s1.m6.p2 **Structural genomics of Schistosomes: stathmin-like protein and cyclophilin.** Baiocco P., Miele A., Angelucci F., Gourlay L., *Basso A., *Valle C., *Liberti P., *Cioli D., Bellelli A., Brunori M., *Dept. Biochemical Sciences "A. Rossi Fanelli", univ. "La Sapienza" Rome, Italy, *Institute of Cell Biology, CNR Monterotondo, Rome, Italy. E-mail: paola.baiocco@uniroma1.it*

Keywords: Schistosomiasis; Cytoplasm remodelling protein; RNA-binding protein

Schistosomiasis is a debilitating parasitic disease which affects 200 million people, causing lifethreatening complications in 10% of the patients. We are investigating several proteins interfering in critical steps of schistosome development in order to look for a good candidate as a vaccine and/or drug target. We cloned, expressed, purified two of these candidates: a stathmin-like protein from the human blood fluke *Schistosoma Mansoni* (SmSLP) and a cyclophilin-like protein from *Haemonchus Contortus*, the equivalent of S.m. in bovines. Both proteins were segregated in inclusion bodies, hence their purification involved also a refolding step. Stathmin is a ubiquitous 17 kDa cytosolic phosphoprotein proposed to play an general role in the cell growth and differentation through its capacity to regulate microtubule assembly dynamics. It works by sequestering tubulin in a complex made by two tubulin heterodymers per stathmin molecule. SmSLP[1] is first synthesized at high levels in the intermediate molluscan host and completely disappeares 48h after the penetration into the mammalian host.

Cyclophilin[2] is a cytosolic protein with a high affinity for the immunosuppressive drug cyclosporin A. Cyclophilins are known to possess enzymatic activity in the form of peptidyl-prolyl cis-trans isomerase catalysis, a reaction thought to be involved in the late stages of protein folding. Moreover this cyclophilin-like protein has been shown to bind RNA in the nucleolus, therefore a putative role in transcription/translation regulation is inferred. We succeeded in the purification and refolding of both proteins. We have set up crystallization trials of both proteins and actually we are trying to optimize their crystallizations conditions.

[1] *J Biol Chem*. 1999 Nov 26;**274**(48):33869-74
[2] *Proc Natl Acad Sci USA*;1991 Nov **1**;88(21):9483-7

s1.m6.p3 **The LytM structure: Implications for lysostaphin and for the definition of a new group of metallopeptidases.** Sergey G. Odintsov, Izabela Sabala, Malgorzata Marcyjaniak and Matthias Bochtler, *International Institute of Molecular and Cell Biology, ul. Trojdena 4, 02-109 Warsaw, Poland & Max-Planck-Institute for Molecular Cell Biology and Genetics, Pfotenhauerstr. 108, 01309 Dresden, Germany. E-mail: MBochtler@iimcb.gov.pl*

Keywords: Peptidase; Peptidoglycan hydrolase; Lysostaphin

Lysostaphin is under development as a protein drug to eradicate nasal *Staphylococcus aureus* infections. In spite of the strong practical interest in lysostaphin-type enzymes, no structure of any lysostaphin-type enzyme was available prior to our work. We have recently solved the structure of LytM, the first structure of a metallopeptidase of this family. The structure generated several surprises: Firstly, and contrary to the prior literature on the enzyme, it showed that full length LytM is a latent enzyme, most likely the proform of the enzyme, a finding that could be confirmed biochemically. Secondly, and more importantly, it showed that sequence based assumptions about the architecture of the active site of the enzyme have to be revised. Finally, the structure showed an unexpected similarity between the active sites of lysostaphin-type peptidases of a large group of peptidases with specificity for the peptidoglycan building block D-Ala-D-Ala. As a similar arrangement of residues is also present in the N-domain of sonic hedgehog, a peptidase without known substrate so far, we propose for this group of enzymes the term "LAS (lysostaphin/D-Ala-D-Ala/sonic hedgehog)" enzymes according to the initials of three main families.