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# Scientists aim to give botox a safer facelift

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New insights into botulinum neurotoxins and their interactions with cells are moving scientists ever closer to safer forms of Botox and a better understanding of the dangerous disease known as botulism. By comparing all known structures of botulinum neurotoxins, researchers writing in the Cell Press journal *Trends in Biochemical Sciences* on October 1st suggest new ways to improve the safety and efficacy of Botox injections.

"If we know from high-resolution structures how botulinum neurotoxins interact with their receptors, we can design inhibitors or specific antibodies directed at the binding interface to prevent the interaction," said Richard Kammerer of the Paul Scherrer Insititute in Switzerland. "Furthermore, it may be possible to engineer safer toxins for medical and cosmetic applications."

In addition to its popular cosmetic use, the neurotoxin is used for the treatment of muscle conditions related to cerebral palsy, multiple sclerosis, stroke, Parkinson's disease, and more.

The bacterium known as *Clostridium botulinum*, classically found as a contaminant in home-canned food, produces the neurotoxins, which pass the intestine and enter the bloodstream when ingested, Kammerer explained. When the neurotoxins reach neurons, they bind to receptors at the cell surface. Through a series of events, a portion of the toxin is released inside the cell. Once inside, that light-chain portion acts as a protease to specifically cleave a protein important for the release of acetylcholine, a neurotransmitter important for signaling from nerve to

muscle. The result is paralysis, which can be fatal if the muscles required for breathing are affected.

Kammerer and his colleagues offer a comprehensive review of high-resolution structures of botulinum neurotoxins and their complexes with cell-surface receptors, many of which have become available only recently. While many questions remain, the new picture of BoNT/A and its interactions offers considerable hope for less-risky clinical use of Botox in the future.

"The wide range of BoNT/A dosage used in medical or cosmetic applications bears the substantial risk of accidental BoNT/A overdosage," the researchers write. "The BoNT/A-SV2C complex crystal structure provides a strong platform for the rational design of BoNT/A variants with attenuated SV2C binding properties. Such variants are promising candidate proteins for safer applications of the toxin."

Provided by Cell Press