12 de noviembre de 2020

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

JESÚS PÉREZ CAMIÑA
SERGAS-IDIS
Santiago de Compostela, Coruña

Digestive Pathology Group
PI: Yolanda Pazos-Randulfe

Cellular Endocrinology Group
PI: Jesús Pérez-Camiña

idis
INSTITUTO DE INVESTIGACIÓN SANITARIA
SANTIAGO DE COMPOSTELA

IDIS was created as a result of a partnership between the research units of the University of Santiago de Compostela and the University Hospital Complex of Santiago de Compostela in 2008.

IDIS was officially certified by the Institute of Health Carlos III in 2010.

IDIS works in order to identify and develop new solutions to health problems.

1071 RESEARCHER partners

94 research GROUPS

29 M€ funds collected

65 research PROJECTS secured

754 PAPERS published

282 AGREEMENTS for clinical trials and observational studies

Obestatin: a solution for peripheral nerve repair and protection

About the peripheral nerve repair

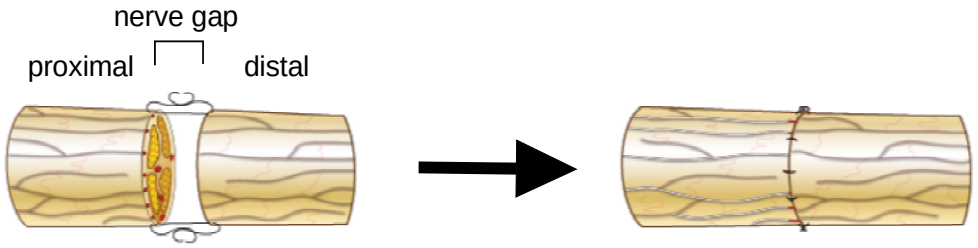
- Every day, traumatic injuries or surgical procedures impact on the function of peripheral nerves.
- Peripheral nerve damage leads to the loss of muscle or organ function, the loss of sensory feeling, or the initiation of pain.
- Although peripheral nervous system retains a remarkable ability for regeneration, it is estimated that only 10% of patients fully recover functionality.

Obestatin: a solution for peripheral nerve repair and protection

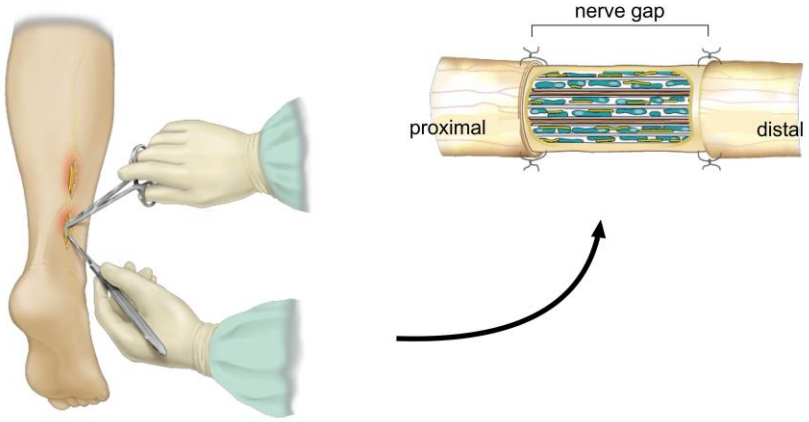
Nerve damage treatment options

Depending on the type of nerve damage:

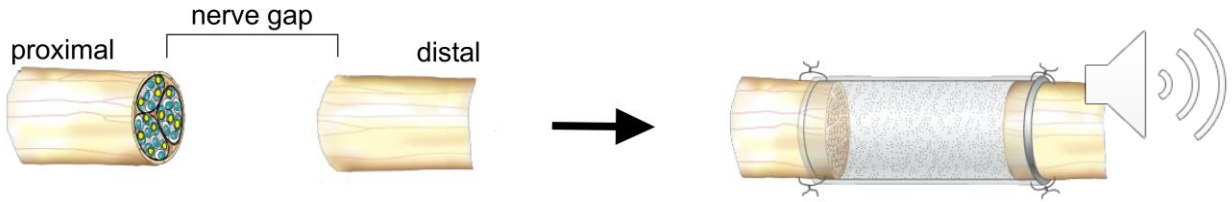
- microsurgical end-to-end repair



- nerve autograft



- hollow tube conduit

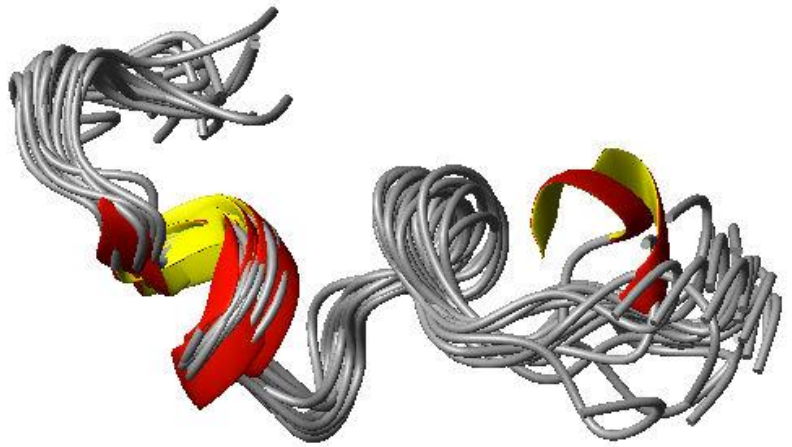


Obestatin: a solution for peripheral nerve repair and protection

Despite remarkable ability for never regeneration: <10% of patients fully recover function.

