Mitochondria Divide by Budding

1MPI of Molecular Physiology, Dortmund, Germany, 2Albert-Ludwigs-Universität Freiburg, Freiburg, Germany, 3Jacobs University Bremen, Bremen, Germany.

Photobacteri d luminescens is an insect pathogenic bacterium that is symbiotic with entomopathogenic nematodes. Upon invasion of insect larvae, P. luminescens is released from the nematodes and kills the insect mainly through the action of large tripartite ABC-type toxin complexes (Tcs). Tcs are typically composed of TcA-, TcB- and TcC proteins that are only biologically active when complete. Functioning as ADP-ribose transferases, TcC proteins were identified as the actual functional components that induce actin-clustering, defects in phagocytosis and cell death. However, little is known about the translocation of TcC into the cell by the TcA and TcB components. Here, we show that TcA (TcA1) forms a transmembrane pore and report its structure in the preproc and pore state determined by cryo-electron microscopy. We found that the TcA1 prepro assemblies as a pentamer forming a 9-hedral vuvuzela-shaped channel less than 1.5 nm in diameter surrounded by a large outer shell. Membrane insertion is triggered not only at low pH as expected, but also at high pH values, suggesting a novel route for Tc toxin action directly through the midgut of insects. Comparisons with structures of the TcA1 pore inserted into a membrane and in complex with TcB2 and TcC3 reveal large conformational changes during membrane insertion suggesting a novel syringe-like mechanism of protein translocation. Our results demonstrate how ABC-type toxin complexes bridge a membrane to insert their deadly components into the cytoplasm of the host cell. Our proposed mechanism is paradigmatic for the whole ABC-type toxin family. It is an important step towards the understanding of the host-pathogen interaction and the complex life cycle of Photobacteri d luminescens and other pathogens, including human pathogenic bacteria, and serves as a strong foundation for the development of biopesticides.

Three-Dimensional Visualization of Whole Synapses by Stem Tomography

1MPI of Molecular Physiology, Dortmund, Germany, 2Albert-Ludwigs-Universität Freiburg, Freiburg, Germany, 3Jacobs University Bremen, Bremen, Germany.

Photorhabdus luminescens is an insect pathogenic bacterium that is symbiotic with entomopathogenic nematodes. Upon invasion of insect larvae, P. luminescens is released from the nematodes and kills the insect mainly through the action of large tripartite ABC-type toxin complexes (Tcs). Tcs are typically composed of TcA-, TcB- and TcC proteins that are only biologically active when complete. Functioning as ADP-ribose transferases, TcC proteins were identified as the actual functional components that induce actin-clustering, defects in phagocytosis and cell death. However, little is known about the translocation of TcC into the cell by the TcA and TcB components. Here, we show that TcA (TcA1) forms a transmembrane pore and report its structure in the preproc and pore state determined by cryo-electron microscopy. We found that the TcA1 prepro assemblies as a pentamer forming a 9-hedral vuvuzela-shaped channel less than 1.5 nm in diameter surrounded by a large outer shell. Membrane insertion is triggered not only at low pH as expected, but also at high pH values, suggesting a novel route for Tc toxin action directly through the midgut of insects. Comparisons with structures of the TcA1 pore inserted into a membrane and in complex with TcB2 and TcC3 reveal large conformational changes during membrane insertion suggesting a novel syringe-like mechanism of protein translocation. Our results demonstrate how ABC-type toxin complexes bridge a membrane to insert their deadly components into the cytoplasm of the host cell. Our proposed mechanism is paradigmatic for the whole ABC-type toxin family. It is an important step towards the understanding of the host-pathogen interaction and the complex life cycle of Photobacteri d luminescens and other pathogens, including human pathogenic bacteria, and serves as a strong foundation for the development of biopesticides.

Three-Dimensional Visualization of Whole Synapses by Stem Tomography

1MPI of Molecular Physiology, Dortmund, Germany, 2Albert-Ludwigs-Universität Freiburg, Freiburg, Germany, 3Jacobs University Bremen, Bremen, Germany.

Photorhabdus luminescens is an insect pathogenic bacterium that is symbiotic with entomopathogenic nematodes. Upon invasion of insect larvae, P. luminescens is released from the nematodes and kills the insect mainly through the action of large tripartite ABC-type toxin complexes (Tcs). Tcs are typically composed of TcA-, TcB- and TcC proteins that are only biologically active when complete. Functioning as ADP-ribose transferases, TcC proteins were identified as the actual functional components that induce actin-clustering, defects in phagocytosis and cell death. However, little is known about the translocation of TcC into the cell by the TcA and TcB components. Here, we show that TcA (TcA1) forms a transmembrane pore and report its structure in the preproc and pore state determined by cryo-electron microscopy. We found that the TcA1 prepro assemblies as a pentamer forming a 9-hedral vuvuzela-shaped channel less than 1.5 nm in diameter surrounded by a large outer shell. Membrane insertion is triggered not only at low pH as expected, but also at high pH values, suggesting a novel route for Tc toxin action directly through the midgut of insects. Comparisons with structures of the TcA1 pore inserted into a membrane and in complex with TcB2 and TcC3 reveal large conformational changes during membrane insertion suggesting a novel syringe-like mechanism of protein translocation. Our results demonstrate how ABC-type toxin complexes bridge a membrane to insert their deadly components into the cytoplasm of the host cell. Our proposed mechanism is paradigmatic for the whole ABC-type toxin family. It is an important step towards the understanding of the host-pathogen interaction and the complex life cycle of Photobacteri d luminescens and other pathogens, including human pathogenic bacteria, and serves as a strong foundation for the development of biopesticides.