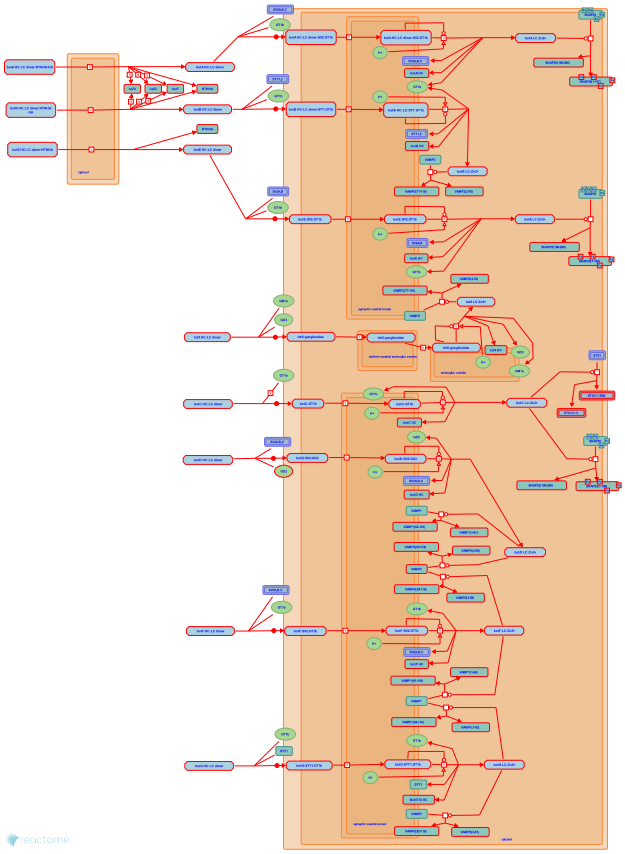
Neurotoxicity of clostridium toxins



D'Eustachio, P., Gopinathrao, G., Ichtchenko, K., Krupa, S., Sharma, S., Thirunavukkarasu, N.

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

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.

27/04/2024

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. ↗

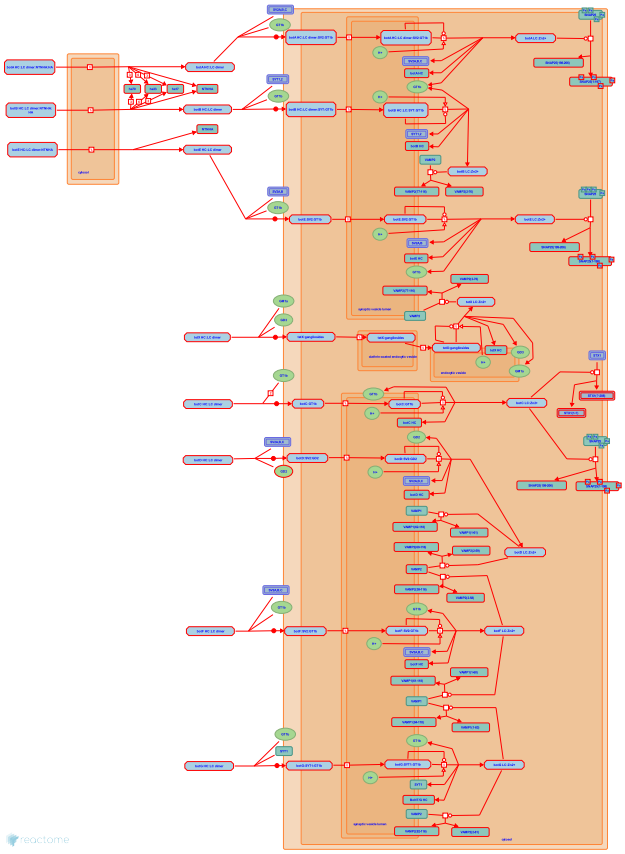
Reactome database release: 88

This document contains 9 pathways (see Table of Contents)

Neurotoxicity of clostridium toxins ↗

Stable identifier: R-HSA-168799

Diseases: tetanus, botulism



Clostridial neurotoxins, when taken up by human neurons, block synaptic transmission by cleaving proteins required for the fusion of synaptic vesicles with the plasma membrane. They are remarkably efficient so that very small doses cause paralysis of an affected person (Lalli et al. 2003; Turton et al. 2002). All characterized clostridial neurotoxins are synthesized as products of chromosomal, plasmid or prophage-borne bacterial genes. The nascent toxin may be cleaved into light (LC) and heavy (HC) chain moieties that remain attached by noncovalent interactions and a disulfide bond (Turton et al. 2002).

