Pro183 and Pro188, is accommodated in a specific binding pocket. Comparison with other similar kinase structures shows a 180° rotation of the loop and suggests a possible pro-active dimer formation, by which intermolecular phosphorylation may occur. The well-defined protein-ligand interactions further provide additional information for design of potent inhibitors.

Keywords: kinase structure; protein conformation; egulation and reaction mechanism of enzymes

FA1-MS07-P04

Is It Possible to Guess Potential Drug Activity from Its Crystal Structure? Agnieszka Skórska-Stania[a], Magdalena Śliwa[a], Barbara J. Oleksyn[a], Kamil Musilek[b,c], Kamil Kuca[b,c], Josef Jampilek[d,e], Robert Musiol[f], Jiri Dohnal[d,e]. *[a]Faculty of Chemistry, Jagiellonian University, Kraków, Poland. [b]Faculty of Military Health Sciences, Hradec Kralove, Czech Republic. [c]Faculty of Science, University of Jan Evangelista Purkyne, Czech Republic. [d]Zentiva a.s., Prague, Czech Republic. [e]Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic. [f]Institute of Chemistry, University of Silesia, Katowice, Poland.*
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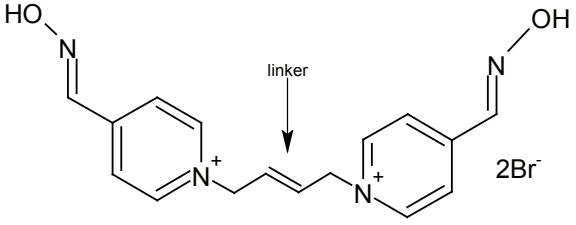
Design of new reactivators of acetylcholinesterase (AChE) gained more interest recently [1]. We have studied crystal structures of two bis-pyridinium oximes (K075 and K282), which can be used as detoxifying agents in case of poisoning with organophosphorous compounds, e.g. sarin, soman, insecticides [2]. Based on the molecular structures of well known AChE reactivators, obidoxime and HI-6, the new potential agents (K075 and K282) were proposed. Their molecules differ in configuration in respect to the double bond between carbon atoms in the linker between two pyridines. The activity of K075 has been determined [3]. It is interesting if the activity of K282 can be predicted by comparison of the crystal structures of both potential reactivators.



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Keywords: drug structure-activity relationships; drug interactions; stereochemistry

FA1-MS07-P05

Structural Studies of the Acetylcholine Binding Protein in Complex with Novel Compounds. Line Aagot H. Thomsen [a,b], Thomas Bale [a], Marianne L. Jensen [b], Philip K. Ahring [b], Jette S. Kastrup[a], Michael Gajhede[a]. *[a]Department of Medicinal Chemistry, Faculty of Pharmaceutical Sciences,University of Copenhagen, Universitetsparken 2, DK-2100, Copenhagen, Denmark. [b]NeuroSearch A/S, Pederstrupvej 93, DK-2750 Ballerup, Denmark.*
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Cys-loop receptors form essential ligand-gated ion channels. In the central nervous system, the Cys-loop receptors mediate neurotransmitters signalling and are involved in fast communication between neurons. The receptors are formed by one to four different subunits in a pentameric complex. The Ligand binding domain is located extracellular with the ligand binding site located in the interface between the subunits and the ion channel pore region is located in the cell membrane of the neuron. Upon binding of neurotransmitter, the receptor undergoes conformational changes, which course the ion channel to open and allow ions to enter the cell. The Cys-loop receptors are implicated in several brain diseases including Parkinson's disease, schizophrenia, depression, Alzheimer's' disease, anxiety and epilepsy [1-3]. Detailed understanding of receptor structure and function is essential for providing a rational basis for the design of new drug allowing new therapeutic strategies for treating such disorders. Threedimensional structures of Cys-loop receptors have proven to be extremely difficult to obtain as the receptors are very
difficult to crystallize. However, a soluble protein forming a very similar pentameric structure, the Acetylcholine Binding Protein (AChBP) from the water snail *Lymnaea stagnalis*, has successfully been expressed and co-crystallized with different ligands [4]. Using the AChBP as a model system for Cys-loop receptors, the main objective is to co-crystallize AChBP with various novel compounds selected by binding affinity.
AChBP has been expressed in *Pichia pastoris* as a soluble protein and subsequently purified using ion exchange chromatography. Crystallization experiments are in progress and the current status of the project will be presented.

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Keywords: cys-loop receptors; AChBP; novel compounds

FA1-MS07-P06

How to Design Aurora Kinase A Selective Inhibitors. Magda Kosmopoulou[a], Amir Faisal[b], Chongbo Sun[b], Vassilios Bavetsias[b], Butrus Atrash[b], Nathalie Bouloc[b], Mizio Matteucci[b], Julian Blagg[b], Spiros Linardopoulos[b,c], Richard Bayliss[a]. *[a]Section*