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Antibodies against epitopes on H_N domain of botulinum neurotoxin- A protect against toxin poisoning

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Botulinum neurotoxins (BoNTs) are the most toxic substances known. BoNT poisoning occurs in a highly programmed fashion. After BoNT binds to cell surface, it is internalized, its light chain (L_C) translocated into the cell. L_C is a Zn-endopeptidase which causes enzymatic cleavage of SNARE proteins, thus inhibiting synaptic exocytosis. Over past two decades we investigated the immune recognition of BoNT/A and defined the epitopes on its heavy (H) and L_C chains. In the current work, we explored significance of BoNT/A heavy chain N-terminal (H_N) domain as a vaccine candidate. For evaluating protection, we used a mouse protection assay (MPA), which is considered the gold standard for BoNT toxicity assays. Mice were immunized with recombinant BoNT/A H_N519-845. Antibodies (Abs) against H_N519-845 protected mice against lethal dose of BoNT/A. Immuno-dominant regions of H_N519-845 were identified and investigated individually for Ab response. Synthetic peptides covering H_N519-845 were also studied for protective activity using MPA. Results were confirmed by patch-clamp analysis. Anti-H_NAbs were studied for ability to block toxin-induced channel formation. The data strongly indicated that H_N519-593 is an important region in generating protective Abs and should be valuable in a vaccine design.

Biography

B Vijayalakshmi Ayyar received her M.Sc. in Biotechnology from the Barkatullah University, India in 2006 with her thesis on molecular diagnosis of PCV and PPV. She completed Ph.D. from Dublin City University, Ireland in 2011. Her Ph.D. research focused on developing high affinity antibodies against cardiac biomarkers and further validating them in various assay formats. Subsequently, she joined as Postdoc under Dr. Richard O'Kennedy and worked on generation of immunoreagents for cancer diagnostics. In 2012, she joined Dr. M.Z. Atassi's Lab at Baylor College of Medicine, USA where she is working on identifying reliable vaccine candidates for botulinum neurotoxin A.

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