Uptake and function of diphtheria toxin

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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: 79

This document contains 1 pathway and 5 reactions (see Table of Contents)
Uptake and function of diphtheria toxin

Stable identifier: R-HSA-5336415

Diseases: diphtheria

Diphtheria is a serious, often fatal human disease associated with damage to many tissues. Bacteria in infected individuals, however, are typically confined to the lining of the throat or to a skin lesion; systemic effects are due to the secretion of an exotoxin encoded by a lysogenic bacteriophage. The toxin is encoded as a single polypeptide but is cleaved by host furin-like proteases to yield an aminoterminal fragment A and a carboxyterminal fragment B, linked by a disulfide bond. Toxin cleavage can occur when it first contacts the target cell surface, as annotated here, or as late as the point at which fragment A is released into the cytosol. Fragment B mediates toxin uptake into target cell endocytic vesicles, where acidification promotes a conformational change enabling fragment B to form a channel in the vesicle membrane through which fragment A is extruded into the target cell cytosol. Cleavage of the inter-fragment disulfide bond frees DT fragment A, which catalyzes ADP ribosylation of the translation elongation factor 2 (EEF2) in a target cell, thereby blocking protein synthesis. Neither fragment is toxic to human cells by itself (Collier 1975; Pappenheim 1977; Murphy 2011).

Literature references


Murphy, JR. (2011). Mechanism of diphtheria toxin catalytic domain delivery to the eukaryotic cell cytosol and the cellular factors that directly participate in the process. *Toxins (Basel)*, 3, 294-308.


Editions

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https://reactome.org
DT A:B binds HBEGF and CD9 on the target cell surface

Location: Uptake and function of diphtheria toxin

Stable identifier: R-HSA-5336417