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Letter to Editor

Mesenchymal stem cells in optic nerve atrophy: a novel therapeutic approach

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Arora B,[1] Suriyanarayanan S,[2] Pandey A[3]
[1]Department head of Therapies, CelluGen Biotech Pvt. Limited, India
[2]Head, Laboratory Operations, CelluGen Biotech Pvt. Limited, India
[3]Medical Director, CelluGen Biotech Pvt. Limited, India

Correspondence: Anubhav Pandey, Medical Director, CelluGen Biotech Pvt. Limited, CelluGen House 62, Udyog Vihar Phase-1, Gurgaon, Haryana-122016, India, Tel +91-7838515178, 9871456699, Email dranubhav.pandey@cellugen.in

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Introduction

Optic nerve atrophy (ONA) is characterized by mild to severe damage to the optic nerve that can adversely affect central vision, peripheral vision and colour vision. Optic nerve disease is complicated and there are a number of pathophysiologic mechanisms that can lead to retinal ganglion cell impairment or death. ONA is associated with myriad causes including tumour, trauma, glaucoma, ischemia, heredity, hydrocephalus, toxins, infection and some rare degenerative disorders. Clinically, the neuroprotective or exogenic therapies that restore lost visual system connectivity in retinal degenerative disease are non-existent and translatable techniques for the replacement of lost retinal ganglion cells (RGCs) and photoreceptors are in their infancy.[1] Stem cell therapies are being explored extensively as treatments for degenerative eye disease, either for replacing lost neurons or for restoring neural circuits. Recent evidence suggests stem cell-derived trophic factors protect compromised endogenous retinal neurons from death and induce the growth of new connections.[1,2] Mesenchymal stem cells (MSCs) provide trophic support to damaged retinal cells for the neuroprotection and axon regeneration either directly through the secretion of neurotrophic factors (NTFs) or indirectly after stimulation of endogenous retinal cells which, when activated, could provide additional paracrine support and/or effect cell replacement.[1,2] MSCs have been the focus of a regime of emerging therapeutics owing to their non-invasive, non-tumorigenic, immunosuppressive and tropic characteristics and their potential to differentiate into tissue specific cell types. MSCs can be isolated from various sources such as umbilical cord tissue, bone marrow, adipose tissue and dental pulp to name a few.

Within the umbilical cord stem cells have been derived from various compartments including the amniotic compartment, the Wharton's Jelly compartment, the peri-vascular compartment surrounding the vessels, the media and adventitia compartment of the walls of UC blood vessels, the endothelial compartment as well as the vascular compartment. Wharton's Jelly is a robust source of MSCs. Stemness and immune properties of these MSCs are more comparable with fetal than adult-derived MSCs. They are considered much more proliferative, immunosuppressive and even therapeutically active as compared to stem cells isolated from older, adult tissue sources such as the bone marrow or adipose. Other favorable properties such as ease of collection, in vitro expandability, differentiation abilities and immune modulation capacities make them a popular choice for therapeutics.[3]

In a study by Lund et al.,[4] they observed the Umbilical Tissue-Derived Cells (U-MSC) demonstrated the best photoreceptor rescue and, unlike MSC from other sources, were capable of sustained population doublings without Karyotypic changes. It is postulated that the various neurotrophic factors secreted by U-MSC to be effective in rescuing photoreceptors in a number of different retinal degeneration models after direct injection into the vitreous.[4] Some growth factors such as Basic Fibroblast Growth Factor (BFGF), Brain-Derived Neurotrophic Factor (BDNF), Nerve Growth Factor (NGF), Epidermal Growth Factor (EGF), etc. involved in the development of retinal cells might also be essential to the differentiation of MSCs into retinal cells.[5]

It is widely accepted that MSCs-based retinal regeneration is one of the most promising therapies for retinal diseases and U-MSC owing to their neurotrophic properties could promote the survival of axotomized RGCs and regeneration of axon.[5] Though the dose of MSCs to be administered still remains investigational, it is strongly felt that administration of MSC at the peak of inflammation may improve therapeutic benefit.[6] Various authors have independently reported the efficacy of MSC in disorders of the eye.[7–10] MSCs continue to face hurdles related to inconsistent stem cell potency, poor cell engraftment and survival, as well as age and disease-related host tissue impairment preventing their effective translation into therapeutics.[11] Development of processes and procedures for harvesting and culturing of cells that minimally effect the properties of MSC in accordance with Current Good Manufacturing Practices (cGMP), Current Good Tissue Practices (cGTP), as well as Current Good Laboratory Practices (cGLP) further slows the progress of MSC related clinical trials to efficacious therapeutics.

Conclusion

In conclusion, stem cell based regenerative repair for disorders of the eye hold great promise. However, further elucidation of the biology and immunology of such approaches in human volunteers are needed, including the best source of stem cells and their mode of delivery.

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Conflict of interest

The author declares no conflict of interest.

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