DT fragment B transports DT fragment A from target cell endosome membrane

D'Eustachio, P., Liu, S.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

21/04/2021

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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

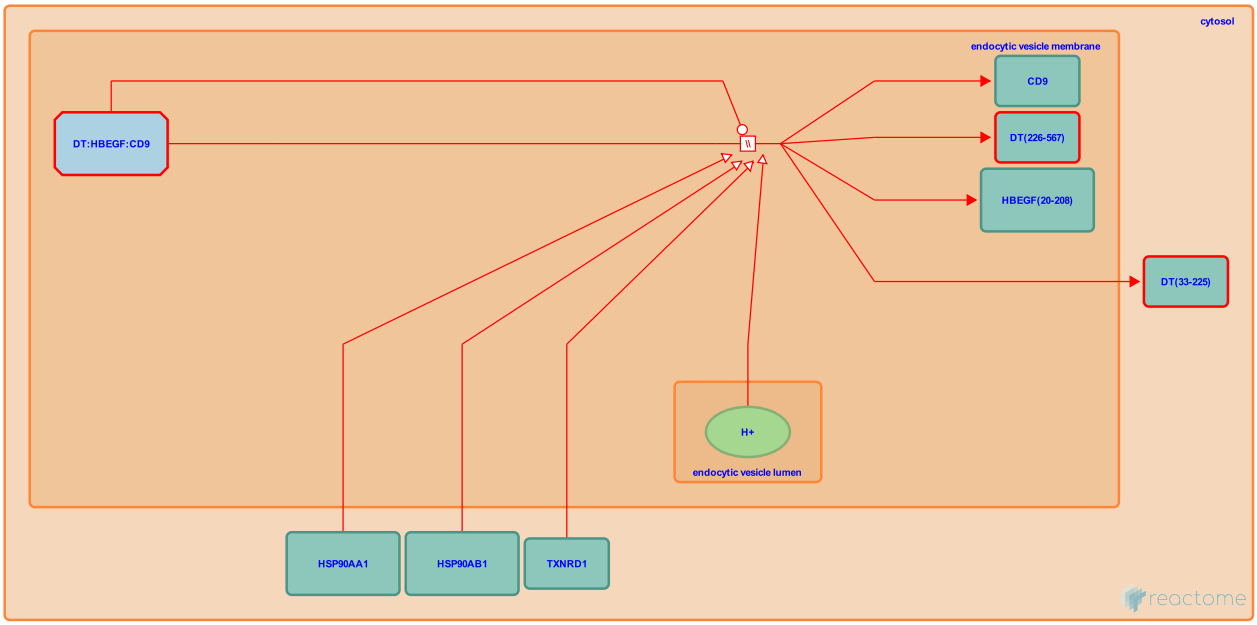
DT fragment B transports DT fragment A from target cell endosome membrane ↗

Stable identifier: R-HSA-5336420

Type: omitted

Compartments: cytosol, endocytic vesicle membrane

Diseases: diphtheria



The normal process of acidification of the endocytic vesicle containing diphtheria toxin (DT A:B) associated with target cell proteins HBEGF and CD9 is thought to cause a conformational change in the toxin. Its B fragment forms a channel in the endocytic vesicle membrane through which the A fragment is extruded into the target cell cytosol. There, reduction of the disulfide bond connecting the A and B fragments releases the A fragment to refold. The process requires participation of target cell heat shock proteins (HSP90AA1 and HSP90AB1) and thioredoxin reductase 1 (TXNRD1), which may mediate disulfide bond cleavage (Ratts et al. 2003; 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. ↗

Ratts, R., Zeng, H., Berg, EA., Blue, C., McComb, ME., Costello, CE. et al. (2003). The cytosolic entry of diphtheria toxin catalytic domain requires a host cell cytosolic translocation factor complex. *J. Cell Biol., 160*, 1139-50. ↗

Editions

2014-03-05	Authored, Edited	D'Eustachio, P.
2014-11-19	Reviewed	Liu, S.