A theoretical approach is the use of **autocrine signals** in a therapeutic setting to help nerve repair.

Obestatin, a 23-amino acid peptide derived from a polypeptide called preproghrelin, is involved in peripheral nerve regeneration, exerting an autocrine function to control nerve repair.

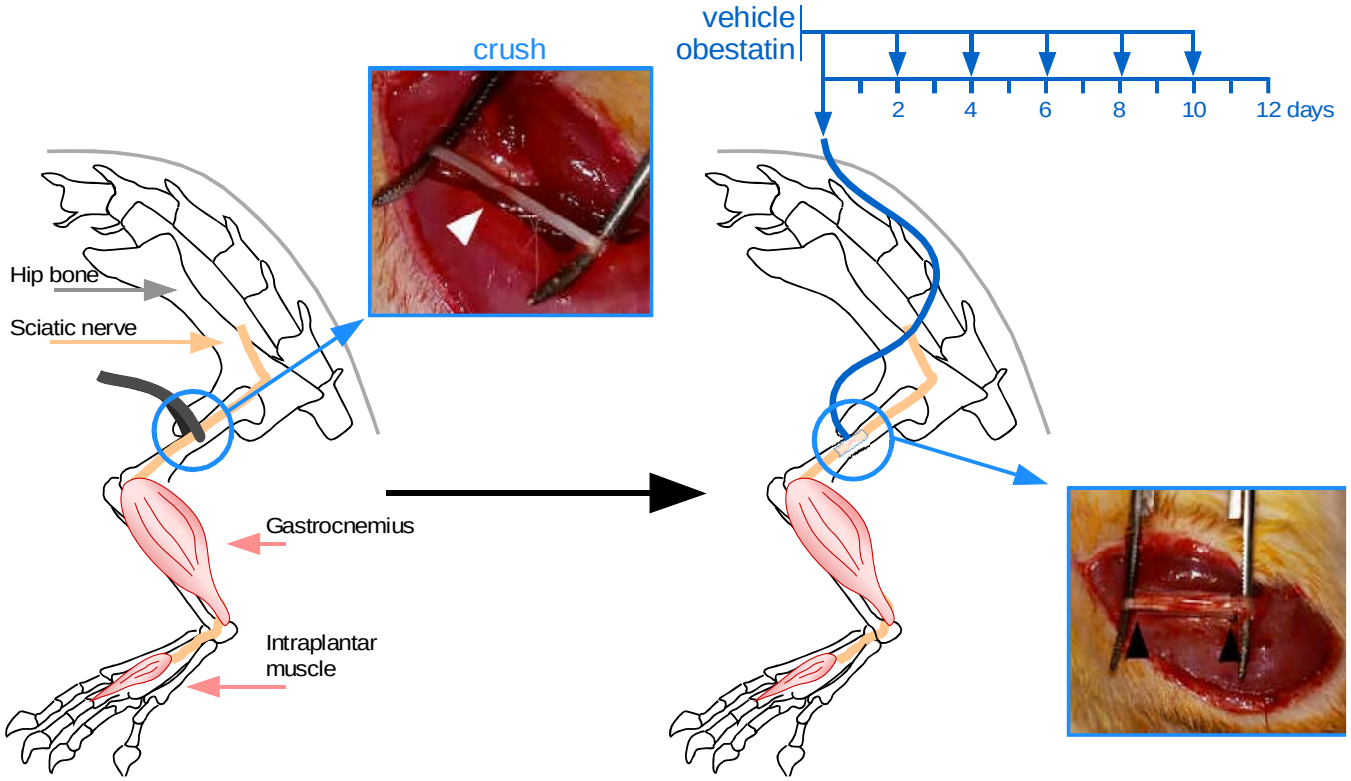


Human obestatin:
FNAPFDVGIKLSGVQYQQHSQAL-NH_2

Alen BO et al. PLoS One. (2012) 7:e45434

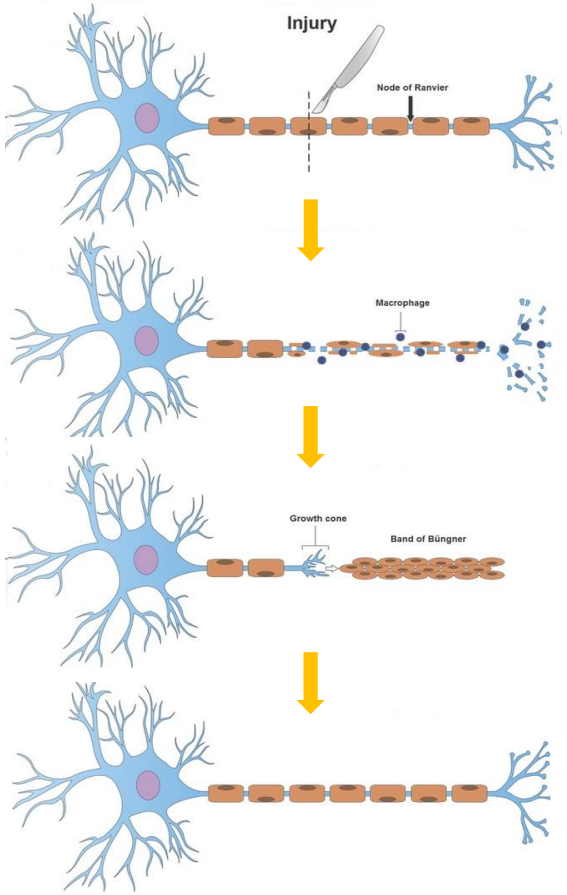
Obestatin: a solution for peripheral nerve repair and protection

