Vision Research Portfolio
Congressionally Directed Medical Research Programs
Telemedicine and Advanced Technology Research Center

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U.S. Army Medical Research and Materiel Command
The mission of the U.S. Army Medical Research and Materiel Command (USAMRMC) is to provide medical knowledge and materiel lifecycle management to protect, treat, and optimize warfighter health and performance across the full spectrum of operations. As part of that mission, USAMRMC manages research focused on vision-related issues, principally through specific appropriations from Congress, congressional special interest (CSI) medical research programs, administered by the Office of the Congressionally Directed Medical Research Programs (CDMRP) and the Telemedicine and Advanced Technology Research Center (TATRC). Much of this research addresses the needs of the warfighter, other Armed Forces personnel, and the Veteran population.

CDMRP manages congressionally directed peer-reviewed programs that solicit proposals through open competitions in an effort to find and fund the best research to eradicate diseases and support the warfighter for the benefit of the American public. CDMRP has a total of fourteen vision-focused research projects within its portfolio, for a total of approximately $19 million (M). These projects were funded through two separate programs, the Peer Reviewed Medical and the Psychological Health/Traumatic Brain Injury Research Programs.

TATRC manages congressionally mandated advanced technology projects including the identification, exploration, and demonstration of key technologies that will reduce the medical “footprint” and increase medical mobility, while ensuring that warfighters have access to essential medical expertise and support wherever they deploy. TATRC has a total of twelve vision-focused awards within its portfolio, totaling approximately $64M; six large awards (totaling $62.5M) were funded by CSI appropriations, while six smaller projects (totaling $1.2M) were funded as TATRC-identified gap areas.

http://cdmrp.army.mil
http://www.tatrc.org
Research Investment

Combined, CDMRP and TATRC have managed 26 vision research awards in the last decade, totaling about $83M in Congressional appropriations. Both organizations have additional awards to be funded for Fiscal Year 2008 (FY08).

New Preventive and Therapeutic Approaches
Eye injuries, especially corneal damage, are the result of trauma, infection, and chemical or thermal (including laser-induced) burns. Battlefield injuries to the eye mostly occur on the cornea and retina through trauma to the head and laser-related exposures. These injuries are usually treatable, but can lead to blindness because of the collateral damage to tissues surrounding the injured area. The resulting state of significantly reduced visual function occurs from injury-induced inflammation, cell death, failure to regenerate or repair, and development of scar tissue. Developing effective treatments that would preserve vision will benefit not only United States military and support personnel at risk on the battlefield, but also civilian populations. Investigators funded by CDMRP and TATRC are developing new preventive methods and novel therapeutic approaches to preserve vision.

Autonomic Biomarkers Military Vision Research Program
Darlene A. Dartt, Ph.D., Schepens Eye Research Institute
FY00, 01, 05, 06, 07, 08 $10.72M (TATRC)
Scientists are developing strategies to enhance the current low vision capabilities to minimize low vision that can occur in military battlefield environments. Two focus areas are: (1) augmented vision and (2) protection and treatment to preserve vision after injury.
Triage and Treatment of Laser Eye Injury on the Modern Battlefield
Thomas Johnson, Ph.D., Colorado State University

FY02 Investigator-Initiated Research Award $1.60M (CDMRP)
The objectives of this proposal are to: (1) determine how laser energy is deposited in tissue, how that energy affects the site of deposition, and how energy deposition leads to injury, (2) develop techniques for performing triage on corneal injuries, (3) develop battlefield treatments utilizing medications and materials currently carried by medics, and (4) determine the medications and treatments carried by a medic that are contraindicated. These studies revealed that a non-biological system (ZAP-IT paper), which allows a thermally-based estimate of laser beam image and size, can be useful in predicting laser-induced eye damage. Additionally, data indicated that a combination of steroids and antibiotics resulted in better healing of corneal injury than either treatment by itself.

Molecular Solutions to Low Vision Resulting from Battlefield Injuries
Darlene A. Dartt, Ph.D., Schepens Eye Research Institute

FY03 Investigator-Initiated Award $2.99M (CDMRP)
The intent of this study is to investigate the effect of battlefield trauma on corneal, retinal, and optic nerve function and on dry eye after refractive surgery with the goal of developing a molecular solution to prevent or reverse damage. The hypothesis is that targeted molecular interventions can preserve vision threatened by trauma-induced corneal and retinal inflammation, corneal and retina/optic nerve apoptosis, ocular surface dry eye after refractive surgery, and retinal degeneration.

