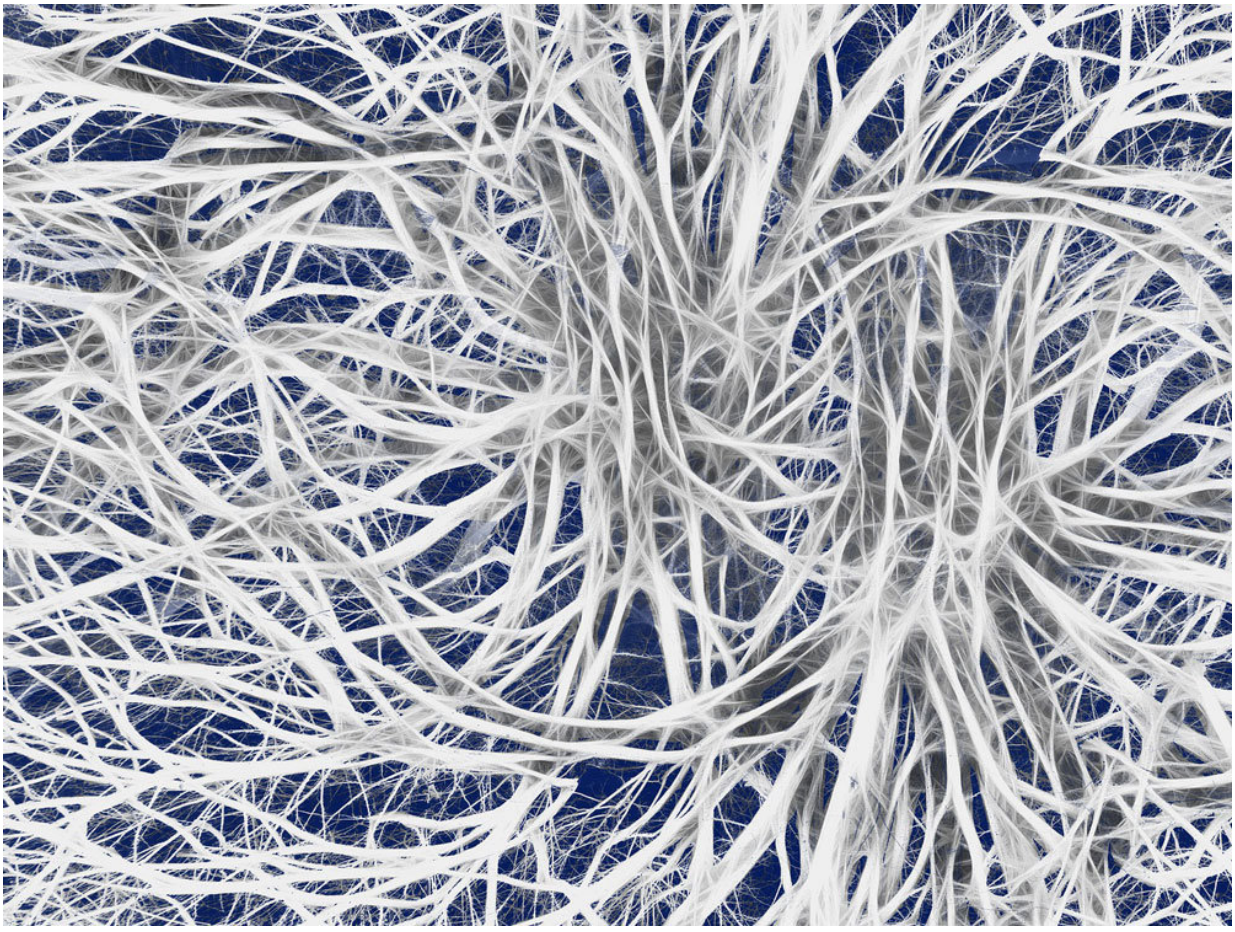
MedicalXpress

'Off the shelf' living artificial tissues could repair severe nerve injuries

February 13 2018



Nerves. Credit: Pixabay

Severe nerve damage has been successfully repaired in the laboratory

using a new living artificial nerve tissue developed by UCL, ReNeuron and Sartorius Stedim Biotech.

