"Mechanism of action of Tc toxins"

Stefan Raunser

Department of Structural Biochemistry – Max Planck Institute of Molecular Physiology, Otto-Hahn-Str. 11, 44227 Dortmund

raunser@mpi-dortmund.mpg.de

Tripartite Tc toxin complexes perforate the host membrane by forming channels that translocate toxic enzymes into the host, including humans. The underlying mechanism is complex but poorly understood. In my talk I will present the high-resolution structure of a complete 1.7 MDa Tc toxin complex composed of TcA, TcB and TcC. TcA forms a long translocation pore that is surrounded by a shell domain including putative receptor-binding domains. TcB and TcC form a large cocoon, in which the toxic domain resides and is autoproteolytically cleaved. A high-resolution structure of TcA embedded in the membrane and functional studies enable us to explain the mechanism of membrane insertion of the toxin.

Our results allow us to understand the mechanism of action of Tc toxins at molecular to atomic level and shed new light on the interaction of bacterial pathogens, such as the plague pathogen *Yersinia pestis*, with their hosts.

References:

1. Gatsogiannis C, Lang A, Meusch D, Pfaumann V, Hofnagel O, Benz R, Aktories K, **Raunser S** (2013) A syringe-like injection mechanism in *Photorhabdus luminescens* toxins, **Nature**. 495(7442): 520-23

2. Meusch D, Gatsogiannis C, Efremov R, Lang A, Hofnagel O, Vetter I, Aktories K, **Raunser S** (2014) Mechanism of Tc toxin action revealed in molecular detail, **Nature.** 508(7494): 61-5

3. Gatsogiannis C, Merino F, Prumbaum D, Roderer D, Leidreiter F, Meusch D, Raunser, S (2016) Membrane insertion of a Tc toxin complex in near-atomic detail, Nature Struct Mol Biol. Aug 29 [Epub ahead of print]