Strains of Clostridium botulinum produce seven serologically distinct toxins, BoNT/A, B, C, D, E, F, and G. An eighth toxin, BoNT/H has recently been identified (Barash & Arnon 2014) but its molecular properties have not yet been described. Human poisoning most commonly result from ingestion of toxin contaminated food. More rarely, it is due to wound infection or clostridial colonization of the gut of an infant whose own gut flora have not yet developed or of an older individual whose flora have been suppressed. While all seven characterized toxins can cleave human target proteins, three, BoNT/A, B, and E, are most commonly associated with human disease (Hatheway 1995; Sakaguchi 1982). BoNT/F is also able to cause human botulism.

Once ingested, the botulinum toxin must be taken up from the gut lumen into the circulation, a process mediated by four accessory proteins. These proteins form a complex that mediates transcytosis of the toxin molecule across the gut epithelium, allowing its entry into the circulation. The accessory proteins produced by different C. botulinum strains differ in their affinities for polarized epithelia of different species (e.g., human versus canine), and may thus be a key factor in human susceptibility to the toxins of strains A, B, and E and resistance to the others (Simpson 2004).

Clostridium tetani produces TeNT toxin. Human poisoning is the result of toxin secretion by bacteria growing in an infected wound and the toxin is released directly into the circulation.

Circulating clostridial toxins are taken up by neurons at neuromuscular junctions. They bind to specific gangliosides (BoNT/C, TeNT) or to both gangliosides and synaptic vesicle proteins (BoNT/A, B, D G) exposed on the neuronal plasma membrane during vesicle exocytosis (Montal 2010). All seven characterized forms of BoNT are thought to be taken up into synaptic vesicles as these re-form at the neuromuscular junction. These vesicles remain close to the site of uptake and are rapidly re-loaded with neurotransmitter and acidified (Sudhoff 2004). TeNT, in contrast, is

taken up into clathrin coated vesicles that reach the neuron cell body by retrograde transport and then possibly other neurons before undergoing acidification. Vesicle acidification causes a conformational change in the toxin, allowing its HC part to function as a channel through which its LC part is extruded into the neuronal cytosol. The HC - LC disulfide bond is cleaved and the cytosolic LC functions as a zinc metalloprotease to cleave specific bonds in proteins on the cytosolic faces of synaptic vesicles and plasma membranes that normally mediate exocytosis (Lalli et al. 2003; Montal 2010).

Literature references

Sakaguchi, G. (1982). Clostridium botulinum toxins. *Pharmacol. Ther., 19,* 165-94. ↗

Verastegui, C., Schiavo, G., Lalli, G., Deinhardt, K., Bohnert, S. (2003). The journey of tetanus and botulinum neurotoxins in neurons. *Trends Microbiol, 11,* 431-7. ↗

Acharya, KR., Chaddock, JA., Turton, K. (2002). Botulinum and tetanus neurotoxins: structure, function and therapeutic utility. *Trends Biochem Sci, 27,* 552-8. ↗

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79,* 591-617. ↗

Südhof, TC. (2004). The synaptic vesicle cycle. *Annu Rev Neurosci, 27,* 509-47. ↗

Editions

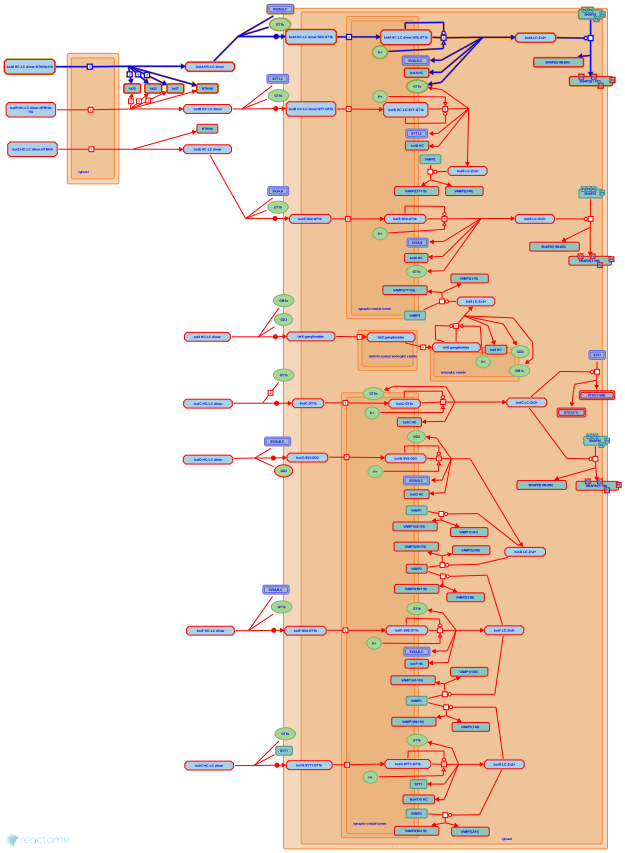
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2006-06-16	Edited	Gopinathrao, G.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type A (botA) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250968

