Therapeutics & Vaccines

Protein Receptors for Botulinum Neurotoxin E (BoNT/E) Enable Means of Reducing BoNT/E Toxicity

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing the mechanism of BoNT/E entry into neurons.

Overview

Botulinum neurotoxins (BoNTs), the most potent toxins known, are among the most dangerous potential bioterrorism threats. They cause botulism, a severe disease that can cause paralysis in humans and animals by blocking the release of neurotransmitters.

The protein receptors for three of the seven BoNT serotypes, BoNT/A, B and G, have been identified. Identifying the receptor for BoNT/E, the third most important commercial serotype, would be useful for designing molecules that reduce or completely inhibit its toxicity.

The Invention

UW-Madison researchers have identified the mechanism of BoNT/E entry into neurons. They found that two glycosylated isoforms of the synaptic vesicle protein SV2, in conjunction with gangliosides, mediate the entry of BoNT/E into neurons. The two isoforms of SV2, SV2A and SV2B, are the protein receptors for BoNT/E. Specifically, the L4 domain of SV2A and SV2B mediates BoNT/E entry and is sufficient to act as the toxin binding site on neuronal surfaces.

This discovery provides a means of reducing BoNT/E toxicity by administering an agent that inhibits binding between BoNT/E and SV2A or SV2B. It allows specific anti-toxins against BoNT/E to be prepared more readily. It also enables screening for agents that inhibit BoNT toxin or block binding between BoNT/E and SV2A or SV2B.

Applications

- Reducing BoNT/E toxicity, thereby preventing or treating botulism
- Inhibiting BoNT toxin activity
- Identifying agents that block binding between BoNT/E and an SV2A or SV2B protein
- Screening for agents that inhibit BoNT toxin
- Detecting BoNT/E or *Clostridium botulinum*
- Creating a chimeric receptor that includes the L4 domain to mediate the entry of BoNT/A or E into neuronal or non-neuronal target cells
- Labeling synaptic vesicles

Key Benefits

- Provides—for the first time—the protein receptors for BoNT/E

Additional Information

For More Information About the Inventors

- Edwin Chapman

Publications

- Dong M., Liu H., Tepp W.H., Johnson E.A., Janz R. and Chapman E.R. 2008. Glycosylated SV2A and SV2B Mediate the Entry of Botulinum Neurotoxin E into Neurons. Mol. Biol. Cell 19, 5226-5237.

Tech Fields

- Therapeutics & Vaccines : Biodefense

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847