PAR-1 activation affects the neurotrophic properties of rat Schwann cells

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PAR-1 (Protease-activated receptor-1) is a G-protein-coupled receptor that elicits cellular responses to extracellular proteases such as thrombin. In the peripheral nervous system (PNS), the expression and/or the role of PAR-1 are still poorly investigated. Several authors speculated that many functions in PNS, such as motor, secretory, vascular, nociceptive, inflammatory or regenerative processes, may be regulated by PARs (Vergnolle et al. 2003; Shavit et al., 2008; Wang et al., 2013). The present study was aimed to determine if PAR-1 activation affects neurotrophic properties of Schwann cells. By double immunofluorescence experiments we observed a specific staining for PAR-1 in S100β-positive cells of rat sciatic nerve and sciatic teased fibres. Moreover, PAR-1 was highly expressed in Schwann cell cultures obtained from both neonatal and adult rat sciatic nerves. When PAR-1 specific agonists were added to these cultures a higher proliferation rate was observed. Moreover, conditioned medium from primary Schwann cells treated with PAR-1 agonists increased cell survival and neurite outgrowth of PC12 cells. Therefore synthesis and secretion of several factors by Schwann cells treated with PAR-1 agonist peptides were investigated by RT-PCR, western blot and proteomics analysis. By these experiments some molecules, including extracellular matrix components and adhesion molecules, were identified as putative neurotrophic candidates.

References

- [1] Vergnolle et al (2003) Proteinase-activated receptors: novel signals for peripheral nerves. Trends Neurosci 26:496-500.
- [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] Wang et al. (2013) Interleukin-1β increased the expression of protease-activated receptor 4 mRNA and protein in dorsal root ganglion neurons. Neurochem Res 38:1895-903.

Keywords

Protease-activated receptor 1, Schwann cells, peripheral nerve, regeneration.