Diseases: botulism



Botulinum toxin type A (botA, also known as BoNT/A), a disulfide bonded heavy chain (HC) - light chain (LC) heterodimer ("dichain"), enters the gut typically as a result of consuming contaminated food (Hatheway 1995), as a complex with nontoxic nonhemagglutinin protein (NTNHA, encoded by the C. botulinum ntnha gene) and multiple copies of three hemagglutinin proteins (HA, encoded by the C. botulinum ha17, ha34, and ha70 genes) (Lee et al. 2013). The complex protects the toxin from degradation in the gut and mediates its association with the gut epithelium and transcytosis to enter the circulation. Recent studies in vitro raise the possibility that the toxin may also directly disrupt the basolateral membrane of the gut epithelium (Fujinaga et al. 2013). Circulating toxin molecules associate with gangliosides and synaptic vesicle protein 2 (SV2) exposed by exocytosis at a synapse of a target neuron in the neuromuscular junction (Yowler & Schengrund 2004; Dong et al. 2006). Vesicle recycling brings the toxin into the neuron where the vesicle is acidified (Sudhoff 2004). The lowered pH induces a conformational change in the toxin: its HC forms a passage in the vesicle membrane through which its LC is extruded into the neuronal cytosol and released by reduction of the HC - LC disulfide bond (Montal 2010). The cytosolic LC then catalyzes the cleavage of synaptosomal associated protein 25 (SNAP25) on the cytosolic face of the neuronal plasma membrane (Binz et al. 1994; Schiavo et al. 1993), thereby inhibiting synaptic vesicle fusion with the plasma membrane and exocytosis.

Literature references

Matsumura, T., Fujinaga, Y., Sugawara, Y. (2013). Uptake of botulinum neurotoxin in the intestine. *Curr. Top. Microbiol. Immunol., 364*, 45-59. ↗

Tepp, WH., Chapman, ER., Janz, R., Dean, C., Yeh, F., Dong, M. et al. (2006). SV2 is the protein receptor for botulinum neurotoxin A. *Science, 312*, 592-6. ↗

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Yowler, BC., Schengrund, CL. (2004). Glycosphingolipids-sweets for botulinum neurotoxin. *Glycoconj. J., 21*, 287-93. ↗

Mehta, PP., Schiavo, G., DasGupta, BR., Montecucco, C., Wilson, MC., Santucci, A. et al. (1993). Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds. *FEBS Lett, 335*, 99-103. ↗

Editions

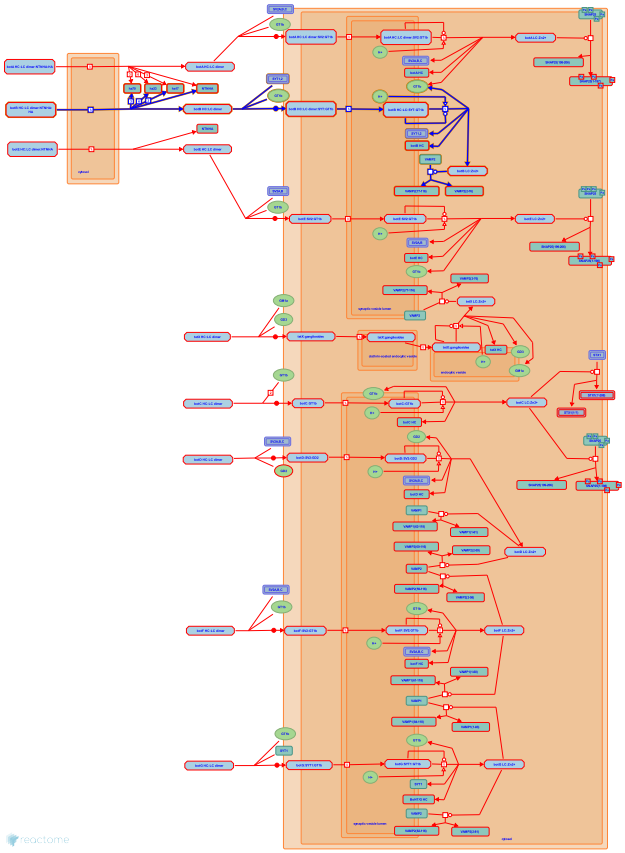
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type B (botB) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250958

