Invited Trends Article:

Retinoic Acid as a Regulator of Cytokine Signaling after Nerve Injury

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After an injury of the central nervous system it is of foremost clinical concern to prevent nerve cell degeneration and to develop strategies for the support of axonal regeneration. This requires an understanding of traumatic processes in the nervous system and their regulation by intercellular cytokine signaling. Although injury-induced temporal changes in gene expression of many cytokines have been described in this context, much less is known about their regulation. This review proposes a role of retinoic acid (RA) as transcriptional regulator in nerve regeneration. Four lines of evidence support this hypothesis: (1) In various cell culture systems retinoids were found to interact with most cytokine signals that mediate cellular interactions after nerve lesions *in vivo*. (2) Necessary components of the retinoid signaling pathway (aldehyde dehydrogenases, nuclear RA-receptors, cellular RA-binding proteins) are present in the adult nervous system, and glial cells produce RA *in vitro*. In addition, recent observations indicate that RA-synthesizing enzyme activity increases after nerve injury. (3) During development endogenous RA promotes glial and neuronal differentiation including the outgrowth of axons in the developing spinal cord, cerebellum, dorsal root ganglia and sympathetic ganglia. (4) Axonal regeneration of differentiated retinal ganglion cells and peripheral sensory neurons is enhanced by RA *in vitro*.