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Editorial

An Editorial on Stem Cell Therapies in Retinal Disorders

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Stem cell therapy has long been considered a promising mode of treatment for retinal conditions. While human embryonic stem cells (ESCs) have provided the precedent for regenerative medicine, the development of induced pluripotent stem cells (iPSCs) revolutionized this field. iPSCs allow for the development of many types of retinal cells, including those of the retinal pigment epithelium, photoreceptors, and ganglion cells, and can model polygenic diseases such as age-related macular degeneration. Cellular programming and reprogramming technology is especially useful in retinal diseases, as it allows for the study of living cells that have genetic variants that are specific to patients' diseases. Since iPSCs are a self-renewing resource, scientists can experiment with an unlimited number of pluripotent cells to perfect the process of targeted differentiation, transplantation, and more, for personalized medicine. Challenges in the use of stem cells are present from the scientific, ethical, and political realms. These include transplant complications leading to anatomically incorrect placement, concern for tumorigenesis, and incomplete targeting of differentiation leading to contamination by different types of cells. Despite these limitations, human ESCs and iPSCs specific to individual patients can revolutionize the study of retinal disease and may be effective therapies for conditions currently considered incurable.Stem cell therapy has long been considered a promising mode of treatment for retinal conditions. Human embryonic stem cells (hESCs) were once considered the only promising source of replacement cells in regenerative medicine.

However, hESCs are associated with numerous drawbacks, including the concomitant administration of lifelong immunosuppressive therapy and limited effectiveness. Thus, when patient-specific induced pluripotent stem cell (iPSC) therapy was developed, exploration of disease pathophysiology, novel drug development, and the possibility of stem cell therapy in retinal disorders were forever changed.

The retina, particularly the subretinal space, is advantageous to stem cell transplantation as the eye is relatively immune privileged. The blood-ocular barrier protects the subretinal space by antigen-specific inhibition of responses of cellular and humoral immune systems, provided that it is not physically compromised during transplantation or due to the underlying disease pathology. In such cases, the immunogenicity remains a challenge in hESC-derived transplantation, but can be mitigated by the iPSC approach.

The propensity for tumorigenesis-such as the formation of teratomas, as is often the case with iPSCs, which are prone to epigenetic and transcriptional aberrations-is a recurring complication, secondary to transplantation, that can be treated with plaque brachytherapy or proton beam radiotherapy without high risk of life-threatening consequences. Additionally, the eye is easily accessible for monitoring by exam and with several high-resolution imaging modalities, without the need for tissue biopsies pre- and post-transplantation.

Human ESCs and iPSCs specific to individual patients are a beneficial tool for the study of retinal disease and may be effective therapies for conditions currently considered incurable. Minimizing the chances of tumorigenicity and precisely targeting differentiation are the most significant challenges that must be overcome in order to make iPSC therapy a reality to treat RPE-related disorders. Ultimately, being able to model retinal conditions *in vitro* allows for the study of the cell development that is truly personalized to patients' disease-specific genetic variants.

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