Injury model: axonotmesis



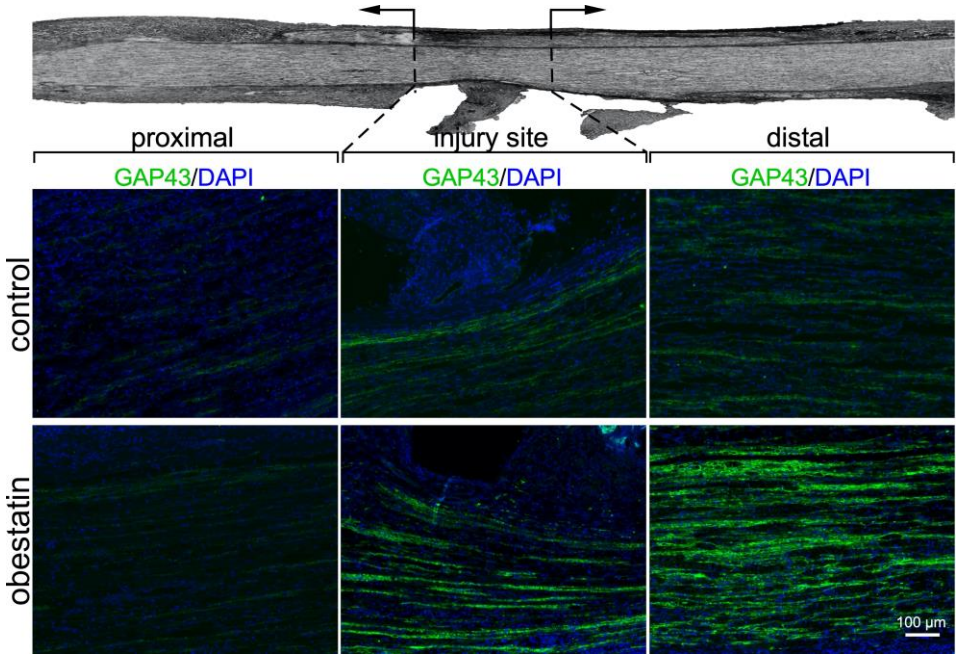
- A standard compression model of sciatic nerve injury.
- Obestatin (500 nM/Kg body weight per 48h for 12d) or vehicle [0.9% NaCl (w/v), corresponding volume] was administered into crush-injured sciatic nerve by using a catheter port.

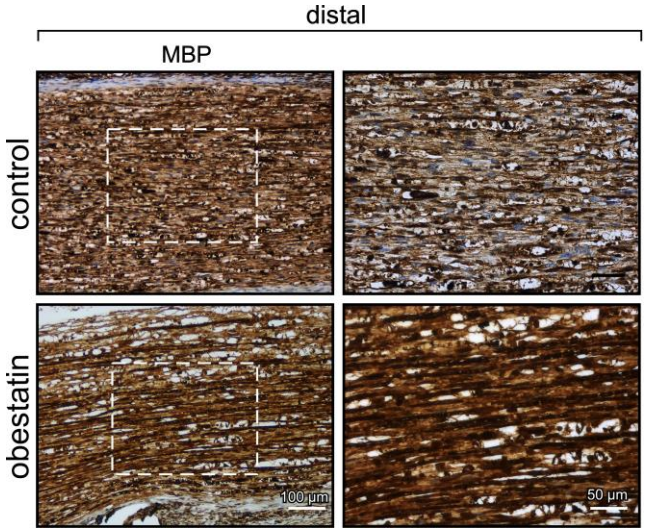
Obestatin: a solution for peripheral nerve repair and protection



- Obestatin directs different stepwise from the repair program of Schwann cells, including proliferation and migration.

