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Structural Characterization of the Shigella Flexneri Autotransporter VirG. Karin Kühnel[a], Dagmar Diezmann[a]. [a]*Department of Neurobiology, Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany.*
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VirG ('Virulence gene G') is essential for actin-based intracellular cell motility of the pathogen *Shigella flexneri*. We are interested in this protein because VirG also plays a role in the escape of *Shigella* from destruction by autophagy. Autophagy is a conserved eukaryotic process where a growing isolation membrane engulfs part of the cytoplasm leading to the formation of a vesicle, the so called autophagosome, which then fuses with the lysosome. Autophagy fulfills diverse functions, for example as a response to starvation and it also serves as a defense mechanism by degrading invading pathogens. As a consequence certain bacteria devised strategies to escape destruction by autophagy. The mechanism *Shigella* developed has been elucidated [1] (Ogawa et al. Science 2005). VirG interacts with the autophagy protein Atg5, which triggers the engulfment of the bacterium by the isolation membrane. However, *Shigella* secretes IcsB and this protein binds to VirG and shields its Atg5 binding site, so that the bacterium is no longer recognized and protected. We determined the crystal structure of the C-terminal part of the VirG passenger domain and our aim is to further characterize this protein and its binding partners.

[1] M.Ogawa *et al.*, *Science*, 307:727-31, **2005**.

Keywords: bacterial pathogenesis; autotransporter; autophagy

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Complexes of Cysteine Proteases with Chagasin. Grzegorz Bujacz[a], Izabela Redzynia[a],Anna Bujacz[a], Mariusz Jaskolski[b], Magnus Abrahamson[c], Anna Ljunggren[c]. [a]*Institute of Technical Biochemistry, Technical University of Lodz, Lodz Poland.* [b]*Faculty of Chemistry, A. Mickiewicz University, Poznan Poland.* [c]*Department of Laboratory Medicine, Lund University, Sweden.*
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Chagasin is a cysteine protease inhibitor identified in *Trypanosoma cruzi,* the parasite that causes an irreversible medical condition known as Chagas' disease. The parasite expresses a papain-like cysteine protease called cruzipain. Chagasin is associated with cruzipain and takes part in regulation of its activity. At the site of infection, chagasin is secreted outside of the parasite and interacts with host proteases.
Chagasin belongs to a new, recently defined structural family of inhibitors. Although it resembles in size and function some well-characterized cysteine protease inhibitors, such as cystatins, it has a unique amino acid sequence and a completely different structure. We have determined high-quality crystallographic structures of chagasin in complex with the human cysteine proteases cathepsin L [1] and B [2], which are potential target enzymes during *T. cruzi* infection as well as with plant cysteine protease – papain [3], the structure of which is almost identical to the catalytic domain of cruzipain.
Cathepsin B is a papain-like cysteine protease showing both endo- and exopeptidase activity, the latter due to a unique occluding loop restricting access to the active site cleft. To clarify the mode by which natural protein inhibitors manage to overcome this obstacle, we have determined a high-quality crystallographic structure of cathepsin B in complex with the *T. cruzi* inhibitor chagasin. Chagasin is a more potent inhibitor of cathepsin B than cystatins. Inhibition of this enzyme involves a conformational change of the occluding loop. Proper understanding of these changes is only possible with a reliable atomic model of the cathepsin B - inhibitor complex.
The inhibitory epitope of chagasin is composed of 3 loops, L4, L2 and L6, which interact with the catalytic cleft of the enzyme, with only the central loop (L2) inserted directly into the catalytic center. The two lateral loops are used for docking on target surfaces and exhibit different modes of interaction.
The structures of chagasin in complexes with proteolytic enzymes provide a detailed view of how the parasite protein inhibits host enzymes that may be of paramount importance as the first line of host defence. The high level of structural and functional similarity between cathepsins L and B and papain to cruzipain also offers interesting clues as to how the cysteine protease activity of the parasite could be targeted. This information will guide the development of drugs for possible prevention and treatment of Chagas' disease.

[1] Ljunggren A., Redzynia I., Alvarez-Fernandez M., Abrahamson M., Krupa J., Mort J.S., Jaskolski M., Bujacz G., *J. Mol. Biol*., **2007**, 371, 137. [2] Redzynia I**.,** Ljunggren A., Abrahamson M., Mort J.S., Krupa J.C., Jaskolski M., Bujacz G., *J. Biol. Chem.,* **2008**, 283, 22815. [3] Redzynia I., Ljunggren A., Bujacz A., Abrahamson M., Jaskolski M., Bujacz G., *FEBS J.,* **2009**, 276, 793.

Keywords: chagasin - cysteine proteases inhibitor; cruzipain; chagas disease

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Tandem Beta-Zippers in Host-Pathogen Interactions. Jennifer Potts[a], Richard J. Bingham[a], Kate Atkin[a], Gemma Harris[a], Nicole C. Norris[a]. [a]*Department of Biology, University of York York, UK.*
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The interaction of *Staphylococcus aureus* with the human plasma and extracellular matrix protein fibronectin triggers bacterial invasion of endothelial cells. This process has been proposed to aid haematogenous dissemination of infection and the development of infective endocarditis.
The first structures of complexes between a peptide from *S. aureus* and modules from the N-terminal domain of