Diseases: botulism



Botulinum toxin type B (botB, also known as BoNT/B), a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer, enters the gut typically as a result of consuming contaminated food (Hatheway 1995), as a complex with nontoxic nonhemagglutinin protein (NTNHA, encoded by the C. botulinum ntnha gene) and multiple copies of three hemagglutinin proteins (HA, encoded by the C. botulinum ha17, ha34, and ha70 genes) (Amatsu et al. 2013). The complex protects the toxin from degradation in the gut and mediates its association with the gut epithelium and transcytosis to enter the circulation (Fujinaga et al. 2013). Circulating toxin molecules associate with gangliosides and synaptotagmin (SYT) proteins exposed by exocytosis at a synapse of a target neuron (Dong et al. 2003; Yowler & Schengrund 2004). Vesicle recycling brings the toxin into the neuron where the vesicle is acidified (Sudhoff 2004). The lowered pH induces a conformational change in the toxin: its HC forms a passage in the vesicle membrane through which its LC is extruded into the neuronal cytosol. Tthe HC - LC disulfide bond is reduced (Montal 2010). The LC then catalyzes the cleavage of vesicle-associated membrane protein 2 (VAMP2) on the cytosolic face of synaptic vesicle membranes (Foran et al. 1994; Schiavo et al. 1992), thereby inhibiting synaptic vesicle fusion with the plasma membrane and exocytosis.

Literature references

Poulain, B., Polverino de Laureto, P., Schiavo, G., DasGupta, BR., Montecucco, C., Rossetto, O. et al. (1992). Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin. *Nature, 359*, 832-5. ↗

Matsumura, T., Fujinaga, Y., Sugawara, Y. (2013). Uptake of botulinum neurotoxin in the intestine. *Curr. Top. Microbiol. Immunol., 364*, 45-59. ↗

Tepp, WH., Chapman, ER., Dong, M., Goodnough, MC., Johnson, EA., Richards, DA. (2003). Synaptotagmins I and II mediate entry of botulinum neurotoxin B into cells. *J Cell Biol, 162*, 1293-303. ↗

Matsumura, T., Kitadokoro, K., Fujinaga, Y., Amatsu, S., Sugawara, Y. (2013). Crystal Structure of Clostridium botulinum Whole Hemagglutinin Reveals a Huge Triskelion-shaped Molecular Complex. *J. Biol. Chem., 288,* 35617-25. ↗

Shone, CC., Foran, P., Dolly, JO. (1994). Differences in the protease activities of tetanus and botulinum B toxins revealed by the cleavage of vesicle-associated membrane protein and various sized fragments. *Biochemistry, 33,* 15365-74. ↗

Editions

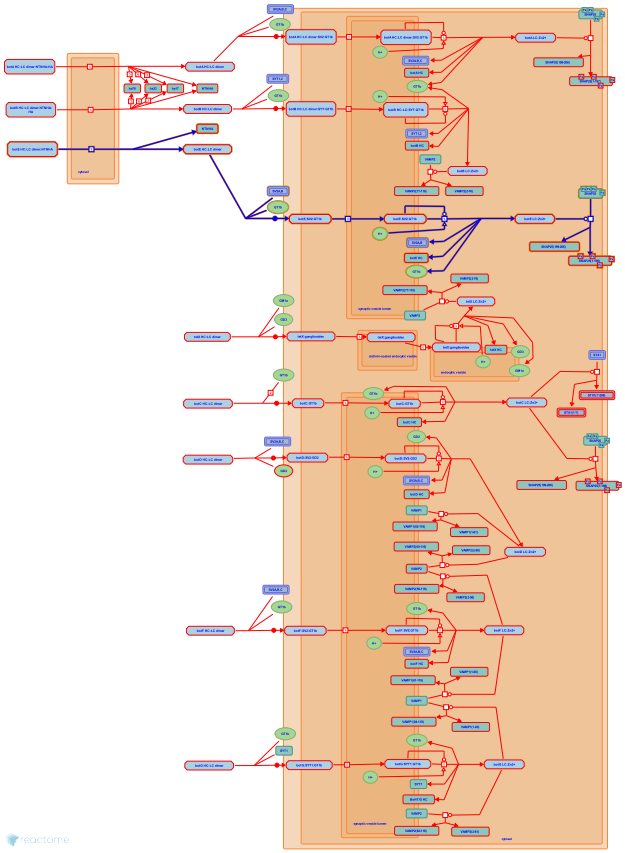
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type E (botE) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250992

Diseases: botulism



Botulinum toxin type E (botE, also known as BoNT/E), a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer (“dichain”), enters the gut typically as a result of consuming contaminated food (Hatheway 1995), as a complex with nontoxic nonhemagglutinin protein (NTNHA, encoded by the C. botulinum ntnha gene) (Benefield et al. 2013). The complex protects the toxin from degradation in the gut and mediates its association with the gut epithelium and transcytosis to enter the circulation (Fujinaga et al. 2013). Circulating toxin molecules associate with gangliosides and synaptic vesicle protein 2 (SV2) exposed by exocytosis at a synapse of a target neuron (Dong et al. 2008; Yowler & Schengrund 2004). Vesicle recycling brings the toxin into the neuron where the vesicle is acidified (Sudhoff 2004). The lowered pH induces a conformational change in the toxin: its HC forms a passage in the vesicle membrane through which its LC is extruded into the neuronal cytosol and released by reduction of the HC - LC disulfide bond (Montal 2010). The LC then catalyzes the cleavage of synaptosome-associated protein 25 (SNAP25) on the cytosolic face of the neuronal plasma membrane (Binz et al. 1994; Schiavo et al. 1993), thereby inhibiting synaptic vesicle fusion with the plasma membrane and exocytosis.