Treatment of Laser-Induced Retinal Injury and Visual Loss Using Sustained Release of Intra-Vitreal Neurotrophic Growth Factors
Randy H. Kardon, M.D., Ph.D., University of Iowa and Veterans Administration

FY06 Investigator-Initiated Research Award $0.58M (CDMRP)
This study will test the treatment effect of sustained-release intra-vitreal neurotrophic growth factor(s) on the preservation and recovery of visual function and structure in a canine model of laser-induced retinal injury. The successful outcome will allow the development of an injectable treatment of laser-induced retinal damage to humans, even under battlefield conditions.
**Improved Therapeutic Regimens for Treatment of Post-Traumatic Ocular Infections**  
Michelle Callegan, Ph.D., University of Oklahoma Health Sciences Center  
*FY06 Investigator-Initiated Research Award $0.90M (CDMRP)*  
The objective of this research is to identify effective therapeutic regimens that will prevent vision loss and inflammation during a Bacillus endophthalmitis infection. A number of therapeutic agents, drug combinations, and regimens will be tested to identify the most effective in preserving vision, arresting inflammation, and limiting intraocular damage.

**Intraceptor Interference of VEGF Pathways in Corneal Angiogenesis**  
Balamurali Ambati, M.D., Medical College of Georgia  
*FY06 Investigator-Initiated Research Award $0.72M (CDMRP)*  
This proposal hypothesizes that intracellular autocrine loops are part of VEGF signaling in cornea. The goal of the project is to disrupt intracellular VEGF and VEGFR-2 expression, which may represent an important modality in treating disorders involving angiogenesis, in vascular endothelial cells in vitro and in the injured cornea in vivo. By exploring a novel avenue of anti-angiogenic therapy, this project will hopefully add to the therapeutic arsenal for corneal injury and transplant rejection, macular degeneration, and diabetic retinopathy.

**Repair of Corneal Injury with Stem Cell-Based Bioengineered Tissue**  
De-Quan Li, M.D., Ph.D., Baylor College of Medicine  
*FY06 Investigator-Initiated Research Award $0.90M (CDMRP)*  
The long-term objective of this research project is to bioengineer stem cell-based corneal constructs using human limbal epithelial progenitor cells (LEPC). The goal is to use these LEPC-derived corneal constructs for therapeutic repair of corneal injury.

**Identification of ABCG2 as a potential marker for corneal epithelial stem cells**

**Molecular Blockade of Lymphangiogenesis in Promoting High-Risk Corneal Transplant Survival**  
Lu Chen, M.D., Ph.D., University of California, Berkeley  
*FY06 Investigator-Initiated Research Award $1.17M (CDMRP)*
Sight Restoration Technologies and Prosthetics Development

In the industrialized world, retinal disease is the major cause of blindness, and currently there is no cure or treatment available for these patients. An estimated 1 million adults in the United States (which includes 160,000 Veterans) are blind. Over the last 15 years, active military personnel have suffered from substantially increased risk of blindness, mostly from ocular blast injuries and laser-induced retinal injury. Investigators funded through CDMRP and TATRC are using a variety of approaches to treat blindness. Some examples include the development of a microelectronic, implantable device designed to interface directly with the retina, microelectrodes that electrically stimulate the visual cortex in the brain, and a biocompatible, electrochemical implantable muscle stimulation system that would restore motion to paralyzed muscle in a painless and more natural manner.

Sight Restoration by Electrical Stimulation of Visual Cortex via Arrays of Penetrating Microelectrodes
Richard Norman, Ph.D., University of Utah Moran Eye Center
FY05-FY07 $0.50M (TATRC)

A systematic experimental approach is being employed to define the design parameters needed to implement a functional visual neural prosthesis, using behavioral responses to indicate what patients perceive in response to patterned electrical stimulation of the cortex. Investigators will then determine the design parameters for a functional visual neural prosthesis and study its safety and efficacy.

A Hybrid Electrochemical Microstimulator Implant for Denervated Muscles
Kimberly Cockerham, M.D., VA Health Care System, Palo Alto
FY06 Advanced Technology: Product/Technology Down-Selection or Optimization Award $1.21M (CDMRP)

The long-range objective of this project is to develop a hybrid implantable microstimulator system that will act as a stimulus for denervated muscles, by mimicking the natural stimulation that occurs at neuromuscular junctions.
Retinal Prosthesis - Modular and Configurable
Joseph Rizzo, M.D., Massachusetts Eye and Ear Infirmary, Harvard Medical School
FY06 $1.43M (TATRC)
Optimization of Microelectronic Methods to Produce an Implantable Retinal Prosthesis to Treat Blindness
FY06 Advanced Technology: Product/Technology Down-Selection or Optimization Award $1.24M (CDMRP)

This project focuses on developing a retinal prosthesis that may be used to treat several forms of retinal blindness that are currently untreatable, including blindness caused by battlefield laser injury to the retina, and military-related, blast-induced blindness. The implantable prosthetic will be a microelectronic device designed to interface directly with the retina. This device will: (1) capture visual images, (2) communicate the images to electronic components that interface with the retina, and (3) selectively deliver electrical pulses to the retina to create vision. It intends to permit “customizable” adjustments to accommodate the unique visual needs of each patient and improve their quality of life.

