THE FUTURE OF RETINAL TRANSPLANTATION: TECHNOLOGY OR BIOLOGY
PRO: RETINAL PROSTHESIS IS THE BEST SOLUTION FOR RESTORING SIGHT
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The standard of care of a number of retinal conditions is going through a revolution. In the past, diseases such as retinitis pigmentosa, that caused a dysfunction of the photoreceptors and lead to progressive, yet irremediable blindness, had no cure. Up to date no known treatment exists for these types of conditions. Physicians could only counsel those patients and had to deliver the bad news that "I cannot offer anything to you, you will become blind, try to get used to the white stick". Unfortunately, these patients often left the medical community or gravitated around some esoteric therapies (such as Cuba therapy).

Today, we can offer them medical interventions such as the Argus II retinal prosthesis system that will improve their vision. This medical device sends images directly via electrical currents to the ganglion cells at the surface of the retina. By this it restores a level of functional vision that patients had lost many years in the past. It is backed by 10 years of clinical data, was demonstrated safe and effective. Patients have used it for up to 8 years, and continued to provide a benefit. Additionally, Chow et al have demonstrated that such devices could preserve the architecture of the retina and mitigate some of the second order changes that happen during the degeneration process.

Three other approaches have been described to treat those patients. The first is the correction of biochemical abnormalities that leads to the dysfunction of the photoreceptors by gene therapy. The second is geared toward arresting or slowing the progressive degeneration of photoreceptors. The third approach aims to regenerate lost (or maldeveloped) photoreceptors by means of transplantation of stem cells or genetic manipulation.

Correcting the biochemical abnormalities was tried in a severe form of Leber’s congenital amaurosis. A normal RPE65 gene was delivered under the retina by intraocular injection. This has successfully and safely corrected dysfunction of the visual cycle in patients. There is evidence of visual gain in the short term, but the long term incidence of tumorigenesis remains a concern for the clinical applicability of this approach. The regulatory hurdle and the clinical validation will make this approach very expensive and restricted to a single of the 100 documented mutation causing retinitis pigmentosa. The economic prospects of the gene therapy in retinitis pigmentosa are likely to be a million dollars treatment.

Slowing or arresting the progressive degeneration of photoreceptors is interesting and the most promising of such approaches is that of Rod-derived Cone Viability Factor. The demonstrations at the functional level of the therapeutic potential of RdCVF in mice model show the potential for preserving central vision in some RP patients. The current stage of development allows considering a clinical application in the next decade. There is one major drawback of this drug: It cannot revert the vision for patients whose vision deteriorated beyond utility.

Regenerate lost photoreceptors by means of transplantation of stem cells are also an interesting approach. The use of placenta cell injection that developed in the mid seventies was in a way the initial steps that lead to the current interests. Skeptics claim that twenty years of research has not produced a single approved treatment or human trial using stem cells. The key challenge is to promote optimal integration and differentiation of transplanted stem cells, in order to generate functional photoreceptors and repair degenerating retina. The key controversies are that the side effects of cell therapy are quite severe: It tends to produce tumors and malignancies, cause transplant rejection, and form the wrong kinds of cells. Thus, it is unlikely that this strategy will find its way into clinics during the next decade.

The main opportunity is to consider how these approaches can be integrated and could be deployed in synergetic fashion. It is obvious that retinal implants will be used to promote the integration of stem cells. In addition, retinal implants may be perfect devices to deliver drugs that could slow the progress of the disease.

However, at this time the only realistic approach to help patients whose vision is already deteriorated is the surgical application of retinal prosthesis system.