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Degeneration and regeneration of peripheral nerves: role of thrombin and its receptor PAR-1

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The peripheral nervous system has a striking regeneration potential and after damage extensive changes in the differentiation state both of the injured neurons and of the Schwann cells are observed. Schwann cells, in particular, undergo a large scale change in gene expression becoming able to support axonal regeneration. Nerve injury is generally associated to inflammation and activation of the coagulation cascade. Thrombin acts as a polyfunctional signalling molecule exerting its physiological function through soluble target proteins and G-protein-coupled receptors, the protease-activated receptors (PARs) [1]. Recently, we have demonstrated that the activation of the main thrombin receptor, PAR-1, in Schwann cells favours their regenerative potential determining the release of factors which promote axonal regrowth [2]. The pro-regenerative potential of thrombin seems to be exerted in a narrow range of concentrations (pM-nM range). In fact, our preliminary data indicate that high levels of thrombin in the micromolar range slow down Schwann cell proliferation and induce cell death. On the contrary, PAR-1 activating peptides mimic the pro-survival but not the pro-apoptotic effects of thrombin.

Controlling thrombin concentration may preserve neuronal health during nerve injury and represent a novel target for pharmacologic therapies.

References

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Keywords
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