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Corneal opacity and retinal degeneration affect several million people worldwide. In the UK alone, more than 360,000 people are registered blind, with age related macular degeneration (AMD) accounting for 40% of these. While current therapies may slow down disease progression, they fail to restore vision that has been lost. The only feasible approach is replacement of cells that have been lost (in the case of corneal opacity limbal stem cells and for retinal blindness either photoreceptors or supporting retinal pigmented epithelial cells or both). In the last eight years my group has worked towards identification of autologous or allogeneic stem cell sources that can engraft into cornea and retina and are able to restore vision. In particular we have been interested in finding new treatments for unilateral limbal stem cell deficiency (LSCD) that results in opacification of cornea and penetration of blood vessels from conjunctiva to central cornea resulting in loss of vision despite the presence of a functional inner retina. We have been successful in devising an animal and feeder free system for expanding *ex vivo* autologous transplants taken from the patient's healthy eye for 10-14 days prior to transplantation into the LSCD affected eye. Using this technique we have treated succesfully eight patients and are in the process of performing 24 further transplants in the next two years.

While the source and location of stem cells that replenish cornea is well established, this remains a little bit more elusive for retina. To date, the most promising donor cell type that has been shown to integrate succesfully and function within the host retina has been the postmitotic immature photoreceptor precursor isolated from developing mouse retina. Transplantation of equivalent human donor cells would require isolation from second trimester human foetuses which raises obvious ethical concerns so attractive cell sources for developing human clinical therapies are human embryonic stem cells (hESC) and human induced pluripotent stem cells (hiPSC). These cells can be easily propagated *in vitro* and are able to differentiate into cells which express markers of retinal progenitor cells, rod photoreceptors, lens cells, bipolar neurons and RPE. hiPSC have the added advantage that somatic cells derived from them are less likely to undergo immune rejection when transplanted back into the patient from which they were originally derived. In the last five years my group has developed a three-step differentiation protocol (feeder and serum free) that employs defined and stage-specific culture supplements and growth factors to drive the differentiation of hESC/hiPSC towards retinal photoreceptor precursors. Using this protocol, hESC and hiPSC over a 60 day time window sequentially acquire markers associated with neural, retinal field and photoreceptor cells including the mature photoreceptor markers OPN1SW and RHODOPSIN. We routinely observe the generation of RPE in our cultures, an additional replacement cell type required in various forms of retinal degeneration such as AMD. Funded by Fight for Sight UK, we are investigating the engraftment of hESC/hiPSC-derived photoreceptor precursors into animal models of retinal degeneration. Our studies indicate that hESC-derived retinal cells that are injected subretinally into *rd1* mutant mice do settle into the appropriate layer, however so far we have not observed them to acquire the expression of end-stage cone photoreceptor markers.