Poster

Crystal structure of the effector/metaeffector pair SidL/LegA11 from Legionella pneumophila

D. M. Machtens[1], J. M. Willerding[1], S. Eschenburg[1,2], S. R. Shames[3], T. F. Reubold[1]

[1]Institute for Biophysical Chemistry, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hannover, Germany, [2]Cluster of Excellence RESIST (EXC2155), Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany, [3]Department of Microbiology & Molegular Genetics, Michigan State University, East Lansing, MI 48824, USA

reubold.thomas@mh-hannover.de

The gram-negative bacterium *Legionella pneumophila* lives in aquatic freshwater environments as a parasite of free-living amoebae or in the form of biofilms. As accidental pathogen, it may cause life-threatening lung infections in humans. *L. pneumophila* secretes more than 300 effector proteins into the cytosol of the host cell that modulate numerous cellular pathways to build and to maintain a compartment for effective replication. Some effectors, called metaeffectors, do not interact with host proteins, but serve as regulators of other effector proteins to modulate their activity.

The effector protein SidL interacts with actin [1] and inhibits protein translation in the host via a currently unknown mechanism [2]. The effector protein LegA11 has been identified as a metaeffector of SidL [3].

We confirmed a direct interaction between SidL and LegA11 via pull-down assays and determined the dissociation constant of the complex to be 40 nM using surface plasmon resonance (SPR). We crystallized SidL in complex with LegA11 and determined the crystal structure of this complex to a resolution of 2.4 Å. We solved the phase problem via single anomalous dispersion (SAD) using a selenomethionine-derivative crystal grown from protein carrying several methionine substitutions for signal enhancement. SidL is composed exclusively from α-helices and its polypeptide chain folds into a smaller N-terminal and a larger C-terminal domain, which are connected via a likely flexible linker (Figure 1). LegA11 bridges the two subdomains of SidL. The N-terminal part of LegA11 consists of four ankyrin repeats, which are followed by an extension formed by a two-stranded β-sheet surrounded by several α-helices. The last 20 residues of LegA11 fill the lumen between the two subdomains of SidL and the main body of LegA11.

Our crystal structure is the starting point for a further characterization of the metaeffector activity of LegA11.

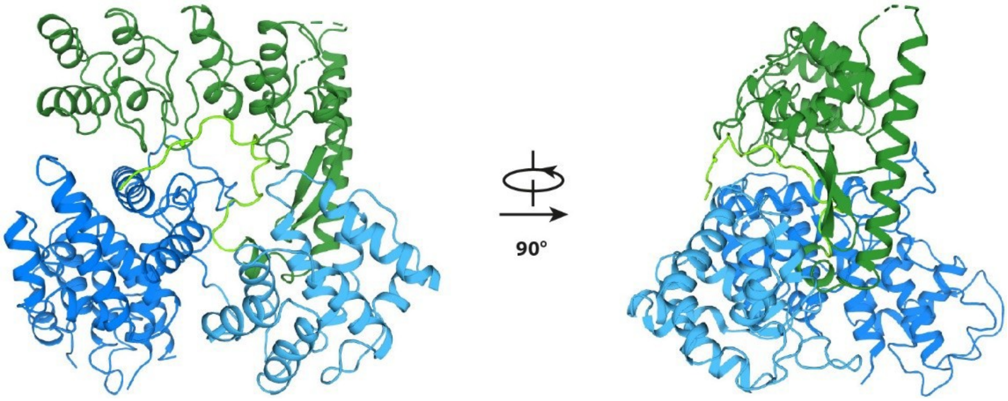

Figure 1. Crystal structure of the Sidl/LegA11 complex in cartoon representation. The N-terminal domain of SidL is shown in light blue, the C-terminal domain of SidL is shown in dark blue, LegA11 is shown in dark green, the last 20 amino acid residues of LegA11 are shown in light green.

[1] Guo, Z., Stephenson, R., Qiu, J., ZTheng, S., Luo Z. Q. (2014). *Microbes Infect.* **16**, 225-36.

[2] Fontana, M. F., Banga, S., Barry, K. C., Shen, X., Tan, Y., Luo, Z. Q., Vance, R. E. (2011). *PLoS Pathog.* **7**, e1001289.

[3] Urbanus,M. L., Quaile, A. T., Stogios, P. J., Morar, M., Rao, C., Di Leo, R., Evdokimova, E., Lam, M., Oatway, C., Cuff, M. E., Osipiuk, J., Michalska, K., Nocek, B. P., Taipale, M., Savchenko, A., Ensminger, A. W. (2016). *Mol. Syst. Biol.* **12**, 893.