Literature references

Matsumura, T., Fujinaga, Y., Sugawara, Y. (2013). Uptake of botulinum neurotoxin in the intestine. *Curr. Top. Microbiol. Immunol., 364*, 45-59. ↗

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Yowler, BC., Schengrund, CL. (2004). Glycosphingolipids-sweets for botulinum neurotoxin. *Glycoconj. J., 21*, 287-93. ↗

Mehta, PP., Schiavo, G., DasGupta, BR., Montecucco, C., Wilson, MC., Santucci, A. et al. (1993). Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds. *FEBS Lett, 335*, 99-103. ↗

Südhof, TC. (2004). The synaptic vesicle cycle. *Annu Rev Neurosci, 27*, 509-47. ↗

Editions

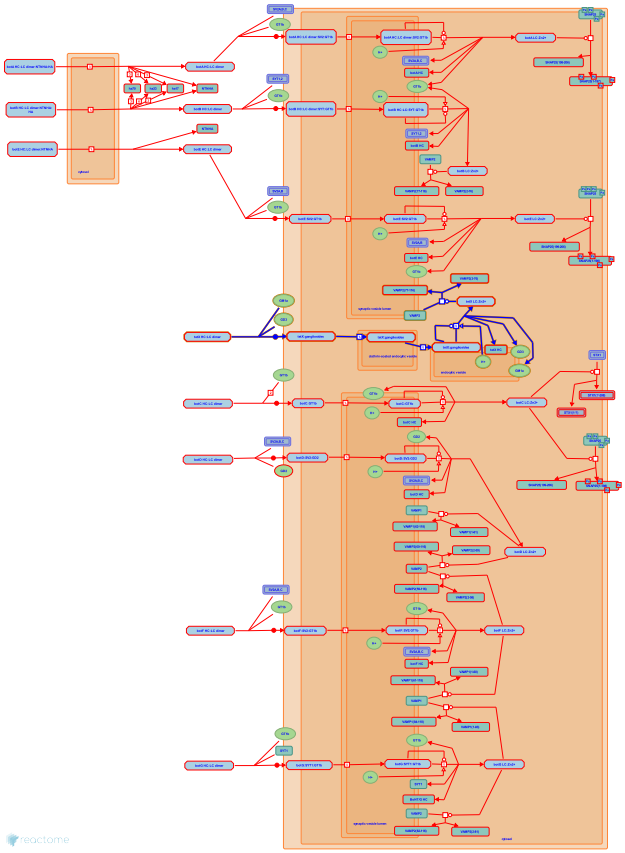
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of tetanus toxin (tetX) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250982

Diseases: tetanus



Tetanus toxin (tetX, also known as TeNT), a disulfide-bonded heavy chain (HC) - light chain (LC) dimer, is secreted from bacteria growing in an infected wound directly into the circulation. Circulating toxin molecules associate with gangliosides at a synapse of a target neuron. The toxin is taken up into clathrin-coated vesicles that reach the neuron cell body by retrograde transport and then possibly other neurons before undergoing acidification. Vesicle acidification causes a conformational change in the toxin, allowing its HC part to function as a channel through which its LC part is extruded into the neuronal cytosol. Cleavage of the HC - LC disulfide bond releases the LC into the cytosol, where it functions as a zinc metalloprotease to cleave vesicle-associated membrane protein 2 (VAMP2), thereby blocking synaptic vesicle exocytosis (Lalli et al. 2003).

Literature references

Verastegui, C., Schiavo, G., Lalli, G., Deinhardt, K., Bohnert, S. (2003). The journey of tetanus and botulinum neurotoxins in neurons. *Trends Microbiol, 11,* 431-7. ↗