It opens up the possibility of a new 'off the shelf', universal therapy to improve the treatment of peripheral nerve injuries by removing the need for nerve grafts which cause additional damage and personalised stem cell therapies which take weeks to prepare.

The study, published today in *Scientific Reports* and funded by Innovate-UK, shows a measurable recovery of motor and sensory function in damaged rat nerves repaired using the artificial tissue as a bridge between two severed nerve ends.

"Peripheral nerve damage can be severe and extremely debilitating, causing a loss of sensation or movement and the possibility of chronic pain. It is often as a result of trauma from road traffic accidents and frequently affects young people at huge personal cost," explained Dr. James Phillips, lead study author (UCL Centre for Nerve Engineering and UCL School of Pharmacy).

Currently, there are no engineered cellular therapies to treat nerve damage and where large gaps exist in damaged nerves, grafts are taken from a healthy part of the body to repair a more important function. For example, a nerve that provides a sensory function in the foot may be used to repair movement in the arm.

The newly developed living artificial nerve tissue (called Engineered Neural Tissue, EngNT-CTX) is made of ReNeuron's CTX clinical grade human neural stem cells manufactured to GMP standards and aligned within a collagen hydrogel sheet. This living tissue is rolled into tubes that are used to bridge the gaps in nerves. As the material is allogeneic, it can potentially be used in anyone.

ReNeuron's CTX cells are already being tested in clinical trials for the treatment of disability resulting from ischaemic stroke but this is the first time they have been combined with an engineered support to guide nerve repair in vitro and in vivo.

For the study, rats with sciatic nerve injuries were treated with either EngNT-CTX sheets delivered in collagen tubes, an autologous nerve graft – the current therapy used in hospitals today – or empty collagen tubes.

After eight weeks, the treated nerves were assessed using a variety of methods to test their function and growth. EngNT-CTX constructs were comparable to autologous nerve grafts in supporting sufficient nerve regeneration to re-establish functional connections, and electrophysiological studies of muscle function gave a stronger response from nerves repaired with EngNT-CTX compared to the autologous nerve graft and the empty collagen tubes.

"We're impressed with how well the living artificial nerve tissue performed against the autologous nerve grafts. Although it is only in an animal model, it demonstrates that nerves can be repaired using engineered living constructs and opens up possibilities for future treatment options for repairing severe nerve damage," said Dr. Phillips.

"These preliminary studies provide considerable optimism that Eng-NT might, literally and metaphorically, fill this gap," added Dr. John Sinden, Chief Scientific Officer at ReNeuron.

"The generation of artificial nerve using cells to replace autografts for peripheral nerve repair has relied on bespoke procedures using autologous cells and individualised matrix, permitting very limited and expensive clinical application. Combining the Phillips group's self-aligning collagen technology using ReNeuron's allogeneic, clinically

validated CTX neural stem cells along with simple production methodologies, represents a step forward in developing a more readily available clinical product at reasonable cost."

Next steps will involve optimising the cell and material components of the technology in order to progress through the final stages of translation to first-in-human testing.

"Many patients undergoing nerve repair for trauma or after cancer surgery are not fully served by conventional repairs which may lead to slow and inaccurate regrowth. The development of a targeted, stem-cell based repair product, available to all surgeons, especially in the emergency setting, would represent a massive breakthrough in care. These preliminary studies provide considerable optimism that Eng-NT might, literally and metaphorically, fill this gap," said Professor Martin Birchall (Chair of Larynogology at the UCL Ear Institute and Consultant Head and Neck Surgeon).

"This is exactly what clinicians have been hoping for. This project is clearly focused on delivering the key clinical unmet need in surgical treatment- the nerve gap. A solution like this will address the question successfully and will allow us to treat a nerve gap to the patients benefit," said Mr Tom Quick (Clinical Scientist at the UCL Centre for Nerve Engineering and Consultant Orthopaedic Surgeon).

More information: C. O'Rourke et al. An allogeneic 'off the shelf' therapeutic strategy for peripheral nerve tissue engineering using clinical grade human neural stem cells, *Scientific Reports* (2018). DOI: 10.1038/s41598-018-20927-8

Provided by University College London