- Obestatin sustains axonal regrowth and later remyelinate regenerated axons.

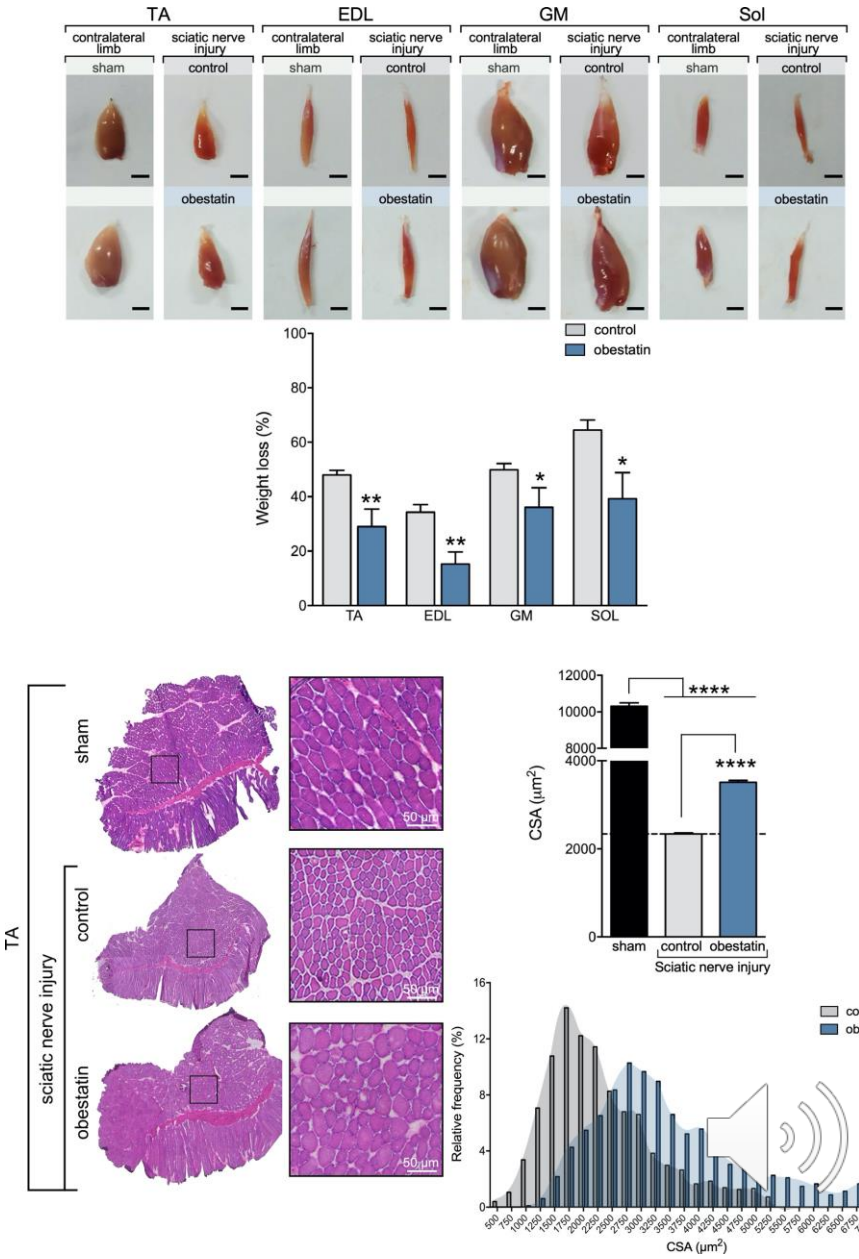




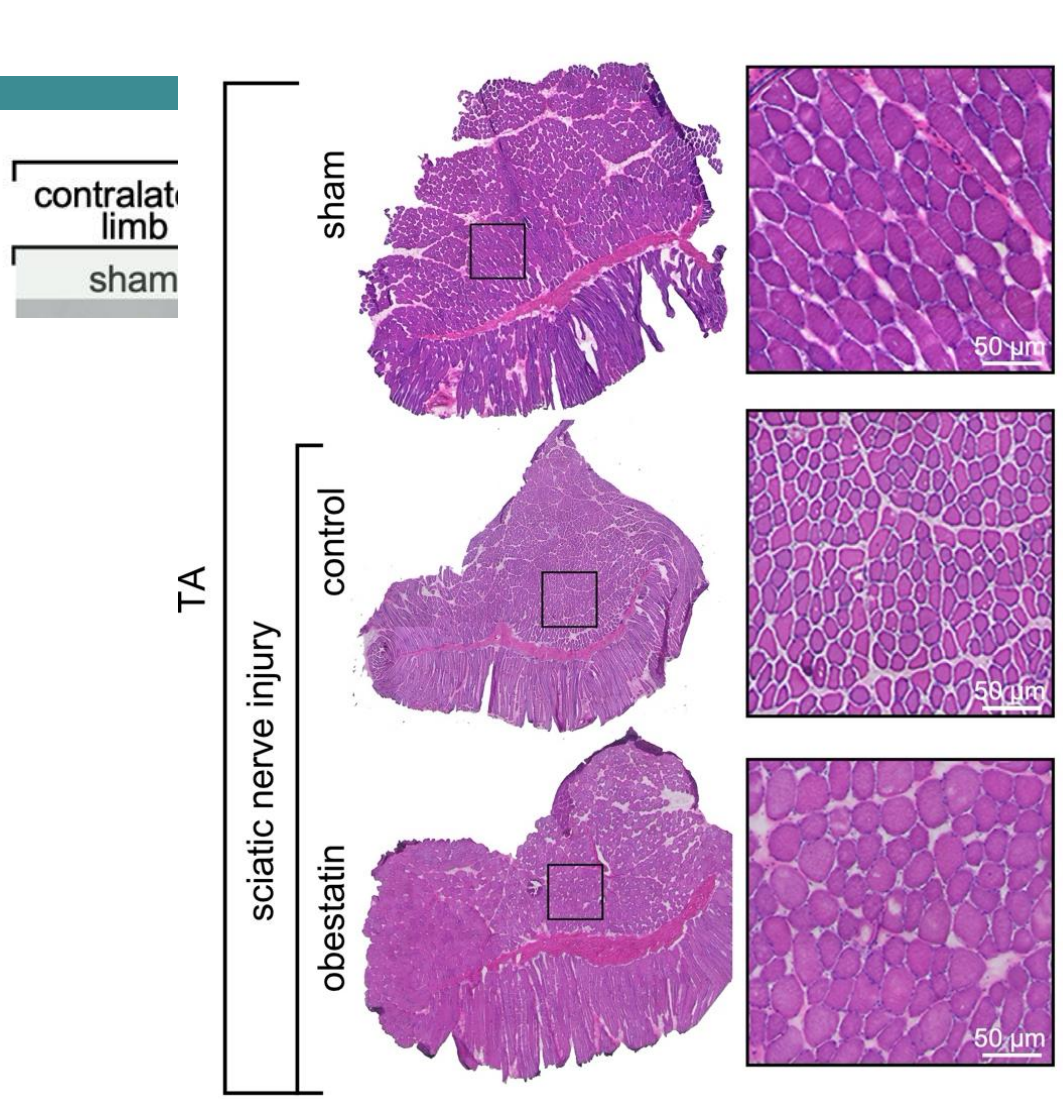
Obestatin: a solution for peripheral nerve repair and protection

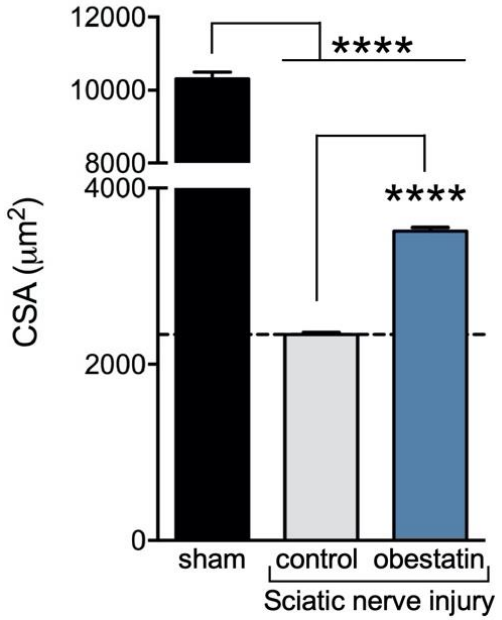
- Obestatin supports the preservation of skeletal muscle by the maintenance of neuromuscular synapses through the axonal regulation of calpain-calpastatin proteolytic system.

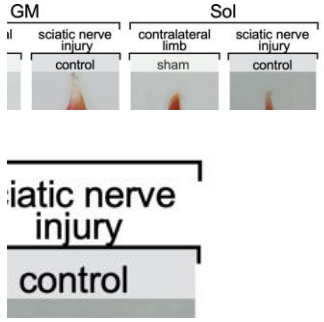
- This encompasses the control of skeletal muscle homeostasis by regulation of the ubiquitin proteasome system and the autophagy machinery.

