Poster Presentation

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Characterization of βαββββ Resistance Proteins from Pseudomonas aeruginosa

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Pseudomonas aeruginosa is a multiresistant pathogen that can cause infection in immuno-compromized patients, for example in people suffering from cystic fibrosis. [1] It has complex patho-physiology and produces a large number of exoproducts, among which the phenazines are especially prominent. In P. aeruginosa, the blue phenazine derivative pyocyanin plays a crucial role in infection of the host. [2] This phenazine can generate reactive oxygen species and is thought to act as respiratory pigment and as a virulence factor at the same time. P. aeruginosa has to protect itself from its own phenazines because of the antibiotic action of these substances. Inspired by the fact that the phenazine biosynthesis operon of several bacteria contains a phenazine resistance factor of the βαββββ module protein family, we have searched the genome of P. aeruginosa for proteins of this fold. [3] In P. aeruginosa we could identify 22 of these genes, most without previous functional characterization. A structure-based sequence alignment made it possible to assign these proteins to two classes with two subgroups each, based on the conserved residues in the active site. Using X-ray crystallography and biophysical methods, we further demonstrate that several of these proteins indeed bind phenazines and possibly other antibiotics that contain aromatic moieties. Currently, we are working on the structural characterization and physiological function assignment of all of these βαββββ-module-containing proteins. Ultimately, these data may lead to novel anti-infective strategies.

[1] *J. B. Lyczak, C. L. Cannon, G. B. Pier, Clin. Microbiol. Rev., 2002, 15, 194–222,* ***[2]*** *G. W. Lau, D. J. Hassett, H. Ran et al., Trends Mol. Med., 2004, 10(12), 599-606,* ***[3]*** *S. Yu, A. Vit, S. Devenish et al., BMC Struct. Biol., 2011, 11:33*

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