Botulinum Toxoid

Published date: Feb. 1, 2012

Technology description

Summary

Vaccination is the only approach that can be used to prevent botulism. A pentavalent botulinum toxoid comprised of formalin-detoxified botulinum neurotoxin (BoNT) BoNT/A, B, C, D and E hemagglutinin (Hmg) complexes has been used to immunize laboratory and military personnel since 1961, but this has never been licensed by the United States Food and Drug Administration (FDA). Vaccination immediately after toxin exposure has no protective benefit because the immune response is relatively slow compared to the rate of intoxication. The only treatment that is available upon intoxication is antibody therapy, which entails the injection of equine-derived botulinum antitoxin (BAT) or human-derived botulinum immunoglobulin (BIG) to remove toxin from the blood. Antibody therapy does not alleviate symptoms of botulism, but can limit the amount of toxin that enters nerve terminals and thus may lessen the severity and shorten the duration of paralysis.

Since a vaccine can be used to either protect a human population or produce a BAT or BIG product, it is important to have reliable methods to evaluate the antigenic integrity of botulinum vaccines. An in vitro assay that can serve in this capacity would be useful for evaluating the consistency of the antigen throughout the manufacturing process, as well as generating data that may reduce in vivo testing.

Available for licensing are a variety of new toxoids useful as botulinum vaccine antigens, for BAT or BIG production, or for development of tests to evaluate antigenicity of botulinum vaccines. The toxoids of the invention are derived from the Serotype A and B 150 kDa neurotoxin proteins. The resulting toxoids are antigenically identical to the native toxin as measured by inhibition ELISA in spite of showing a reduction of toxicity by more than 100,000-fold. Sandwich ELISA analysis indicated that the featured toxoids were two to three-fold less antigenic than the native neurotoxin compared to commercially available toxoids, which were about 100-fold less antigenic.

Preclinical studies have been performed using the toxoids of the invention. Mice were immunized twice, on Day Zero (0) and Day Fourteen (14). By Day Twenty-Eight (28), relatively high toxin-specific IgG titers were detected in animals that had received any of the in-house toxoids, with greater than 99% being IgG1 and the remainder IgG2. These immunized mice remained asymptomatic after being challenged with Fifty (50) to One Million (1,000,000) median lethal dose (LD50) units of the 900 kDa neurotoxin. In contrast, animals immunized with several different batches of commercially available toxoids did not develop measurable toxin-specific antibody titers; however, these mice did survive

neurotoxin challenges with Two (2) LD50 units, but died when challenged with Six (6) LD50 units. This application claims the formalin-detoxified botulinum compositions described above and an in vitro method for characterizing the toxoids. Also claimed are methods of making the botulinum compositions, and methods of producing antitoxin to botulinum toxin.

Application area

ELISA development, production of equine or human-derived botulinum antitoxin, development of next generation botulism vaccines.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com