Llama proteins could play a vital role in the war on terror

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Scientists at the Southwest Foundation for Biomedical Research (SFBR) have for the first time developed a highly sensitive means of detecting the seven types of botulinum neurotoxins (BoNTs) simultaneously.

The BoNT-detecting substances are antibodies --proteins made by the body to fight diseases--found in llamas. BoNT are about 100 billion times more toxic than cyanide, and collectively, they are the only toxins in the federal Centers for Disease Control and Prevention (CDC) 'category A' list of potential bioterror threats alongside anthrax, Ebolavirus and other infectious agents.

The llama antibodies, called single domain antibodies (sdAb) or "nanobodies," are molecularly flexible, unlike conventional antibodies. "As such, sdAb may allow biosensors to be regenerable and used over and over without loss of activity. Also, for some types of BoNT, conventional antibodies are not generally available and we are filling this biosecurity gap," said Andrew Hayhurst, Ph.D., an SFBR virologist. Since some sdAb have been shown to have inhibitory activity and can block toxin function, they may play a role as part of a future anti-botulism treatment.

The new work, funded by the Defense Department's Defense Threat Reduction Agency Medical Diagnostics Program, is described in the Jan. 21 issue of the journal *PLoS ONE*.

BoNTs are made by specific strains of the bacterium Clostridium, which

are widely distributed in soils and aquatic sediments. Most cases of botulism are the result of improperly stored foods, which can encourage growth of Clostridia and production of toxin, which is then ingested. BoNTs are extremely potent and target the nervous system, resulting in paralysis that can be so severe as to require life support on a mechanical ventilator for weeks to months. Countermeasures to prevent and treat botulism, such as vaccines and therapeutics, are extremely limited. Consequently, the ability to detect these toxins in the environment is critically important.

"We not only aim to use the antibodies in BoNT detection tests, but also to understand how they bind and inhibit these fascinating molecules," Hayhurst said. "We are also striving to improve our test by making it more sensitive such that one day it may be able to detect much smaller amount of toxins found in patients' blood. Since BoNT also have therapeutic applications with carefully controlled preparations and dosing regimens, there is also an increasing need to monitor BoNT levels in these treatments."

In the new study, a llama was immunized with harmless versions of seven types of BoNT, blood taken to provide antibody producing cells. Using bioengineering techniques, the antibody genes were cloned and the resulting antibodies were tested for their ability to detect BoNT in a selection of drinks, including milk. Hayhurst and his team are continuing to study the molecular interactions of the llama antibodies to find out why they are so specific and why some of them inhibit toxins. The laboratory capabilities of SFBR enabled this research to be performed according to all applicable federal guidelines of biosafety and biosecurity under the CDC Select Agent Program.

Provided by Southwest Foundation for Biomedical Research

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