Use of obestatin peptide as a factor to improve peripheral nerve repair

IDIS

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PROFILE

Wihtin the *Instituto de Investigación Sanitaria* (IDIS), the **Cellular Endocrinology Group** works in collaboration with Yolanda Pazos-Randulfe, leader from **Digestive Pathology Group,** also belonging to IDIS. Both Groups works to understand the molecular and cellular mechanisms that regulate myogenesis and determine nerve-muscle communication under pathological conditions related to muscular atrophy. Located at the IDIS within *Hospital Clínico Universitario de Santiago* at the CHUS, both Groups employ molecular and cellular approaches to determine the function and roles played by autocrine/paracrine regulatory factors in the regeneration functions**.**

SPEAKER

Dr. Jesus Perez-Camiña is PhD in Chemistry and is currently leader from the Group of Cellular Endocrinology within IDIS focused on the identification of therapies directed at myopathies related to the processes of skeletal muscle and peripheral nerve regeneration.

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PRODUCT

Use of obestatin peptide as a factor to improve peripheral nerve repair.

MECHANISM OF ACTION

Use of obestatin for the regeneration of peripheral nerve injuries, improves nerve and neuromuscular function recovery, by enhancing remyelinization and thus the regeneration of the damaged nerve, counteracting the severe loss of function and the atrophy of the innervated muscle.

Obestatin peptide directs proliferation and migration of Schwann cells that sustain axonal regrowth and later remyelinate regenerated axons. This action supports the preservation of skeletal muscle by the maintenance of neuromuscular synapses through the axonal regulation of calpain-calpastatin proteolytic system.

This encompasses the control of skeletal muscle homeostasis by regulation of the ubiquitin proteasome system and the autophagy machinery. Thus, obestatin peptide promotes nerve repair through integration of multiple molecular cues of neuron-Schwann cells crosstalk aimed to promote axon growth and guide axons back to their targets.

TARGET INDICATIONS

Peripheral nerve regeneration associated to traumatisms.

Peripheral nerve injury is a high-incidence clinical problem, significantly affects the patient's quality of life and causes an enormous socioeconomic burden. It still stands as one of the most challenging tasks in neurosurgery, as functional neuromuscular recovery is rarely satisfactory.

CURRENT STATUS

- Critical roles for the obestatin/GPR39 system in regulating the plasticity of SCs, as well as in preserving neuromuscular synapses during peripheral nerve regeneration, have been identified. We found that obestatin directs different stepwise from the repair program of Schwann cells, including proliferation and migration, that guide regrowing axons and later remyelinate regenerated axons.
- Importantly, this action supports the preservation of skeletal muscle by the maintenance of neuromuscular synapses. This provides the necessary signals and spatial cues for the regulation of autophagy and ubiquitin-proteasome systems in skeletal muscle.
- These results serve as a therapeutic approach to skeletal muscle atrophy related to peripheral nerve injury. Thus, we demonstrated the feasibility of obestatin peptide as a factor to improve peripheral nerve repair in both in vitro and in vivo models corresponding to the POC to verify its practical potential.

INNOVATIVE ASPECTS

- Direct nerve repair with epineural end-to-end sutures is still the gold standard treatment for severe neurotmesis injuries but only in the cases where well-vascularized tension-free coaptation can be achieved. However, when peripheral nerve injury originates a significant gap between the nerve stumps, nerve grafts are required, with several associated disadvantages.
- To circumvent these facts, scaffolds were developed by tissue engineering to stimulate optimum clinical outcome. Nerve conduit tailoring involves reaching ideal wall pores, surface coating with extracellular matrix materials, and adding of growth factors or cell-based therapies. Also, the intraluminal cues are employed such as the filling with hydrogels, inner surface modification, topographical design, and the introduction of neurotrophic factors, antibiotics, anti-inflammatories and other pharmacological agents.
- Obestatin can be added to the group of neurotrophic factors/growth factors for its use as a pharmacological agent in third-generation nerve conduits, as well as for its use mixed with hydrogels for a perineural application.
- Obestatin will also improve therapies based on Schwann cells treatments for nerve regeneration.
- Comparing to other studied neurotrophic factors, obestatin might include many of the single positive aspects of any of them, namely enhanced axonal regeneration and remyelination, neuroprotection, rescue of functional neuromuscular junctions, which ameliorates the atrophy of the innervated muscle increasing its recovery and functionality.

IPR

European Patent Request EP18382680 : Obestatin For Use In The Treatment Of Peripheral Nerve Damages Or Injuries.

PARTNERING OPPORTUNITIES

We are fully committed to ensuring the translation of our research results into a manufacturing scale product. The optimization and development of the product needed could be done by the research team. We are seeking for a collaboration with the pharmaceutical industry to address the market access through a license agreement of the technology.