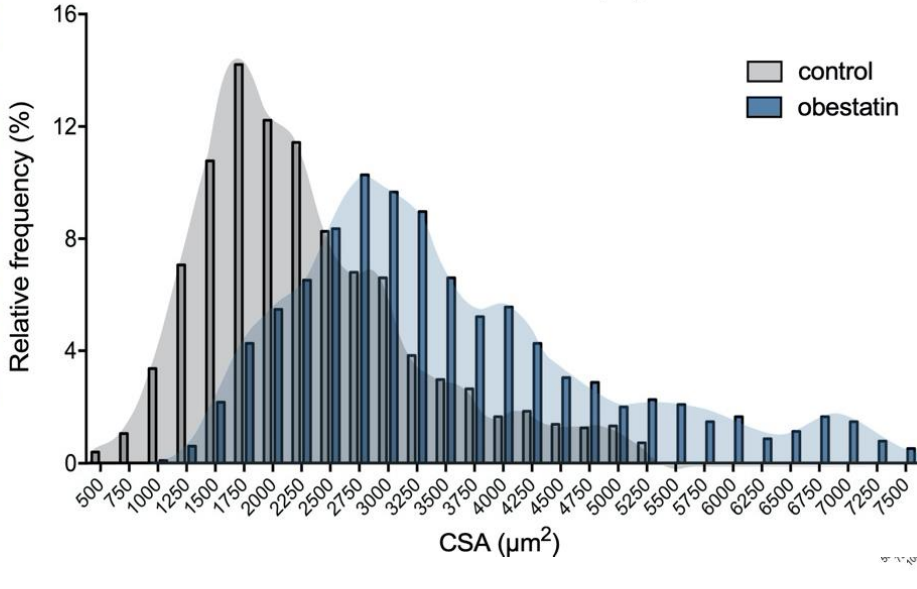


Obestatin: a solution for peripheral nerve repair and protection



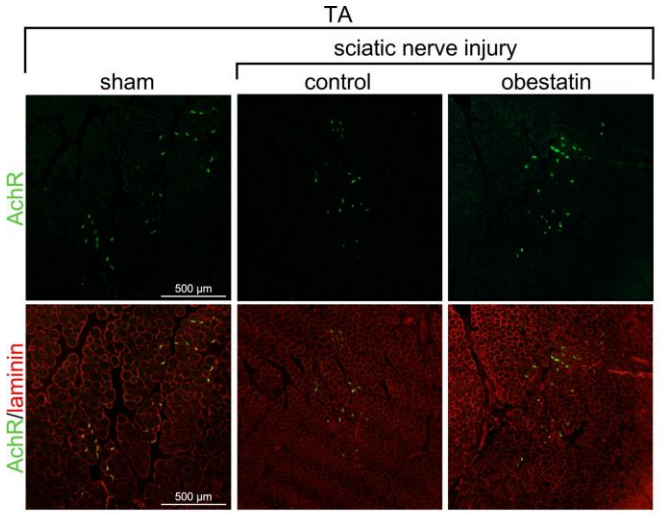


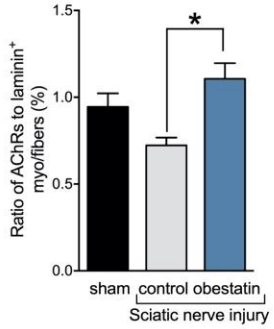


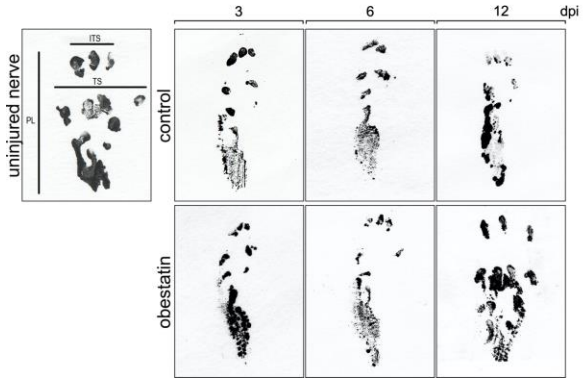


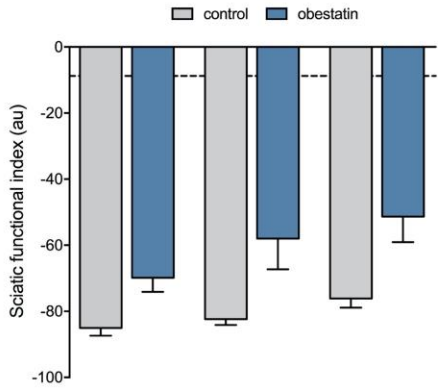
Obestatin: a solution for peripheral nerve repair and protection

- Obestatin preserves neuromuscular synapses during PNS regeneration.
- Obestin increases functional recovery.

