

# Direct optic nerve sheath (DONS) application of Schwann cells prolongs retinal ganglion cell survival in vivo

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Cell-based therapies are increasingly recognized as a potential strategy to treat retinal neurodegenerative disease. Their administration, however, is normally indirect and complex, often with an inability to assess in real time their effects on cell death and their migration/integration into the host retina.

In the present study, using a partial optic nerve transection (pONT) rat model, we describe a new method of Schwann cell (SC) delivery (direct application to injured optic nerve sheath, SC/DONS) , which was compared with intravitreal SC delivery (SC/IVT) . Both SC/DONS and SC/IVT were able to be assessed in vivo using imaging to visualize retinal ganglion cell (RGC) apoptosis and SC retinal integration. RGC death in the pONT model was best fitted to the one-phase exponential decay model. Although both SC/DONS and SC/IVT altered the temporal course of RGC degeneration in pONT, SC/DONS resulted in delayed but long-lasting effects on RGC protection, compared with SC/IVT treatment.

In addition, their effects on primary and secondary degeneration, and axonal regeneration, were also investigated, by histology, whole retinal counting, and modelling of RGC loss. SC/DONS was found to significantly reduce RGC apoptosis in vivo and significantly increase RGC survival by targeting secondary rather than primary degeneration. Both SC/DONS and SC/IVT were found to promote RGC axonal regrowth after optic nerve injury, with evidence of GAP-43 expression in RGC somas and axons. SC/DONS may have the potential in the treatment of optic neuropathies, such as glaucoma.

We show that SC transplantation can be monitored in real time and that the protective effects of SCs are associated with targeting secondary degeneration, with implications for translating cell-based therapies to the clinic.

Cell Death Dis. 2014 Oct 16;5:e1460. doi: 10.1038/cddis.2014.399.

PMID: 25321467

<http://www.ncbi.nlm.nih.gov/pubmed/25321467>