Editions

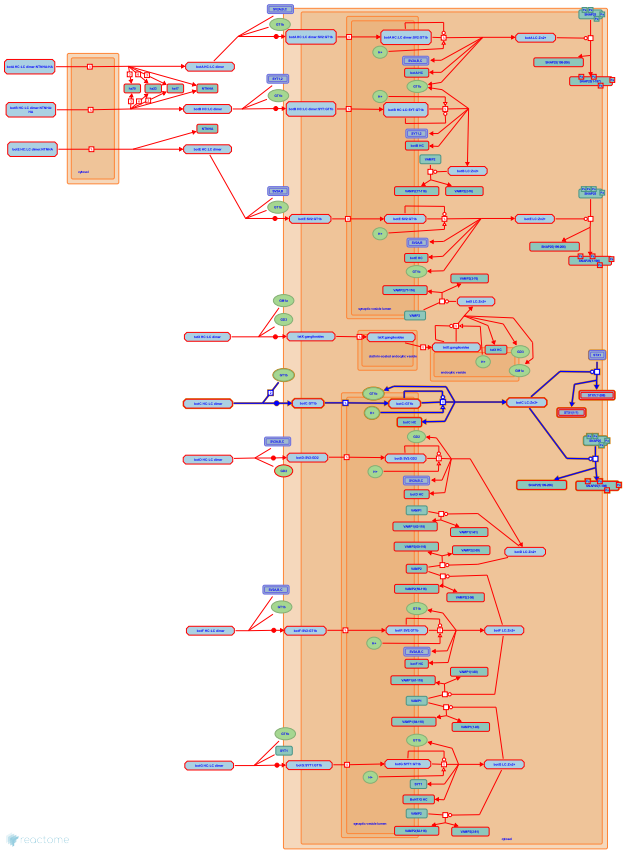
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Authored, Edited	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type C (botC) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250971

Diseases: botulism



Botulinum toxin type C (botC, also known as BoNT/C) is only very rarely associated with human disease (Hatheway 1995) and a pathway by which it might enter the circulation from the human gut has not been described. Nevertheless, the toxin itself, a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer ("dichain"), is capable of binding to neurons by interactions with cell surface gangliosides (Karalewitz et al. 2012), the bound toxin can enter synaptic vesicles and release its LC moiety into the cytosol of targeted cells (Montal 2010), and the botC LC can cleave synaptosomal associated protein 25 (SNAP25) and syntaxin 1 (STX1) on the cytosolic face of the neuronal plasma membrane (Foran et al. 1996). These four events are annotated here.

Literature references

Baldwin, MR., Barbieri, JT., Kim, JJ., Fu, Z., Karalewitz, AP. (2012). Botulinum neurotoxin serotype C associates with dual ganglioside receptors to facilitate cell entry. *J. Biol. Chem., 287*, 40806-16. ↗

Shone, CC., Lawrence, GW., Foster, KA., Foran, P., Dolly, JO. (1996). Botulinum neurotoxin C1 cleaves both syntaxin and SNAP-25 in intact and permeabilized chromaffin cells: correlation with its blockade of catecholamine release . *Biochemistry, 35*, 2630-6. ↗

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Hatheway, CL. (1995). Botulism: the present status of the disease. *Curr. Top. Microbiol. Immunol., 195*, 55-75. ↗

Editions

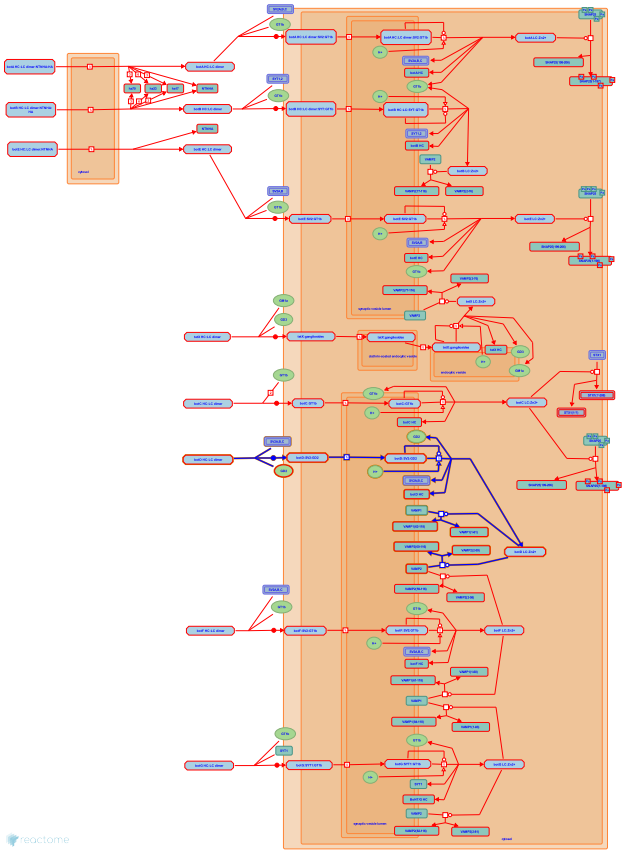
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type D (botD) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250955

Diseases: botulism



Botulinum toxin type D (botD) is only very rarely associated with human disease (Hatheway 1995) and a pathway by which it might enter the circulation from the human gut has not been described. Nevertheless, the toxin itself, a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer ("dichain"), is capable of binding to neurons by interactions with cell surface ganglioside (Kroken et al. 2011) and synaptic vesicle protein 2 (SV2) (Peng et al. 2011), the bound toxin can enter synaptic vesicles and release its LC moiety into the cytosol of targeted cells (Montal 2010), and the botD LC can cleave vesicle associated membrane proteins 1 and 2 (VAMP1 and 2) on the cytosolic face of the synaptic vesicle membrane (Schiavo et al. 1993; Yamasaki et al. 1994). These four events are annotated here.

