Abstract

The inability of neurons to regenerate injured connections within the central nervous system (CNS) severely limits the functional recovery that can occur after traumatic injury, stroke, or certain neurodegenerative diseases. The failure of axonal regeneration is commonly attributed to inhibitory factors associated with myelin and/or the glial scar that is formed at the lesion site and an insufficient intrinsic ability of adult neurons to regrow axons. As central neurons retinal ganglion cells (RGCs) fail to regenerate axons and start to undergo apoptosis soon after intraorbital optic nerve crush (ONC). Contrary to other paradigms the visual system offers a number of advantages for investigating mechanisms that govern axon regeneration in the CNS. Because of the ease of introducing trophic factors, drugs, or viruses expressing any gene of interest into RGCs, this system is ideal for identifying intracellular signaling pathways and transcriptional cascades that enable axon regeneration to occur in the CNS.
Research has recently shown that inducing inflammatory reactions in the eye transforms RGCs to a robust regenerative state enabling these neurons to regrow axons at higher growth rates and to extend lengthy axons into the inhibitory environment of the injured optic nerve. The molecular mechanisms underlying this phenomenon have recently been unraveled is at least partially mediated by an activation of retinal astrocytes that continuously release the neuroprotective and axon growth promoting cytokine CNTF after inflammatory stimulation. Axon regeneration in the optic nerve can be even further increased by additional genetherapeutic approaches to overcome inhibitory signaling caused by myelin using adeno associates viruses.
Overexpression of dominant negative receptors or proteins that inactivate inhibitory signaling result in strong axon regeneration in the optic nerve and these approaches might therefore open new ways to develop new strategies to treat human beings suffering from CNS injury in the future.