examined. Using two proteins from the lipocalin family, the binding signatures of a model hydrophobic system (MUP – Mouse Urinary Protein) has been compared with that of a model hydrophilic system (HBP – Histamine Binding Protein). A combination of techniques including X-Ray crystallography, NMR, Isothermal Titration calorimetry and Molecular Dynamics has been able to show that both systems bind ligands with a similar overall entropy of binding yet the contributions arising from protein, ligand and solvent are very different.

Keywords: thermodynamics; ligand-binding; lipocalin

FA1-MS07-P16

Structure Determination of 2 Potential Parasitic Drug Targets of the SAHH Family. Marina Siponen[a], Magdalena Wisniewska[a], Tobias Karlberg[a], Ann-Gerd Thorsell[a], Johan Weigelt[a], Herwig Shüler[a]. [a]*Structural Genomics Consortium, Karolinska Institute, Stockholm, Sweden.*
E-mail: Marina.Siponen@ki.se

S-adenosyl-L-homocysteine (AdoHcy) is a product but also a potent feedback inhibitor of several methyltransferases which use S-adenosyl-L-methionine (AdoMet) as a methyl donor. The S-adenosyl-L-homocysteine hydrolases (SAHHs) catalyse the reversible reaction of AdoHcy to adenosine and homocysteine [1]. Consequently, SAHHs play a critical role in maintaining a normal level of AdoHcy in the cell. Inhibition of SAHH results in cellular accumulation of AdoHcy, inhibiting AdoMet-dependant methyltransferases. Since methylation plays a role in a wide range of cellular processes, the inhibition of SAHH has been proposed as a drug target for several parasitic diseases including malaria and leishmaniasis [2, 3]. We report here the crystal structures of 2 SAHHs from the human parasites *Leishmania major* and *Trypanosoma brucei*. The structure of the human SAHH being determined (PDB ID = 1LI4), our results can provide an initial structural perspective towards the development of anti-parasitic strategies.

[1] Turner MA, Yang X, Yin D, Kuczera K, Borchardt RT, Howell PL. *Cell Biochem Biophys*. **2000** 33(2):101-25. [2] Bujnicki JM, Prigge ST, Caridha D, Chiang PK. *Proteins* **2003** 52(4):624-32. [3] Henderson DM, Hanson S, Allen T, Wilson K, Coulter-Karis DE, Greenberg ML, Hershfield MS, Ullman B.,*Mol Biochem Parasitol*. **1992**, 53(1-2):169-83.

Keywords: parasites; nucleoide metabolism; protein structures

FA1-MS07-P17

DNA Flipping by Restriction Endonucleases. Roman H. Szczepanowski[a,b], Honorata Czapinska[a,b], Michael Carpenter[c], Mindaugas Zaremba[d], Gintautas Tamulaitis[d], Virginijus Siksnys[d], Ashok Bhagwat[c], Matthias Bochtler[a,b,e]. [a]*IIMCB, Trojdena 4, 02-109 Warsaw, Poland.* [b]*MPI- CBG, Pfotenhauerstr, 108, 01309 Dresden, Germany.* [c]*Department of Chemistry, Wayne State University, Detroit MI 48202, USA.* [d]*Institute of Biotechnology, Graiciuno 8, LT-02241, Vilnius, Lithuania.* [e]*Schools of Chemistry and Biosciences, Main Building, Park Place, Cardiff University, Cardiff CF10 3AT, UK.*
E-mail: roman@iimcb.gov.pl

Nucleotide flipping, the extrusion of a base from the base stack in the helix into an extrahelical position, is a well-known process, that can occur spontaneously, but is rare. Many enzymes promote this drastic distortion of DNA, usually because they need access to the base to excise it or to alter it chemically. In some cases, the flipping also provides access to a damaged estranged base in the stack. We have discovered the first instance of nucleotide flipping in restriction endonucleases. Flipping in this group of enzymes is unusual for several reasons: (a) It naturally occurs with intact base pairs, and is not intended to detect or repair a lesion. (b) Nucleotides in both DNA strands are flipped, and the DNA is compressed. The other enzyme classes usually flip only one base and leave the estranged base in place to prevent DNA compression. (c) In some cases (Ecl18kI), flipping serves to "skip" a base pair in a pseudopalindromic target sequence [1]. (d) In other cases (PspGI, EcoRII), it helps to distinguish A:T pairs from G:C pairs with a million-fold specificity [2,3]. Our structures of Ecl18kI and PspGI highlight this previously "unrecognized" use of nucleotide flipping.

[1] Bochtler M., Szczepanowski R.H., Tamulaitis G., Grazulis S., Czapinska H., Manakova E., Siksnys V. *EMBO J.*, **2006**, 25, 2219. [2] Tamulaitis G., Zaremba M., Szczepanowski R.H., Bochtler M., Siksnys V. *Nucleic Acids Res.*, **2008**, 36, 6101. [3] Szczepanowski R.H., Carpenter M.A., Czapinska H., Zaremba M., Tamulaitis G., Siksnys V., Bhagwat A.S., Bochtler M. *Nucleic Acids Res.*, **2008**, 36, 6109.

Keywords: nucleotide flipping; pseudopalindromic sequence recognition; protein-nucleic acid complex