s1.m7.p21 **Towards the structure of S-layer protein SbsC.** Tea Pavkov,[a] Eva M. Egelseer,[bc] Margit Sára[bc] and Walter Keller[a], [a]*Institute of Chemistry - Structural Biology Group, Karl-Franzens-University Graz, Heinrichstrasse 28, 8010 Graz, Austria,* [b]*Center for Ultrastructure Research, University of Natural Resources and Applied Life Sciences, Gregor Mendelstrasse 33, 1180 Vienna, Austria, and* [c]*BMT-Biomolecular Therapeutics GmbH, Brunnerstrasse 59, 1235 Vienna, Austria. E-mail: walter.keller@uni-graz.at*

Keywords: S-layer; 3D-crystals; *G. stearothermophilus*

Crystalline bacterial surface layers (S-layers) represent the outermost cell-envelope component of many prokaryotes. They are composed of identical protein or glycoprotein subunits with the ability to self-assemble into two-dimensional crystalline arrays exhibiting either oblique, square or hexagonal lattice symmetry with a centre-to-centre spacing of the morphological units of 3,5-35 nm. Due to their high degree of structural regularity, S-layers represent interesting model systems for studies on structure, genetics, functions and dynamic aspects of assembly of supramolecular structures. The S-layer protein SbsC of *Geobacillus stearothermophilus* consists of 1099 amino acids including a 30-amino-acid leader peptide. For obtaining 3D-crystals and determining the structure-function relationship of distinct segments of SbsC, N- and C-terminal deletion mutants were produced. Crystals of a C-terminal deletion mutant, $rSbsC_{31-844}$, were obtained. They crystallized in space group $P2_1$ and diffracted to ca. 3 Å at our home source and at the synchrotron. Knowing unit cell dimensions, the Matthews coefficient was calculated to be 3.5 Å/Da (one molecule in asymmetric unit) with an estimated solvent content of 65%. Soaking with various heavy atom salts gave good platinum, osmium and lead derivatives. Determination of the structure is in progress. The secondary structure prediction (SSP) revealed that $rSbsC_{31-844}$ consists of 35% β-sheets and 23% α-helices, which was also confirmed with circular dichroism measurements. According to SSP, the N-terminal domain is mainly α-helical, while the rest of the protein consists mainly of β-sheets.

[1] T. Pavkov, M. Oberer, E.M Egelseer, M. Sára, U.B. Sleytr, W. Keller (2003), *Acta Cryst*., D**59**, 1466-8.
[2] M. Jarosch, E.M. Egelseer, C. Huber, D. Moll, D. Mattanovich, U.B. Sleytr , M. Sára (2001), *Microbiology* **147**, 1353-63.

s1.m7.p22 **X-ray structures of Glutathione S-transferases from Sporozoa and Helminth organism will from the basis for a structure-based drug design.** M. Perbandt[a], C. Burmeister[b], J. Höppner[b], R. D. Walter[b], C. Betzel[a] and E. Liebau[b], [a]*Department of Biochemistry and Molecularbiology, University of Hamburg, Martin Luther King Platz 6, 20146 Hamburg, Germany,* [b]*Department of Biochemistry, Bernhard-Nocht-Institute for Tropical Medicine, Bernhard-Nocht-Str. 74, 20359 Hamburg, Germany*. *E-mail: markus@unisgi1.desy.de*

Keywords: Glutathione S-transferase; Malaria; River blindness

Glutathione S-transferases (GSTs, EC 2.5.1.18) are a major family of detoxification enzymes that are found in organisms ranging from prokaryotes to mammals. These enzymes carry out a wide range of functions in cells. They catalyse the nucleophilic addition of glutathione to a large variety of electrophilic substrates thereby detoxifying both endobiotic and xenobiotic compounds. Besides catalyzing conjugation reactions, GSTs can reduce organic hydroperoxides of phospholipids, fatty acids and DNA before they become engaged in free radical propagation reactions, ultimately leading to the destruction of macromolecules during oxidative stress [1]. Here we present the structures of GSTs from the parasits *Plasmodium flaciparum* [2] and *Onchocherca volvulus*.

The parasite *Plasmodium falciparum* causes malaria tropica, the most prevailing parasitic disease worldwide, with 300-500 million infections and 1.5 - 2.7 million deaths per year. The emergence of strains resistant to drugs used for prophylaxis and treatment and no vaccine available, makes the structural analysis of potential drug targets essential [3,4]. For that reason we analysed the threedimensional structure of the glutathione S-transferase from *P. falciparum* in the apo-form and in complex with its inhibitor S-hexyl-glutathione. The other focus will be on GSTs from *Onchocerca volvulus,* which causes Onchocerciasis or river blindness. Onchocerciasis is distributed throughout major parts of the world, including parts of Africa, Arabia, Central America, northern South America, and Mexico. In Africa alone it is estimated that more than 30 million people are infected with this parasite.

Although the utility of this enzyme as a drug target against *P. falciparum* and *Onchocerca volvulus* is yet to be established, the critical role played the GSTs in detoxification makes it a viable drug target against malaria and river blindness. The data reported here will form the basis of structure-based design of selective inhibitors, which may serve as drug leads.

[1] Hayes, J. D. & Strange, R. C. (1995). *Free Radic. Res*. **22**, 193-207.
[2] M. Perbandt, C. Burmeister, R.D. Walter, C. Betzel and E. Liebau (2004). *J. Biol. Chem*., **279**(2), 1336-1342.
[3] Breman, J. G. (2001) *Am. J. Trop. Med. Hyg*. **64**, 1-11
[4] Greenwood, B., and Mutabingwa, T. (2002) *Nature* **415**, 670-2