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Molecular and cellular neurobiotechnology group

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Modulating axon growth and neuronal migration by optogenetic approaches and light

After lesion the central nervous system (CNS) have a limited capacity to sprout and to re-establish lost connections. This largely contributes to functional neurological impairment. Experimental evidence suggests that providing a favorable extracellular environment containing cellular or biomaterial bridges is important but may not be sufficient to enhance functional regeneration. In fact, activating or recapitulating the developmental program of the lesioned neuron to sprout and regenerate may represent an alternative and complementary therapeutic approach and may sometimes directly counteract the inhibitory signaling. During development, where CNS neurons still retain the intrinsic ability of regenerating after an axotomy, neuronal activity has been shown to be a critical determinant of neuron connectivity at these stages.

Optogenetics is currently the state-of-the-art method for activity-based nervous system research, which allows more specific stimualtions by cellular, topografical and less invassive techniques compared to classical electrical stimulation, also leading to a more phisiological response. Modulation of the activity in CNS neurons has been widely shown to be able to reprogram neurons through different trancriptional and epigenetic states, leading to strong changes in their phenotypes, both during developement and in maturity. For these reasons we hypothesize, that optogenetic induced genetic reprograming of cns neurons spared fibers may act as a key component of the growth in normal and after lesion. These aims lie within the scope of the need for new strategies and targets that may foster axonal regeneration and functional recovery following CNS lesion, as well as to unravel the mechanisms underlying the phisiological role and mechanisms of neuronal activity during development and after injury, which will also benefit clarify the role of neuronal activity in current rehabilitation therapies on spinal injured patients, strengthening the translational possibilities of this proposal.