AChBP Structures for Understanding Ligand Binding in Nicotinic Receptors

Titia K. Sixma, Patrick H Celie[a], Remco Klaassen[b], Pim van Nierop, Sarah E. van Rossum-Fikkert[a], August B. Smit[b], *[a]Netherlands Cancer Instiute Amsterdam, The Netherlands. [b]Neurobiology, Free University, Amsterdam, The Netherlands.* E-mail: t.sixma@nki.nl

Acetylcholine-binding protein (AChBP) from the mollusc Lymnaea stagnalis is at present the only high-resolution model for the ligand-binding domains of the ligand-gated ion channel family, which includes nicotinic acetylcholine, 5HT3, GABAA, GABAC and glycine receptors.

Here we present crystal structures from remote homologs from other molluscs that will define the variabilities in the binding sites. We will also explore a series of crystal structures of nicotinic receptor agonists and other ligands. These define how cation-pi interactions as well as remote electrostatic compensation contribute to ligand binding in the receptors. These structures also explain the many different data from ligand-binding studies on this pharmaceutically important class of neuronal receptors.

Comparison of these structures will be valuable for improving structure-function studies of ligand-gated ion channel receptors, including signal transduction, homology modeling and drug design.

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