Mature retinal ganglion cells (RGCs) do not normally regenerate injured axons, but degenerate after axotomy. However, inflammatory stimulation (IS) enables RGCs to survive axotomy and regenerate axons in the injured optic nerve. Similar effects are achieved by the genetic deletion of phosphatase and tensin homolog (PTEN) and subsequent mammalian target of rapamycin (mTOR) activation. In this talk I will present data suggesting that (i) IS prevents the axotomy-induced decrease of mTOR activity in RGCs in a CNTF/LIF-dependent manner, (ii) that inactivation of mTOR significantly reduces the number of long axons regenerating in the optic nerve, (iii) but surprisingly, does not affected the initial switch of RGCs into the regenerative state, or the neuroprotective effects associated with IS. In vitro, inhibition of mTOR activity reduces regeneration on myelin or chondroitin sulfate proteoglycans (CSPGs), but not on a growth-permissive substrate. Thus, mTOR activity is not generally required for neuroprotection or switching mature neurons into an active regenerative state, but it is important for the maintenance of the axonal growth state and overcoming of inhibitory effects caused by myelin and CSPGs.

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