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**EDITORIAL**

# Regenerating Perfection

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Although Charles Darwin called the eye ''an organ … of exquisite perfection,'' ocular disease makes visual function less than perfect, and we lack therapies for many ocular conditions. Recent advances in stem cell research have generated enthusiasm for the development of cellular transplantation approaches for the treatment of ocular disease. In this special issue, we focus on cell-based therapies for eye disease.

The discovery of human embryonic stem cells by James Thomson in 1998 and human-induced pluripotent stem cells (iPSCs) by Shinya Yamanaka and Thomson in 2007 was soon followed by reports that ocular cells could be derived from these iPSCs. The review by Di Foggia et al. discusses not only how iPSCs might be used for cellular therapies but also how they can be used to model human disease when derived from patients. In addition to PSCs, stem cell populations within the adult eye were described, in some unexpected places. The review by Du et al. describes recent work on stem cells in the trabecular meshwork, which hold promise for the treatment of glaucoma.

Many efforts are underway to use retinal pigmented epithelium (RPE) cells derived from PSCs for the treatment of macular dystrophies. Clinical trials are underway using cell suspensions as well as cellular monolayers grown on scaffolds. Two reviews (Pennington and Clegg; Hotaling et al.) address this important area, where bioengineering an RPE-compatible niche may afford a survival advantage for transplanted cells. Multiple protocols have been described to differentiate RPE cells, but few studies have compared these protocols in head-to-head studies. Leach et al. compare iPSC-RPE derived through a rapid, directed method to the more common (and lengthier) spontaneous differentiation protocol. Joshi et al. describe an automated method to characterize RPE cell cultures that will be a useful characterization tool.

Translation of cellular therapies requires evidence of function and safety in preclinical animal models. One oft-used model is the Royal College of Surgeons (RCS) rat, which loses photoreceptors due to a merTK mutation that leads to dysfunctional phagocytosis by RPE. Cooper et al. describe an unexpected effect of immunosuppression on visual function in the RCS rat. These results should be taken into consideration in the design of studies using this model. Davis et al. use the RCS rat to show rescue of photoreceptors by RPE stem cell-derived RPE and describe a method for quantifying rescue. Finally, in what might prove to be a new animal model of trauma, Bricker-Anthony and colleagues describe airwave-induced trauma in the mouse. Ocular trauma has increasingly become a common battlefield injury that might be treated with cellular therapies.

Neural retinal cells can be derived from PSCs and recent reports show integration and function of photoreceptors in mouse models. However, only a small percentage of injected cells survive, and methods are lacking for generation of specific populations of cells. Worthington et al. describe a poly (lactic-co-glycolic acid) scaffold for differentiation of iPSC-derived neural progenitors. It is likely that methods for the generation of ocular cells of all types from stem cells will continue to improve.

It is an exciting time in this field, which is still in its very early days, and the potential for the development of meaningful, effective cellular therapies is high. We need better ways to make the eye more perfect in patients suffering from ocular disease.

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