

## Protease-activated receptor-1 in Schwann cells and its possible role in the regeneration of peripheral nerves

Elena Pompili<sup>1</sup>, Cinzia Fabrizi<sup>1</sup>, Bruno Maras<sup>2</sup>, Virginia Correani<sup>2</sup>, Maria Eugenia Schininà<sup>2</sup>, Viviana Ciraci<sup>1</sup>, Marco Artico<sup>3</sup>, Lorenzo Fumagalli<sup>1</sup>

<sup>1</sup> Department of Anatomy, Histology, Forensic Medicine and Orthopedics, Sapienza University of Rome, Rome, Italy - <sup>2</sup> Department of Biochemical Sciences, Sapienza University of Rome, Rome, Italy - <sup>3</sup> Department of Sensory Organs, Sapienza University of Rome, Rome, Italy

Protease-activated receptor-1 (PAR-1) is the prototypic member of a family of four G-protein-coupled receptors that signal in response to extracellular proteases. In the peripheral nervous system, the expression and/or the role of PARs are still poorly investigated. High PAR-1 mRNA expression was found in the rat dorsal root ganglia and the signal intensity of PAR-1 mRNA increased in response to sciatic nerve transection, both in the proximal and in the distal part of the lesioned nerve (1). Other authors revealed that functional PAR-1 receptor exists specifically in the non-compacted Schwann cell myelin microvilli at the nodes of Ranvier in the sciatic nerve (2). Schwann cells are the principal population of glial cells of the peripheral nervous system which myelinate axons playing an important role during axonal regeneration and remyelination (3). The present study was aimed to determine if the activation of PAR-1 affects the neurotrophic properties of Schwann cells. We observed a specific staining for PAR-1 in Schwann cells of rat sciatic nerve and also in primary Schwann cell cultures. To study the role of PAR-1 in Schwann cell cultures, we activated this receptor with a specific activating peptide (PAR-1 AP). Conditioned medium from PAR-1 AP-treated Schwann cells reduced the LDH release of PC12 cells respect to the medium of the untreated cells, suggesting that the stimulation of PAR-1 induces the production of pro-survival molecules. Also an increased neurite outgrowth on PC12 cells was observed using the conditioned medium from Schwann cells treated with PAR-1 AP respect to the control obtained from untreated cells. The synthesis and secretion of several factors produced by Schwann cells treated with PAR-1 AP were investigated by proteomics, western blot and RT-PCR analyses. By these experiments we identified as putative neurotrophic candidates some molecules, such as Macrophage migration inhibitory factor, Syndecan 4 and Annexin A2.

### References

- [1] Niclou et al (1998) Changes in the expression of protease-activated receptor 1 and protease nexin-1 mRNA during rat nervous system development and after nerve lesion. *Eur J Neurosci.* 10:1590-607.
- [2] Shavit et al. (2008) Thrombin receptor PAR-1 on myelin at the node of Ranvier: a new anatomy and physiology of conduction block. *Brain* 131:1113-22.
- [3] Namgung U (2015) The Role of Schwann Cell-Axon Interaction in Peripheral Nerve Regeneration. *Cells Tissues Organs.*

### Keywords

PAR-1; Schwann cells; peripheral nerve.