Tetanus toxin (TeNT), one of the most potent toxins for humans, causes paralytic death to thousands of humans annually. TeNT is produced by the bacterium, *Clostridium tetani*, an anaerobic bacterium usually found as spores in soil. *C. tetani* often infects humans through open wounds where the bacterium colonizes the infected tissues. There are two domains of TeNT: the A domain possesses catalytic activity, while the B domain is made up of two sub-domains: the translocation sub-domain and receptor-binding sub-domain. SNARE protein, VAMP-2, is the target of the catalytic A domain of the TeNT. This SNARE protein regulates synaptic vesicles with the plasma membrane of the neuron, allowing the release of neurotransmitters that are responsible for relaying nerve signals such as inhibitory impulses to the body's muscle cells. TeNT binds to dual receptors, two gangliosides, on the presynaptic membrane of a motor neuron. TeNT hijacks the trafficking machinery of the motor neuron and moves to the central nervous system, where TeNT again binds to gangliosides on the surface of neurons, enters the neuron by an endocytic mechanism to release the catalytic A domain into the host cell cytosol. The catalytic A domain cleaves the SNARE protein, which inhibits neurotransmitter fusion to the host cell membrane and the release of inhibitory neurotransmitter molecules. The loss of inhibitory impulses results in reflex irritability, autonomic hyperactivity, the classic large muscle spasticity and lockjaw associated with tetanus.

**Abstract**

Tetanus neurotoxin (TeNT), one of the most potent toxins for humans, causes paralytic death to thousands of humans annually. TeNT is produced by the bacterium, *Clostridium tetani*, an anaerobic bacterium usually found as spores in soil. *C. tetani* often infects humans through open wounds where the bacterium colonizes the infected tissues. There are two domains of TeNT: the A domain possesses catalytic activity, while the B domain is made up of two sub-domains: the translocation sub-domain and receptor-binding sub-domain. SNARE protein, VAMP-2, is the target of the catalytic A domain of the TeNT. This SNARE protein regulates synaptic vesicles with the plasma membrane of the neuron, allowing the release of neurotransmitters that are responsible for relaying nerve signals such as inhibitory impulses to the body's muscle cells. TeNT binds to dual receptors, two gangliosides, on the presynaptic membrane of a motor neuron. TeNT hijacks the trafficking machinery of the motor neuron and moves to the central nervous system, where TeNT again binds to gangliosides on the surface of neurons, enters the neuron by an endocytic mechanism to release the catalytic A domain into the host cell cytosol. The catalytic A domain cleaves the SNARE protein, which inhibits neurotransmitter fusion to the host cell membrane and the release of inhibitory neurotransmitter molecules. The loss of inhibitory impulses results in reflex irritability, autonomic hyperactivity, the classic large muscle spasticity and lockjaw associated with tetanus.

**Introduction**

Humans can be easily infected with tetanus if matter contaminated with *C. tetani* makes contact with an open wound. Once in the body, the bacterium produces TeNT, which attacks the body's nervous system and causes spastic paralysis. This type of paralysis often causes injury to muscles, tendons, and bones as it tightens and stiffens the muscles. The development of the tetanus vaccine decreased the number of tetanus cases per year from 150,000 to 1,000. In addition, the application of TeNT in therapeutic treatments for various neurological disorders is currently being investigated.

**Conclusion**

1. TeNT utilizes gangliosides as receptors to enter neurons.
2. TeNT causes spastic paralysis by trafficking up the nervous system from the PNS to the CNS. Once in the CNS, TeNT cleaves the SNARE protein, VAMP-2, to inhibit fusion of neurotransmitter vesicles to the plasma membrane of neurons.

**Outcomes of studying the structure of Tetanus Toxin**

1. TeNT heavy chain receptor-binding domain (HCR) is used in tetanus vaccines to develop the body's immunity to the toxin.
2. TeNT light chain (LC) may be useful to develop derivatives to treat neurological and non-neurological diseases.

**Botulism and tetanus toxins are similar, and both are organized into three domains.** The N-terminal domain comprises the catalytic activity (Red, LC), the internal domain comprises the translocation domain (Green) and the C-terminal domain is the receptor binding domain (Blue, HCR). PDB: 3BTA (BoNT/A)


**Tetanus and Botulism: Separated at Birth?**

The tetanus and botulism bacteria share many characteristics in affecting the human body. Both produce neurotoxins that affect the body’s muscle function, and both bind to neurons in order to inhibit neurotransmitter activity. The only major difference between the two toxins is the part of the nervous system they affect. TeNT travels up to the central nervous system (CNS) and inhibit inhibitory neurotransmitters, causing spastic paralysis. On the other hand, the botulism neurotoxin (BoNT) remains in the peripheral nervous system (PNS) and inhibit neurotransmitters, causing flaccid (limp) paralysis.

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