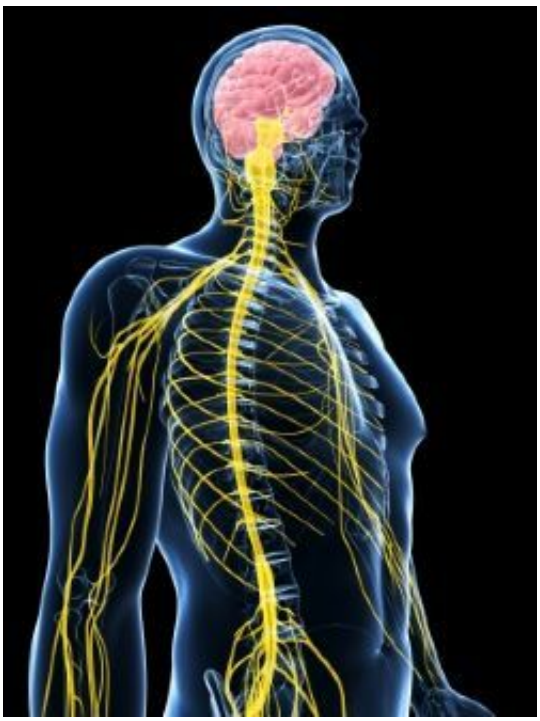
Scientists synthesise new 'chimera' protein which could herald future drug treatments for chronic pain

October 22 2013



(Medical Xpress)—Scientists have manufactured a new bio-therapeutic molecule that could be used to treat neurological disorders such as chronic pain and epilepsy.

A team of 22 scientists from 11 research institutes, including Dr Enrico

Ferrari from the University of Lincoln, UK, created and characterised a new molecule that was able to alleviate hypersensitivity to inflammatory pain.

The work is featured on the cover of the October 2013 issue of the scientific journal *Bioconjugate Chemistry*.

Dr Ferrari joined the School of Life Sciences in October last year from the Medical Research Council's Laboratory of Molecular Biology in Cambridge, where he took part in the development of a new way of joining and rebuilding molecules in the research group of Professor Bazbek Davletov - now at the University of Sheffield.

Now, by separating elements of clostridium botulinum and clostridium tetani neurotoxins, commonly known as Botox and tetanus toxin respectively, the scientists were able to develop a model to re-join the molecule proteins yielding new biomedical properties, without unwanted toxic effects.

While the Botox element is able to block neuronal communication – and therefore pain signals - for months, the tetanus component targets the engineered toxin to the central nervous system, rather than stopping at exterior neurons that are the normal target of Botox. The combination of the two effects is of great interest for neuroscience and can be applied to the treatment of several neurological disorders, particularly chronic pain conditions.

Botox and tetanus neurotoxins hold great promise for clinical applications, but since they are the most lethal proteins known to man, their paralytic activity was a stumbling block until now.

Dr Ferrari, who is one of the lead authors of the study, said: "The toxins were split into parts so they were unable to function. Then later they

were reassembled using a 'zipping' system so they can operate in a safe way. The re-engineered chimera toxin has very similar characteristics to Botox and is still able to block neurotransmission release, but the paralytic effect is a lot less. We then added a tetanus molecule which targets the chimera to where the pain signals travel towards the central nervous system."

Preliminary data on animal models has now been collated at University College London and future clinical trials are expected to fully characterise the new bio-therapeutic.

Dr Ferrari added: "Many painkillers relieve the pain temporarily and have various side effects. The selling point of this molecule is that the pain relief could last up to seven months, in a similar way that Botox injections for removing wrinkles last for several months. Engineering this kind of toxin has many uses and would be a major improvement in the quality of life for those people who suffer from chronic pain. It is very exciting to know that a protein you made could be one of the future drug treatments."

The crux of Dr Ferrari's research is now aimed at creating a method where more than two protein elements can be combined together and their exact order dictated, which will open up further avenues to explore possible medical uses in the future.

More information: Synthetic Self-Assembling Clostridial Chimera for Modulation of Sensory Functions *Bioconjugate Chemistry*, DOI: 10.1021/bc4003103 pubs.acs.org/doi/full/10.1021/bc4003103

Provided by University of Lincoln