IJAE
Vol. 121, n. 1 (Supplement): 43, 2016
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

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

Elena Pompili [1] - Cinzia Fabrizi [1] - Bruno Maras [2] - Virginia Correani [2] - Maria Eugenia Schininà [2] - Viviana Ciraci [1] - Marco Artico [3] - Lorenzo Fumagalli [1]

[1] Department of Anatomy, Histology, Forensic Medicine and Orthopedics, Sapienza University of Rome, Rome, Italy - [2] Department of Biochemical Sciences, Sapienza University of Rome, Rome, Italy - [3] Department of Sensory Organs, Sapienza University of Rome, Rome, Italy

Schwann cells (SCs) regulate a wide variety of axonal functions in the peripheral nervous system, providing a supportive growth environment following nerve injury (1). Here we show that rat SCs express the protease-activated receptor-1 (PAR1) both in vivo and in vitro. PAR1 is a G-protein coupled receptor eliciting cellular responses to thrombin and other proteases (2). To investigate if PAR1 activation affects the neurotrophic properties of SCs, this receptor was activated by a specific agonist peptide (TFLLR) and the conditioned medium was transferred to PC12 pheocromocytoma cells for assessing cell survival and neurite outgrowth. Culture medium from SCs treated with 10 μM TFLLR reduced significantly the release of LDH and increased the viability of PC12 cells with respect to the medium of the untreated SCs. Furthermore, conditioned medium from TFLLR-treated SCs increased neurite outgrowth on PC12 cells respect to control medium from untreated cells. To identify putative neurotrophic candidates we performed proteomic analysis on SC secretoma and real time PCR experiments after PAR1 activation. Stimulation of SCs with TFLLR increased specifically the release of a subset of five proteins: Macrophage migration inhibitory factor (Mif), Aldose reductase (Akr1b1), Matrix metalloproteinase-2 (Mmp2), Syndecan-4 (Sdc) and Decorin (Dcn). At the same time there was a significant decrease in the level of three proteins: Complement C1r subcomponent (C1r), Complement component 1 Q subcomponent-binding protein (C1qbp) and Angiogenic factor with G patch and FHA domains 1 (Aggf1). These data indicate that PAR1 stimulation does induce the release by SCs of factors promoting cell survival and neuritogenesis. Among these proteins, Mif, Sdc, Dcn and Mmp2 are of particular interest.

References

[1] Gordon T (2016) Nerve Regeneration: Understanding Biology and Its Influence on Return of Function After Nerve Transfers. Hand Clin 32(2):103-17. doi: 10.1016/j.hcl.2015.12.001.
[2] Hollenberg et al. (2014) Biased signalling and proteinase-activated receptors (PARs): targeting inflammatory disease. Br J Pharmacol 171, 1180–1194.

Keywords

Protease-activated receptor 1; thrombin; peripheral nerve; Schwann cells.