Literature references

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Polverino de Laureto, P., Schiavo, G., DasGupta, BR., Montecucco, C., Rossetto, O., Benfenati, F. et al. (1993). Identification of the nerve terminal targets of botulinum neurotoxin serotypes A, D, and E. *J. Biol. Chem., 268*, 23784-7. ↗

Hatheway, CL. (1995). Botulism: the present status of the disease. *Curr. Top. Microbiol. Immunol., 195*, 55-75. ↗

Barbieri, JT., Kroken, AR., Kim, JJ., Fu, Z., Karalewitz, AP. (2011). Novel ganglioside-mediated entry of botulinum neurotoxin serotype D into neurons. *J. Biol. Chem., 286*, 26828-37. ↗

Tepp, WH., Dong, M., Peng, L., Johnson, EA. (2011). Botulinum neurotoxin D uses synaptic vesicle protein SV2 and gangliosides as receptors. *PLoS Pathog., 7*, e1002008. ↗

Editions

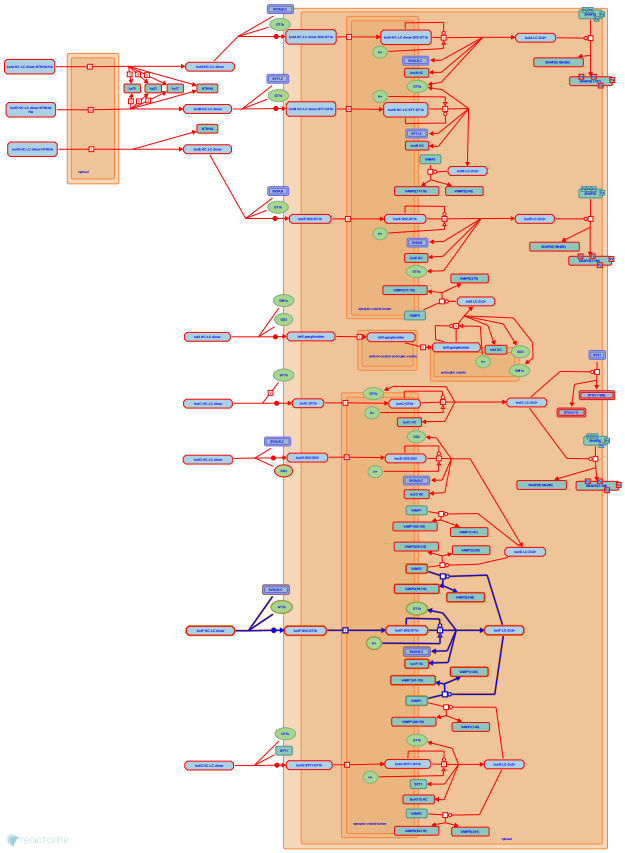
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type F (botF) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250981

Diseases: botulism



Botulinum toxin type F (botF) is only very rarely associated with human disease (Hatheway 1995) and a pathway by which it might enter the circulation from the human gut has not been described. Nevertheless, the toxin itself, a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer ("dichain"), is capable of binding to neurons by interactions with cell-surface ganglioside and synaptic vesicle protein 2 (SV2) (Fu et al. 2009; Rummel et al. 2009), the bound toxin can enter synaptic vesicles and release its LC moiety into the cytosol of targeted cells (Montal 2010), and the botF LC can cleave vesicle-associated membrane proteins 1 and 2 (VAMP1 and 2) on the cytosolic face of the synaptic vesicle membrane (Yamasaki et al. 1994). These four events are annotated here.

Literature references

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Mahrhold, S., Darashchonak, N., Häfner, K., Rummel, A., Holt, M., Binz, T. et al. (2009). Botulinum neurotoxins C, E and F bind gangliosides via a conserved binding site prior to stimulation-dependent uptake with botulinum neurotoxin F utilising the three isoforms of SV2 as second receptor. *J. Neurochem., 110*, 1942-54. ↗

Hatheway, CL. (1995). Botulism: the present status of the disease. *Curr. Top. Microbiol. Immunol., 195*, 55-75. ↗

Baldwin, MR., Barbieri, JT., Chen, C., Kim, JJ., Fu, Z. (2009). Glycosylated SV2 and gangliosides as dual receptors for botulinum neurotoxin serotype F. *Biochemistry, 48*, 5631-41. ↗

