Novel Strategies for Optic Neuroregeneration and Retinal Projection Reintegration After Ocular Trauma

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Institution Receiving Award: PITTSBURGH, UNIVERSITY OF
Program: PH-TBI
Proposal Number: MR130120
Award Number: W81XWH-14-1-0488
Funding Mechanism: Vision Research Program - Translational Research Award
Partnering Awards:
Award Amount: $999,995.00

PUBLIC ABSTRACT

Objectives and Rationale: The primary objective of this research is to develop methods that can be used to restore vision to victims of eye, retina, or optic nerve damage. At the present time, there are no treatments to restore vision after traumatic or ischemic damage to the eye or optic nerve or resulting from degenerative diseases such as glaucoma, age-related macular degeneration, or most forms of retinitis pigmentosa. Eye transplantation would represent a novel and comprehensive way to restore vision irrespective of the cause of the loss. The major obstacles to such an approach include the inherent inability of nerve cells in the eye to regenerate injured axons (nerve fibers) through the optic nerve and to re-establish connections with the correct areas in the brain that process visual information from the eye, the hurdles in re-establishing the blood supply to a transplanted eye, and possible rejection of the transplanted eye by the recipient's immune system. This project will bring together leading investigators with expertise in these areas. The proposed studies will optimize methods to maintain the viability of the retina and other structures of the donor eye, re-establish the blood supply to the donor eye, promote the regeneration of injured nerve fibers from the donor retina to the correct target areas in the host brain, and evaluate the integration of visual signals from the donor eye into the host brain using objective tests of visual function.

Ultimate Applicability and Potential Impact of the Research: Ocular trauma due to occupational, accidental, or violent trauma is a major cause of visual impairment in the United States, second only to cataract, with permanent vision loss in over one million civilians per year (American Society of Ocular Trauma Data). Combat ocular trauma is more severe and ranges from perforations to open-globe injuries and ruptures. Overall, ocular trauma has a very poor prognosis despite the best available interventions, with very high impact on medical care, vocational rehabilitation, and socioeconomic costs. In addition, despite huge advances in vision research in the past two to three decades, we have not yet translated from bench-to-bedside treatments for vision loss due to degenerative cell loss, as occurs in age-related macular degeneration, glaucoma, or other diseases. Beyond these problems, millions lose vision due to systemic diseases that affect the retina or optic nerve like diabetes, hypertension, or multiple sclerosis.

Whole Eye Transplantation (WET) is the holy grail of vision restoration regardless of the underlying etiology. However, WET requires paradigm-shifting, seamless transition of innovation to clinical implementation of conventional and cutting-edge techniques to renew, restore, and recreate vision where conventional options have been exhausted. Along the way, we will undoubtedly encounter problems, some of which can be foreseen and some that are unanticipated and unprecedented. Potential risks include immune rejection and graft failure, from immune or vascular complications. Nonetheless, we believe that this research in experimental animal models is an important first step towards enabling ultimate WET in the clinical setting. The insights gained in the process will help us better advance strategies for vision restoration in millions of patients with no recourse for their vision loss. We estimate that we will achieve optimal success in WET in animal models within 3-5 years and clinical translation in 4-10 years.
Benefit to Service Members, Veterans, and/or Their Family Members: Ocular injury from blast exposure and post-traumatic vision syndrome arising from traumatic brain injury represent significant causes of visual morbidity among service members. Such injuries prevent return to duty, compromising years of training and expertise. More importantly, the functional limitations of vision loss/dysfunction result in significant personal, professional, and psychosocial impairments. Many patients have penetrating globe trauma with neuro-ophthalmologic injury resulting in very poor best-corrected visual acuity consistent with devastating visual loss. Currently, there is no conventional treatment to recover lost function of the eye or optic nerve. The proposed research will address this need. WET might also be considered as a way to restore visual function in other conditions that result in irreversible losses in vision such as glaucoma, macular degeneration, retinal artery and vein occlusions, ischemic optic neuropathy, and diabetic retinopathy, among others.