Uptake and function of anthrax toxins

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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**Introduction**

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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**Literature references**


Reactome database release: 82

This document contains 1 pathway and 20 reactions (see Table of Contents)

[https://reactome.org](https://reactome.org)
Bacillus anthracis bacteria target cells in an infected human through the action of three secreted bacterial proteins, lef (also known as LF, lethal factor), cya (also known as EF, edema factor), and pagA (also known as PA, protective antigen) (Turk 2007; Young and Collier 2007). lef is a protease that cleaves and inactivates many MAP2K (MAP kinase kinase, MEK) proteins (Duesbery et al. 1998; Vitale et al. 2000), disrupting MAP kinase signaling pathways. cya is an adenylate cyclase that mediates the constitutive production of cAMP (Leppla 1982), a molecule normally generated transiently in tightly regulated amounts in response to extracellular signals. Both lef and cya depend on pagA to enter their target cells, a strategy characteristic of bacterial binary toxins (Barth et al. 2004). pagA binds to the target cell receptors, is cleaved by furin or other cellular proteases, and thereupon forms an oligomer that exposes binding sites for lef and cya molecules (Young and Collier 2007). This complex is taken into the target cell by clathrin-mediated endocytosis and delivered to endosomes. The low pH of the endosome causes the bacterial toxin complex to rearrange: the pagA oligomer forms a pore in the endosome membrane through which lef and cya molecules enter the target cell cytosol.

**Literature references**


Extracellular pagA (also known as PA83 - full length Protective Antigen - Petosa et al. 1997) produced by Bacillus anthracis binds to either of two isoforms of ANTXR1 (Anthrax Toxin Receptor 1, also known as TEM8 - Bradley et al. 2001; Liu and Leppla 2003) in the plasma membrane of a target human cell. The physiological ligand for ANTXR1 is not known nor are the physiological roles of the two ANTRX1 isoforms. Although ANTXR1 can act as a relatively low affinity pagA receptor in tissue culture model systems, it does not play a primary role in anthrax toxin induced effects in mouse models (Liu et al. 2009). While some studies suggest that ANTXR1 is associated with palmitoylated LRP6 (low density lipoprotein receptor related protein 6 - Abrami et al. 2008) in the plasma membrane and that the latter molecule can function as a co-receptor (Wei et al. 2006), the role of LRP6 in PA83 uptake remains uncertain (reviewed by van der Goot & Young 2009) and no function for LRP6 is annotated here.

Followed by: Furin cleaves ANTXR1-bound pagA to yield pagA(197-794)

Literature references


## Editions

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pagA binds ANTXR2

**Location:** Uptake and function of anthrax toxins

**Stable identifier:** R-HSA-5210918

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Diseases:** anthrax disease