Project Title: Non Invasive Cell Based Therapy for Traumatic Optic Neuropathy
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Background: The traumatic optic neuropathy (TON) can lead to irreversible blindness and represent a major public health burden with both economical and social impacts. TON results from trauma to optic nerve by head and eye injuries in both military and civilian population; such as blast related combat trauma and accidents. There is no effective treatment as yet.

Objective: The objective of this research proposal is to offer a treatment that targets optic nerve and related neurons in the visual system using non-invasive stem cell therapy in rodent models for TON.

Hypothesis: Systemic and local administration of bone marrow derived mesenchymal stem cells (MSC) and Induced Schwann cells (M-Sch), respectively, to treat TON will preserve/repair optic nerve, stabilize the unstable environment due to trauma and promote retinal ganglion cell (RGC) regeneration and outgrowth by promoting the release of paracrine and autocrine mediators.

Specific Aims: Aim 1. Determine the efficacy of IV injection of MSC after traumatic axonal injury (TAI) in rat model. Aim 2. Investigate the efficacy of combined local application of the induced Schwann cells (M-Sch) and systemic injection of MSC after TAI. Aim 3. Examine the molecular mechanism of specific homing after IV injection of MSC.

Study Design: (A) Both Long Evan rats and Thy1-YFP-G transgenic mice will be used for creating TAI models; (B) MSC and M-Sch will be isolated/induced; (C) IV injection of MSC and local application of M-Sch at several time points after TAI; (D) in vivo imaging of RGCs and distribution of MSC; (E) Evaluation of visual functions; (F) Quantification of survival and outgrowth of RGCs; (G) examine whether SDF-1/CXCR4 plays a key role in regulating MSC homing.

Relevance: Traumatic optic neuropathy (TON) is a devastating problem for both military and civilian population; there is no effective treatment as yet. This approach, to treat traumatic neuropathy by systemic administration of MSC and combined with local injection of M-Sch, is innovative in its emphasis on preserving optic nerve and related target tissues at the same time. In addition, the feasibility of systemic administration makes repeating injection possible. Based on the current extensive clinical experience using MSC as therapy for both regenerative and degenerative medicine, if positive results are obtained in the animal models, this treatment has a realistic likelihood of translation to the clinic.