pockets. This separation might be possible to accept three HMTGs on a gp120 at the same time.

Keywords: lectin proteins; HIV drug design; protein structure analysis

FA1-MS07-P08

Conformational Change of Adenosine Deaminase During Ligand-Exchange in Crystal State.
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Adenosine deaminase (ADA) perpetuates chronic inflammation by degrading extracellular adenosine which is toxic for lymphocytes. ADA has two distinct conformations: open form and closed form [1]. From the crystal structures with various ligands, the non-nucleoside type inhibitors bind to the active site occupying the critical water-binding position and sustain the open form of apo-ADA. In contrast, substrate mimics do not occupy the critical position, and induce the large conformational change to the closed form. However, it is difficult to predict the binding of (+)-erythro-9-(2-hydroxy-3-nonyl)adenine (EHNA), as it possesses characteristic parts of both the substrate and the non-nucleoside inhibitors. The crystal structure shows that EHNA binds to the open form through a novel recognition of the adenine base accompanying conformational change from the closed form of the PR-ADA complex in crystalline state [2]. The open form crystal structure of the EHNA-ADA complex supports our hypothesis that the occupancy at the trigger-water-position is critical for determining the open/closed conformational alternation, rather than the nucleoside framework binding. We believe that the structural penetration of the EHNA-ADA complex and structural comparison of the other inhibitor-ADA complexes will support the discovery of novel ADA inhibitors by structure-based drug design.

[1] T. Kinoshita, et al, *Biochemistry* 44, **2005**, 10562-10569. [2] T. Kinoshita, et al, *Biochem. Biophys. Res. Commun.* 373, **2008**, 53-57.

Keywords: adenosine deaminase; EHNA; conformational change

FA1-MS07-P09

The Structure of the Ca^{2+}-ATPase Bound to Cyclopiazonic Acid Reveals a Complexed Divalent Ion.
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We have determined the structure of the sarco(endo) plasmic reticulum Ca^{2+}-ATPase (SERCA) in an E2.Pi-like form stabilised as a complex with MgF_4^{2-}, an ATP analogue (AMPPCP), and cyclopiazonic acid (CPA) . The structure determined at 2.5 Å resolution leads to a significantly revised model of CPA binding compared to earlier reports [1,2] showing that a divalent metal ion is required for CPA binding through coordination of the tetramic acid moiety at a characteristic kink of the M1 helix found in all P-type ATPase structures which is expected to be part of the cytoplasmic cation access pathway. Our model is consistent with the biochemical data on CPA [3] function and provides new measures in structure based drug design targeting Ca^{2+}-ATPase from e.g. pathogens. We also present an extended structural basis of ATP modulation pinpointing key residues at or near the ATP binding site. A structural comparison to the Na^+,K^+ -ATPase reveals that a Phe93 side chain occupies the equivalent binding pocket of the CPA site in SERCA suggesting an important role of this residue in stabilization of the potassium-occluded E2 state of Na^+,K^+-ATPase.

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Keywords: drug design; ATPase; membrane channel transport

FA1-MS07-P10

An Approach for Producing a CK2alpha Inhibitor Using X-ray, Calculation and ITC.
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Protein kinase CK2alpha is a highly pleiotropic serine/threonine protein kinase. CK2alpha plays important roles in cell growth, proliferation, and survival, while it is highly expressed in a wide variety of tumors.(1) Furthermore, CK2alpha is a target protein for glomerulo nephritis (GN) therapy, because an administration of either anitisense oligodeoxynucleotide against CK2alpha or low molecular weight CK2alpha-specific inhibitors effectively prevents the progression of renal pathology in the rat GN models. (2)
To design a novel and potent CK2alpha inhibitor, we determined four X-ray crystal structures of CK2alpha-inhibitor complexes (cc-04791, cc-04820, apigenin, ellagic acid), and measured enzyme kinetic parameters using ITC (Isothermal Titration Calorimetry) for the respective