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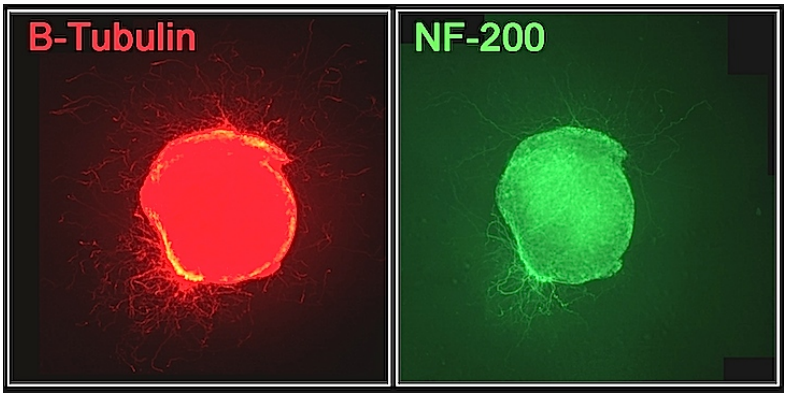
Regulation of sensory nerve fibres regeneration after an injury



After a peripheral nerve injury, neurons activate mechanisms that allow the regeneration of sensory axons, to try to restore their function. However, in most cases, functional recovery is insufficient and there are alterations in the processing of information. This research demonstrates that altering the levels of intracellular chloride affects the regeneration of the fibres responsible for sensations of touch and position without affecting the regeneration of those that convey sensations of pain and temperature.

After a peripheral nerve injury, neurons activate mechanisms that allow the cell to return to a pro-regenerative state and regrow the sectioned axons, so that they can reinnervate and reconnect to the peripheral targets in order to recover their function.

However, in most cases the regeneration of sensory axons is neither quantitatively nor selectively efficient enough with regard to the various categories of sensory information processing (touch, temperature, pain, etc.), resulting in insufficient recovery and functional alterations in the processing of information, particularly as neuropathic pain.

In order to selectively improve the regenerative capacity of sensory nerve fibres, it is essential to understand what are the underlying mechanisms that regulate the regeneration of

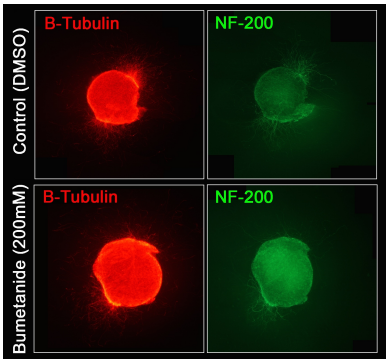


Figure 1: Administration of Bumetadine (inhibitor of sodium, potassium and chloride type 1 (NKCC1) co-transporter activation) specifically and selectively affects the regeneration of myelinated sensory fibres.

different types of neurons specifically. In this work, using in vivo and in vitro techniques, we have shown that altering the levels of intracellular chloride (an essential ion with regard to modulating the electrical activity of neurons), by modulating the sodium, potassium and chloride type 1 (NKCC1) co-transporter, specifically and selectively affects the regeneration of myelinated sensory fibres responsible for conveying sensations of touch and position without affecting the regeneration of unmyelinated fibres that convey sensations of pain and temperature.

In addition, our results show that the activation of a subtype of mitogen-activated kinases (MAPKs), specifically the c-Jun N-Terminal kinases (JNKs), after the injury is the mechanism responsible for the regulation of the co-transporter NKCC1.

In summary, this study demonstrates that the modulation of specific kinases – the JNKs – can selectively alter the growth and regeneration of sensory nerve fibres, opening a new avenue for research to improve functional recovery following peripheral nerve injuries.

Xavier Navarro
Institute of Neurosciences (INc-UAB)
Department of Cell Biology, Physiology and Immunology – UAB
Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED)
xavier.navarro@uab.cat

References

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