Fykse, EM., Südhof, TC., Roques, B., Link, E., Yamasaki, S., Baumeister, A. et al. (1994). Cleavage of members of the synaptobrevin/VAMP family by types D and F botulinal neurotoxins and tetanus toxin. *J Biol Chem, 269*, 12764-72. ↗

Editions

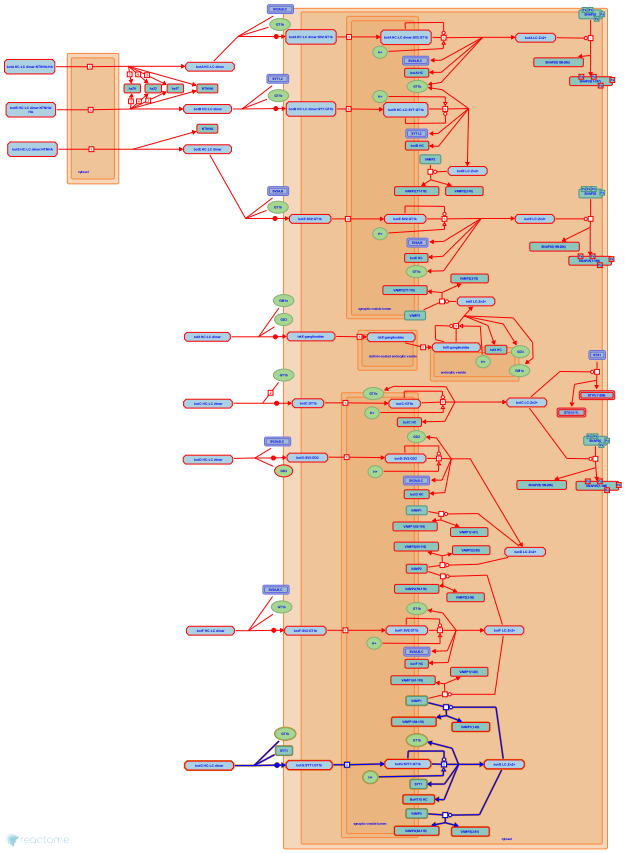
2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Toxicity of botulinum toxin type G (botG) ↗

Location: Neurotoxicity of clostridium toxins

Stable identifier: R-HSA-5250989

Diseases: botulism



Botulinum toxin type G (botG) is rarely if ever associated with human disease (Hatheway 1995) and a pathway by which it might enter the circulation from the human gut has not been described. Nevertheless, the toxin itself, a disulfide-bonded heavy chain (HC) - light chain (LC) heterodimer ("dichain"), is capable of binding to neurons by interactions with cell-surface ganglioside and syntagmin 1 (SYT1) (Peng et al. 2012; Willjes et al. 2013), the bound toxin can enter synaptic vesicles and release its LC moiety into the cytosol of targeted cells (Montal 2010), and the botG LC can cleave vesicle-associated membrane proteins 1 and 2 (VAMP1 and 2) on the cytosolic face of the synaptic vesicle membrane (Schiavo et al. 1994; Yamasaki et al. 1994). These four events are annotated here.

Literature references

Mahrhold, S., Strotmeier, J., Rummel, A., Eichner, T., Binz, T., Willjes, G. (2013). Botulinum neurotoxin G binds synaptotagmin-II in a mode similar to that of serotype B: tyrosine 1186 and lysine 1191 cause its lower affinity. *Biochemistry, 52*, 3930-8. ↗

Hayashi, T., Yamasaki, S., Niemann, H., Eklund, M., Szabo, E., Binz, T. et al. (1994). Botulinum neurotoxin type G proteolyses the Ala81-Ala82 bond of rat synaptobrevin 2. *Biochem. Biophys. Res. Commun., 200*, 829-35. ↗

Pitkin, RM., Tepp, WH., Berntsson, RP., Stenmark, P., Dong, M., Peng, L. et al. (2012). Botulinum neurotoxin D-C uses synaptotagmin I and II as receptors, and human synaptotagmin II is not an effective receptor for type B, D-C and G toxins. *J. Cell. Sci., 125*, 3233-42. ↗

Montal, M. (2010). Botulinum neurotoxin: a marvel of protein design. *Annu. Rev. Biochem., 79*, 591-617. ↗

Malizio, C., Polverino de Laureto, P., Trimble, WS., Schiavo, G., Milan, G., Montecucco, C. et al. (1994). Botulinum G neurotoxin cleaves VAMP/synaptobrevin at a single Ala-Ala peptide bond. *J. Biol. Chem., 269*, 20213-6. ↗

Editions

2006-06-15	Authored	Gopinathrao, G., Krupa, S.
2007-08-03	Reviewed	Ichtchenko, K.
2014-02-11	Edited, Revised	D'Eustachio, P.
2014-11-18	Reviewed	Sharma, S., Thirunavukkarasu, N.

Table of Contents