Graphic images of the designs of the Boston Retinal Implant Project. Left. Glasses support a small camera (red arrow) that collects visual images. Middle. A wire (white arrow) extends along the length of the sidebar to an external processing unit (not shown). Also embedded are two “primary” radiofrequency (RF) coils (yellow arrow). Right. The “secondary” RF coils (yellow arrow) are positioned just behind the circumference of the cornea. The titanium case (white arrow) provides a hermetic environment for the integrated circuit chip. The electrode array enters the eye through a small slit (red arrow) in the sclera.

Replicating Physiological Patterns of Activity with Prosthetic Stimulation
Shelley Fried, Ph.D., Boston VA Research Institute, Inc.
FY06 Investigator-Initiated Research Award $0.75M (CDMRP)
The hypothesis for this study is that specific morphological features and biophysical properties of the ganglion cell shape its response to electric stimulation. The goal is to develop methods to create specific patterns of activity in retinal ganglion cells with a prosthetic device that will replicate the patterns created by the normal retina in response to light.
**Telemedicine Ideas**

Telemedicine, a rapidly developing application of clinical medicine, has the ability to provide interactive multidisciplinary healthcare, utilizing modern technology and telecommunications. As diagnosis and treatment of many ophthalmologic diseases are not widely available in rural communities, telemedicine technologies can help deliver these important services. Additionally, mobile technologies would enable wireless and/or remote monitoring of a person’s health and/or environment, from the battlefield to the hospital to the home. By reducing barriers to eye care, telemedicine facilitates both early detection and appropriate and timely referral for treatment. Investigators funded through TATRC are developing telemedicine systems to aid the distance diagnosis of complicated ocular diseases.

**Diabetes Care and Treatment Project: A Joslin Telemedicine Initiative**

Joslin Diabetes Center, Boston VA, Walter Reed Army Medical Center and the University of Hawaii

*FY98-FY07 $41.34M (TATRC)*

Researchers have developed a telemedicine system for comprehensive diabetes management, and the assessment of diabetic retinopathy that provides increased access for diabetic patients to appropriate care. The system will: (1) centralize the patients in the care process, (2) empower the patient to better manage their disease, (3) perform the care in a cost-effective manner, and (4) maintain the high standard of care required for the appropriate management of diabetic patients.

**Tele-ophthalmology: Enhancing Care and Education for Military Medicine**

Robert Sergott, M.D., Wills Eye Institute

*FY04-FY07 $7.21M (TATRC)*

Researchers are establishing a cost-effective platform that will rapidly diagnose patients with common, costly diseases such as diabetes mellitus and other complicated ophthalmologic problems. In addition, they have developed a distance learning program that is available to all military ophthalmologists.

**Web-based Refractive Surgery Information System (RSIS) Initiative**

TATRC Internal Project

*FY04 $19K (TATRC)*

This project is focused on creating a web-based information system for refractive surgery patient examinations, pre-operative, surgery, and post-operative visits to Army Warfighter Refractive Eye Surgery Program (WRESP) centers. This system will contain patient demographic data, physical examination findings, and results of pre-operative and post-operative evaluations, therapeutic plans, and follow-up information. The internet will add dimension to RSIS in that the eye care providers will be able to access charts from remote locations, and transfer clinical information and images such as orb scans and pre-operative corneal topography to colleagues or sub-specialists when a second opinion is needed.
Centers of Excellence
Centers of Excellence managed by TATRC are accelerating the solution of major overarching questions that will have a significant impact on the prevention, detection, diagnosis, and/or treatment of eye diseases.

National Eye Evaluation Research (NEER) Network for Clinical Trials in Retinal Degenerative Diseases
Stephen Rose, Ph.D., National Neurovision Research Institute
FY06-FY08 $9.73M (TATRC)
NEER is establishing a network of five clinical treatment and evaluation centers (CTECs) to study retinal degenerative diseases. The network will advance the science of therapeutic and preventive interventions for inherited orphan retinal degenerative diseases and dry, age-related macular degeneration through conducting clinical trials.

Center for Ophthalmic Innovation (ONOVA)
Byron Lam, M.D., Bascom Palmer Eye Institute
FY08 $1.70M (TATRC)
Scientists are establishing a Center of Excellence with focus areas in: (1) telemedicine, (2) eye trauma and visual restoration, (3) ocular microbiology and immunology, and (4) ocular imaging and hereditary retinal disease.

