtain an atomic structure of the natural glycosylated tetrameric BChE were unsuccessful.

Here, we present for the first time the 3D structure of the natural tetrameric form of human butyrylcholinesterase, obtained by Cryo-EM technique at a final resolution of 8.8Å. The tetramer has a C2 symmetry, with all subunits arranged as a "propeller-like" tetramer. This is in contrast with previous "flat" model of subunits arrangement in tetramer. Cryo-EM structure shows that the two opposite BChE subunits are placed higher (or lower) the plane of the other two subunits. Despite glycan chains were obscured in the electron density due to their relative disoder, they could be modeled based on the positions of the residues anchoring these glycans. The electron density allowed to distinguish that C-terminal tails of all the subunits interact with each other and form a helix around the PRAD-peptide, supporting rigidity of the tail. The tail is situated in the center of the tetramer and is oriented nearly perpendicular to the tetramer "plane".It was also observed that the subunits in the tetramer have different contacts with neighbouring subunits. This allows to consider the tetramer as a dimer of dimers which is additionally strengthened by the C-terminal tail interactions.

Keywords: butyrylcholinesterase; 3D structure; cryoelectron microscopy; tetramer; native structure

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