Researchers discover nerve repair mechanism

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The research group of the Physiology Department of Elche's Universidad Miguel Hernández (UMH), Hugo Cabedo, has discovered how peripheral nerves induce the repair of the myelin sheath so that communication is properly restored following an injury. This finding could provide clues toward repairing the spinal cord.

Unlike what happens to the spinal cord after an injury, the peripheral nerves have significant self-repair capabilities. After an injury, the nerve ending goes through a specialised biological process aimed at creating the required conditions to regenerate. However, it is a slow process that can occasionally go wrong. Understanding how this process works is important to reduce recovery time and take action when it is not happening appropriately.

Spontaneous repair of the peripheral nerves is possible thanks to Schwann cells, which cover the nerve fibres with an insulating layer of myelin. This greasy layer protects nerves and increases the transmission speed of nerve impulses. The research group headed by UMH professor Hugo Cabedo has just discovered how the nerve (axon) induces the production of the myelin layer by the Schwann cell, so that communication is properly restored after damage.

Cabedo says, "Schwann cells play a very important role in the peripheral nervous system by way of a strictly regulated process of differentiation and dedifferentiation, a feature which no other nervous system cell has. This makes them very versatile, and allows them to go from a state in which they produce myelin, to another, less differentiated, in which they contribute towards repairing the damaged nerve."

When damage occurs to a peripheral nerve, such as the one that goes from the spine to the fingers or toes, the Schwann cells temporarily lose the ability to create myelin and go back to a previous developmental state. The objective of this transformation is to help the nerve regenerate and grow again to reach the target tissue. Once the nerve is repaired, the cell recovers its ability to produce myelin once again in order to cover the nerve with the insulating layer and lead to the proper transmission of nerve impulses.

In this process, as Cabedo's research team has discovered, a chemical messenger called cyclic AMP plays a vital role. Hugo Cabedo says, "Cyclic AMP sends a protein called histone deacetylase 4 to the nucleus of Schwann cells, which, once the nerve is repaired, restarts myelination. This is achieved by inactivating the c-Jun gene, which in standard conditions, blocks the production of myelin. Inactivation of the c-Jun gene is necessary and sufficient in order to activate the genes that produce myelin to cover the regenerated nerve."

This process makes it possible to spontaneously repair a nerve or, in some cases, to re-implant a severed finger, for example. "If you sever a peripheral nerve and the surgeon sews it back together properly, it ends up regenerating. Although the nerve endings deteriorate, the Schwann cells, which are still present, turn into repair cells and help the nerve reach the target tissues once again. Once the nerve reaches its destination, the Schwann cell turns once again into a myelin producer to add the insulation layer. Unfortunately, in larger nerves, nerve regeneration and the associated clinical evolution is not complete, which has lifelong consequences," said Cabedo. This finding can facilitate the treatment of peripheral nerve injuries, such as those that take place in road accidents.

This work could contribute to the treatment of some diseases in which myelin is deteriorated, such as Charcot-Marie-Tooth, which has a genetic origin. It can also be relevant in relation to the Guillain-Barré syndrome, a neurological disorder that takes place following an infection, in which the immune system suddenly attacks the Schwann cells.

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