Neurons from stem cells could replace mice in botulinum test

February 6 2012

(PhysOrg.com) -- Using lab-grown human neurons, researchers from the University of Wisconsin-Madison have devised an effective assay for detecting botulinum neurotoxin, the agent widely used to cosmetically smooth the wrinkles of age and, increasingly, for an array of medical disorders ranging from muscle spasticity to loss of bladder control.

The new assay uses neurons, the critical impulse conducting cells of the central nervous system, derived from induced human pluripotent stem cells. It is the first test to employ stem cell derivatives to reliably and quantitatively detect botulinum neurotoxin and the antibodies that can neutralize the toxin's effects.

The assay is likely to draw considerable interest from industry as a potential replacement for the mouse, an animal now used by the thousands to control the potency of pharmaceutical preparations of the powerful neurotoxin.

Using cells provided by Madison-based Cellular Dynamics International, a company that industrially manufactures induced pluripotent stem cells and their derivative tissue cells for use in research and industry, the University of Wisconsin-Madison team devised an assay that is more sensitive than the mouse assay required for quality control of pharmaceutical preparations of botulinum toxin.

"This is an optimal testing platform for botulinum neurotoxin products," explains Sabine Pellett who, with UW-Madison professor of bacteriology Eric A. Johnson, led the new study published this week in the journal *Toxicological Sciences*. "A cell-based assay that is at least as sensitive and reproducible as the mouse bioassay can serve as a viable alternative and largely eliminate the need to use animals."

The toxin is used most famously for cosmetic purposes to erase the facial wrinkles that come with age. However, it is also used in a growing number of medical applications. Since it was first approved in 1990 for use in human patients with strabismus or cross-eye, the toxin, which works by blocking communication between nerves and muscles, has been used to successfully treat excessive sweating, chronic migraine headaches, painful neck spasms known as dystonia, and muscle conditions associated with cerebral palsy, multiple sclerosis and stroke. In 2010, the Food and Drug Administration (FDA) approved the toxin for use in treating loss of bladder control. Pharmaceutical applications of the toxin underpin a market that easily exceeds $1 billion annually.

Botulinum toxin is a protein produced by the bacterium Clostridium botulinum. It is the most potent toxin known to science and before its first experimental medical application to treat cross-eye was best known as a food poison. The methods to produce the toxin in large quantities and to precise specifications were pioneered at UW-Madison by Johnson and his late mentor, Ed Schantz.

Because of its incredible potency, the quality and dosages of the toxin for medical use must be carefully prepared.

The preparations made by pharmaceutical companies, says Johnson, actually contain very little toxin. To ensure that batches of the agent are of the correct therapeutic dose and of uniform quality, they are tested by injecting mice at a specified dosage that kills half of all mice exposed to the toxin.

"The mouse assay has many drawbacks and hundreds of thousands of mice are used for this every year," Pellett explains. "The most important result of this study is the high sensitivity of the assay, greater than the mouse bioassay, which is required for quality control."

The pharmaceutical industry, Johnson adds, is under pressure from the FDA to develop alternatives to the mouse. One cell-based assay has already been developed by Allergan, the company that makes BOTOX, the most famous trade name for botulinum toxin. However, the details of that assay have not been made available.

"The assay we developed is another cell based assay," notes Pellett, "one that uses normal human neurons derived from induced pluripotent stem cells, and which can be optimized for any pharmaceutical botulinum neurotoxin product."

More information: toxsci.oxfordjournals.org/

Provided by University of Wisconsin-Madison

Citation: Neurons from stem cells could replace mice in botulinum test (2012, February 6) retrieved 23 April 2024 from https://phys.org/news/2012-02-neurons-stem-cells-mice-botulinum.html