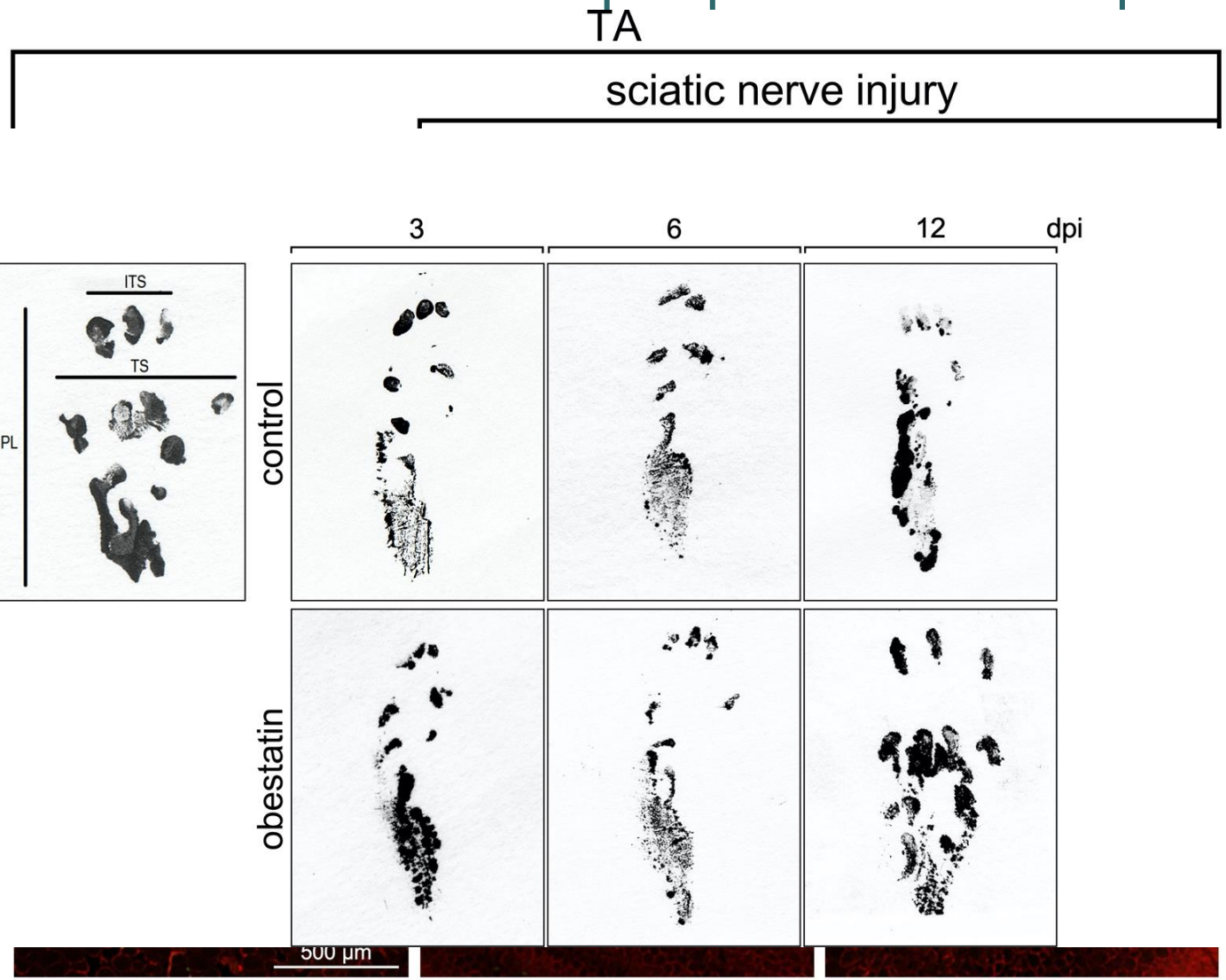


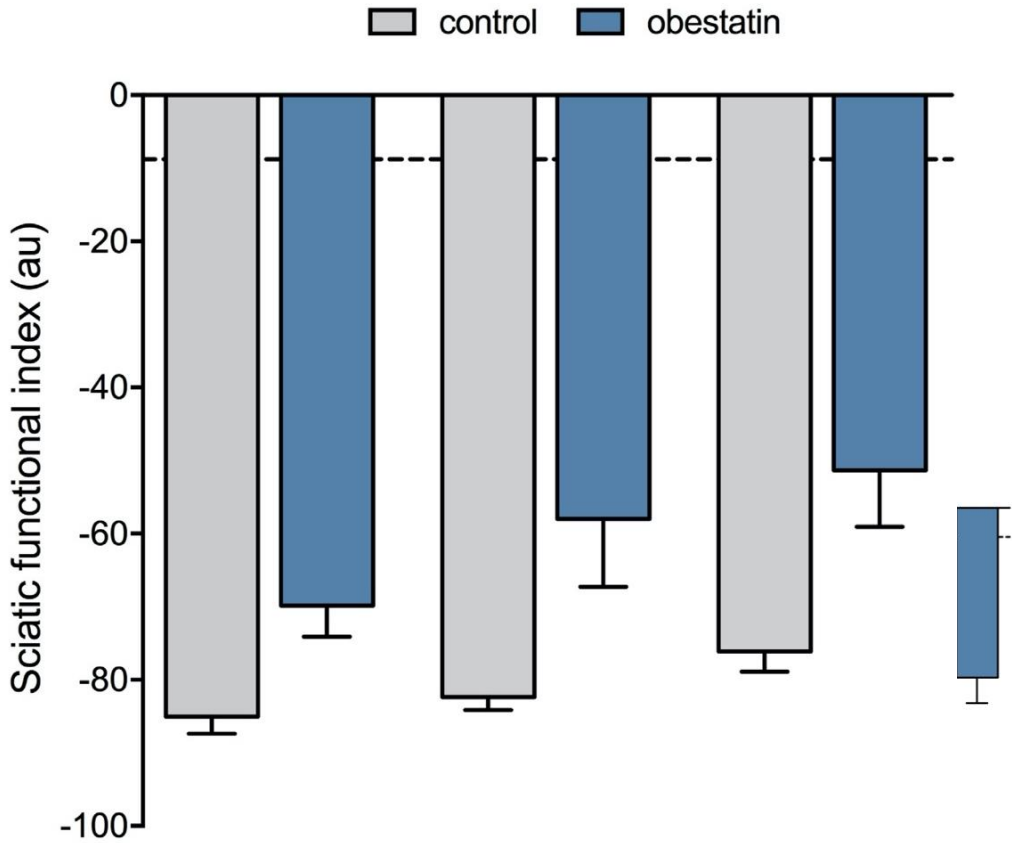






Obestatin: a solution for peripheral nerve repair and protection





Obestatin: differential features facing the market

Obestatin for nerve repair offers:

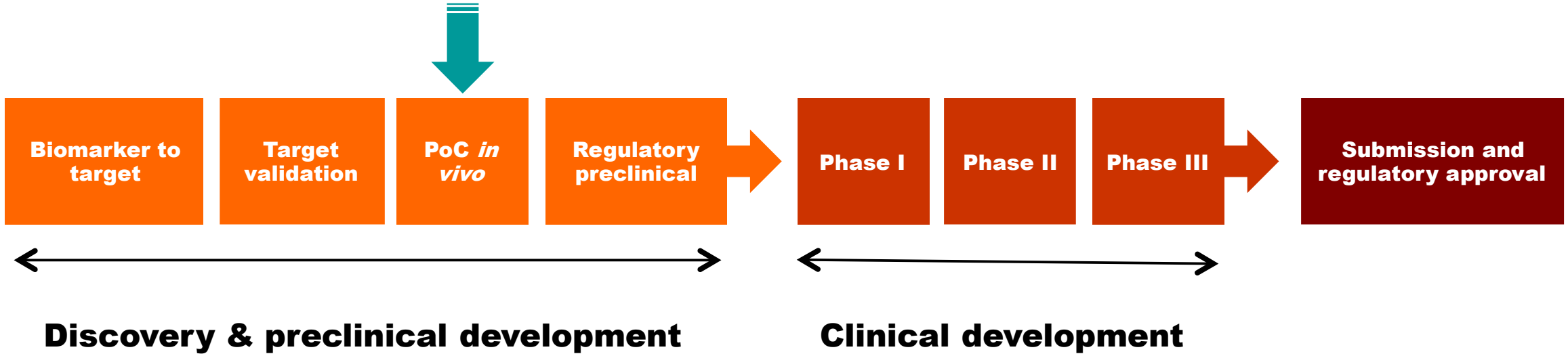
- Obestatin orchestrates Schwann cell plasticity to promote and guide axonal repair.
- Obestatin inhibits axon degradation and neuromuscular synaptic loss.
- Obestatin serves as a therapeutic approach to counteract skeletal muscle atrophy.

This set of actions defines obestatin peptide as a multi-acting drug for the protection and treatment of injured peripheral nerves.

Obestatin can be use:

- To protect injured nerves.
- To minimize risk of neuromuscular synaptic loss.
- To reinforce the effectiveness of the current nerve damage treatments.

Obestatin: current status of development



- Pre-formulation for nerve treatment.
- To test the regenerative capacity in a animal model of severe nerve injury.
- Preclinical development: pharmacokinetic and toxicology.

Obestatin: IPR protection

- European Patent Application No. 18382680.9.
- The invention refers to the medical field. Particularly, the the use of obestatin in the treatment of peripheral nerve damages or injuries.
- Protect the use of the peptide or any fragment thereof comprising or consisting of the amino acid sequence of obestatin.
- Protect the use of a pharmaceutical composition comprising or consisting of obestatin, or a fragment thereof comprising or consisting of the amino acid sequence of obestatin.

Obestatin: benefits

- Small peptide: 23-aa peptide.
- Simple chemical synthesis.
- High dispersal in muscle fibers.
- Specific activity on nerve and muscle regeneration.
- Obestatin could benefit other pathologies related to nerve regeneration.

Obestatin: pitfalls & risks to be considered

This peptide might show oncogenic characteristics under chronic treatment.

Obestatin: partnering opportunities

Our aim is to accelerate the discovery, production, and delivery of new treatments focused on the obestatin/GPR39 system as therapeutic target for nerve and muscle repair. We need a partner to bring our product to market, while navigating safely through the ever-changing pharmaceutical landscape.