

Summary



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RPE transplantation by introduction of cells into the subretinal space before substantial photoreceptor loss has occurred , can limit the disease process and functional deterioration. Donor cells include fresh RPE , cryopreserved RPE, Cultured RPE or immortalised RPE cells of animal or human origin, iris pigment epithelial (IPE) cells, stem cells and Schwann cells (*Keegan et al; 2000*).

The transplantation of RPE may done by used allogenic homologus RPE cells or by autologus transplantation. The allogenic homologus transplantation seemed to be a logical approach in restoring vision in patients with AMD by a patch of cultured human fetal RPE placed in the foveal area after membrane excision or by a cell suspension of concentrated dissociated fetal human RPE used to cover a larger area including the fovea (*Algvere; 1999*).

Autologous transplantation has been made to avoid graft rejection. An interesting strategy to eliminate rejection has been the use of autografts of iris pigment (IPE) epithelium to replace defective RPE (*Aisenbery; 2006*).

RPE suspension is done in order to deliver a certain amount of RPE cells under the fovea which can be used as autologous RPE transplantation (*Binder; 2002*). RPE sheets provide a means of transplanting an organized, polarized patch of RPE (*Stanga; 2002*).

Although recovery of vision has been observed in the animal model, only limited improvement has been obtained in AMD patients as transplantation of autologous RPE cells might result in senescent,

dysfunctional RPE phenotype which will not have enough impact on recovering vision in AMD patients because of RPE graft failure (*Boulton et al; 2004*).

There are no established standard treatment modalities for patients with RP as it is characterized by progressive degeneration of the photoreceptors with subsequent degeneration of the retinal pigment epithelium (*Novak-Laus; 2002*). Many researches has focused on the effects of nutritional and drug supplements and their ability to potentially preserve photoreceptor function (*Berson; 2000*).

RPE cell transplantation plays a role as it has been postulated that by replacing damaged photoreceptor cells, new connections can reform and so, improving visual function. Cell transplantation is the re-infusing of cells into a patient in hopes of producing more healthy cells which may replace non-functional cells. The 2 main sources of cells for transplantaion are retinal and stem cells (*Canola et al; 2007*).

Retinal cell transplantation is the introduction of healthy photoreceptor cells into the host (*MacLaren et al; 2006*) while stem cell transplantation is the process whereby a patient receives healthy stem cells which may in turn being producing normal retinal cells (*Das et al; 2005*).

A successful tissue-engineered therapy for the subretinal space would be able to restore vision to patients with advanced RPE and photoreceptor loss. A combined RPE and progenitor cell scaffold would require a thin, flexible and mechanically strong basement layer optimized to support a monolayer of functional RPE cells ,which represent the future direction of RPE transplantation (*Buchholz et al; 2009*).

Once the photoreceptors are lost, the only option is to reconstruct the outer retina, two approaches are explored; one involving transplantation of new photoreceptors either in dissociates or in a retinal sheet and the other to provide a microchip that can take on the phototransduction role and relay information to the CNS sufficient for sensory photoreceptors discrimination (*Li and Turner; 1991*).

Photoreceptors has been prepared using either a vibratome or excimer laser (*Aramant et al ;1999*). Early studies concentrated on injecting cell suspensions or aggregates into the subretinal space. Transcleral and transvitreal techniques have both been tested. (*Sharma and Ehinger; 1997*).

A wide variety of cells have been used in transplantation paradigms aimed at rescuing host residual photoreceptors and delayed the progression of retinal degenerative diseases (*Keegan et al; 2003*). Schwann cells, derived from peripheral nerves, have been used as autologus grafts to rescue photoreceptors (*Pinilla et al; 2009*).

Transplantation aimed at photoreceptor cell “replacement have evolved into clinical trials in humans (*Radtke et al; 2004*). Recovery of visual function is the goal of retinal transplantation, but it does not constitute evidence of graft-host synaptic connectivity sufficient to re-establish retinal neural circuitry since visual recovery might be due to a “rescue” effect rather than a “replacement” effect (*Aramant and Seiler; 2002*).

Identification of the optimal parameters for successful retinal transplantation, such as type of graft or surgical procedure, as well as resolving issue of tissue rejection are important goals, regardless of

whether the objective of surgery is “rescue” or “replacement” (*Khodair et al; 2006*).

Following approximately 20 years of research into RPE transplantation for the treatment of retinal diseases, partial restoration of visual function has been shown in both animal experimentation and human clinical trials. The possibility to combine cell transplantation with other modalities such as gene transfer is continuing to be investigated. The ability of RPE transplantation to restore the subretinal anatomy and improve photoreceptor function in a variety of retinal diseases adds to the already growing list of retinal treatment modalities that will bring hope of stable or restored vision to a large number of patients with currently untreatable and blinding retinal diseases (*da Cruz et al; 2007*).