Monocyte-derived SDF1 supports optic nerve regeneration and alters retinal ganglion cells' response to Pten deletion

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Although mammalian retinal ganglion cells (RGCs) normally cannot regenerate axons nor survive after optic nerve injury, this failure is partially reversed by inducing sterile inflammation in the eye. Infiltrative myeloid cells express the axogenic protein oncomodulin (Ocm) but additional, as-yet-unidentified, factors are also required. We show here that infiltrative macrophages express stromal cell-derived factor 1 (SDF1, CXCL12) , which plays a central role in this regard. Among many growth factors tested in culture, only SDF1 enhances Ocm activity, an effect mediated through intracellular cyclic AMP (cAMP) elevation and phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K) activation. SDF1 deficiency in myeloid cells (CXCL12flx/flxLysM-Cre?/+ mice) or deletion of the SDF1 receptor CXCR4 in RGCs (intraocular AAV2-Cre in CXCR

Conversely, SDF1 induces optic nerve regeneration and RGC survival, and, when combined with Ocm/cAMP, SDF1 increases axon regeneration to levels similar to those induced by intraocular inflammation. In contrast to deletion of phosphatase and tensin homolog (Pten) , which promotes regeneration selectively from ?RGCs, SDF1 promotes regeneration from non-?RGCs and enables the latter cells to respond robustly to Pten

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