PAR1 activation induces the release by Schwann cells of factors promoting cell survival and neuritogenesis

V. Ciraci[1], E. Pompili[1], V. Correani[2], B. Maras[2], M. E. Schininà[2], M. Artico[3], L. Fumagalli[1], C. Fabrizi[1]

[1]*Sapienza University of Rome, Department of Anatomy, Histology, Forensic Medicine and Orthopedics, Rome, Italy*

[2]*Sapienza University of Rome, Department of Biochemical Sciences, Rome, Italy*

[3]*Sapienza University of Rome, Department of Sensory Organs, Rome, Italy*

Protease-activated receptor 1 (PAR1) is a member of a family of four G-protein-coupled receptors which are activated by proteolytic cleavage of their N-terminal extracellular domain. The expression and the role of PAR1 in peripheral nervous system (PNS) is still poorly investigated, although high PAR1 mRNA expression was found in the dorsal root ganglia and in the non-compacted Schwann cell myelin microvilli at the nodes of Ranvier. Schwann cells (SCs) are the principal population of glial cells of the PNS which myelinate axons and play a key role in axonal regeneration and remyelination. Aim of the present study was to determine if the activation of PAR1 affects the neurotrophic properties of SCs. By double immunofluorescence we observed a specific staining for PAR1 in S100β-positive cells of rat sciatic nerve and sciatic teased fibers.

Moreover, PAR1 was highly expressed in SC cultures obtained from both neonatal and adult rat sciatic nerves. When PAR1 specific agonists were added to these cultures an increased proliferation rate was observed. Moreover, the conditioned medium obtained from primary SCs treated with PAR1 agonists increased cell survival and neurite outgrowth on PC12 cells respect to controls. By proteomics, western blot and RT-PCR analyses we identified five proteins which are released by SCs following PAR1 stimulation: Macrophage migration inhibitory factor (Mif), Aldose reductase (Akr1b1), Matrix metalloproteinase-2 (Mmp2), Syndecan-4 (Sdc) and Decorin (Dcn). Conversely, a significant decrease in the level of three proteins was observed: Complement C1r subcomponent (C1r) and Complement component 1 Q subcomponent-binding protein (C1qbp). When PAR1 expression was silenced by siRNA the observed pro-survival and neurotrophic properties of SCs appear to be reduced respect to controls.

References

PAR1 activation affects the neurotrophic properties of Schwann cells. Pompili E, Fabrizi C, Somma F, Correani V, Maras B, Schininà ME, Ciraci V, Artico M, Fornai F, Fumagalli L. 2017 Jan 4;79:23-33. doi: 10.1016/j.mcn.2017.01.001.