Enhancing Knowledge
Proficiency in ophthalmic surgical skills remains vitally important because training surgeons outside of the operating room may reduce errors inside the operating room. Traditionally, residents have obtained and fine tuned their surgical skills and techniques working on the eyes of animals. Ophthalmic surgical simulators enable the surgeon to practice intraocular surgical techniques with the use of instruments that feel and function much like their real world counterparts. Training can include basic surgical techniques and enables trainee surgeons to become familiar with handling rare cases and possible complications. Using a surgical simulator, a trainee can repeatedly experience live tissue reactions that occur during surgery. The virtual ocular environment realistically depicts the anatomical structure and three-dimensionality of the intraocular space, as well as the physical behavior of delicate tissues. Investigators funded through TATRC are developing ophthalmic surgical simulators that would enhance patient safety and improve patient care.

International Military Refractive Surgery Symposia
Elizabeth Hofmeister, M.D., T.R.U.E. Research Foundation
FY06-FY08 $60K (TATRC)
The symposia bring together tri-service and international military eye care specialists to share knowledge and training with the intent of providing the best care in refractive surgery. Presentations at the meetings have focused on: (1) research results, (2) medical issues related to refractive surgery, (3) policies governing refractive surgery, and (4) insights gained from treatment in allied countries.
Virtual Mentor Cataract Surgery Trainer
John Loewenstein, M.D., Massachusetts Eye and Ear Infirmary
FY07 $0.20M (TATRC)
This residency program leader is developing a content-based curriculum to teach cataract surgery through virtual means. The application will include a library of video links that demonstrate expert techniques and discuss, in depth, various details of each simulated scenario.

An Ophthalmic Surgical Simulator
Karl Reinig, Ph.D., Touch of Life Technologies
FY07 $0.20M (TATRC)
Clinicians are developing a simulator that can be used by students to practice ophthalmic surgical skills. Initially, this ophthalmic simulator will allow students to practice globe repair, most steps of phacoemulsification, and ultrasound for diagnosis and measurement. The simulator will be coupled with a mentor program, which combines HyperText Markup Language (HTML), interactive anatomic animations, and direct proficiency measures from the simulator.

New Developments for Injury Evaluation
The use of lasers by both the military and civilian community is rapidly expanding; thus, the potential for laser eye injury and retinal damage is increasing. Sensitive and accurate methods to evaluate and follow laser retinal damage are needed. Investigators funded through CDMRP and TATRC are developing and improving technologies to diagnose and evaluate laser-induced eye damage. Additionally, CDMRP is managing awards that use eye function as a diagnosis for Traumatic Brain Injury (TBI). These studies will hopefully develop a device that can diagnose attention and memory problems caused by concussion. An accurate and rapid measure of attention is essential in military operations to prevent injury and re-injury, to detect TBI, and to distinguish TBI from Post Traumatic Stress Disorder (PTSD) and fatigue. Studies will also characterize and define the temporal window of brain vulnerability to repeated blast overpressure.

Development and Implementation of an Objective, Non-invasive, Behaviorally Relevant Metric for Laser Eye Injuries
Gary Martinsen, O.D., Ph.D., Air Force Research Laboratory
FY01 Investigator-Initiated Award $0.76M (CDMRP)
The objective of this study is to determine whether the current multifocal electroretinogram (MERG) is sufficiently sensitive to provide an objective, noninvasive metric for the effects of localized retinal laser injury that correlates with perceptual deficits in the same eye, and whether the MERG can quantitatively assess the natural time course of recovery from retinal laser injury as measured by both optical coherence tomography images and behaviorally assessed visual acuity and contrast sensitivity.
Corneal Damage from Mid-Infrared Laser Radiation
Russell L. McCally, Ph.D., Johns Hopkins University
FY01 Investigator-Initiated Research Award $0.55M (CDMRP)
The purpose of these research studies is to assess the health effects and hazards of non-ionizing electromagnetic radiation from laser systems. Three main hypotheses are considered within this proposal: (1) damage from 1.55 micrometers radiation is thermal, (2) damage from sequences of pulses is cumulative and (3) exposures only slightly above the damage threshold for the corneal epithelium will result in damage to the corneal endothelium for these penetrating wavelengths.

Development and Application of Advanced Ophthalmic Imaging Technology to Enhance Military Ocular Health Capabilities
Shulang Jiao, M.D., Bascom Palmer Eye Institute
FY06 $0.20M (TATRC)
This project is designed to improve on current imaging technology with optical coherence tomography. Researchers are developing advanced instrumentation and new software applications to enable high resolution evaluations of the retina and optic nerve that could be easily performed by non-physician health care professionals. In addition, this technology could be potentially applied for telemedicine transmittal of images (from the battlefield or other remote sites) for further evaluation by ophthalmology specialists.

Eye-Tracking Rapid Attention Computation
Jamshid Ghajar, M.D., Ph.D., Brain Trauma Foundation, Inc.
FY07 TBI Advanced Technology-Therapeutic Development Award $4.64M (CDMRP)
This project is designed to develop an eye-tracking device that will quickly diagnose subtle attention deficits that occur in TBI. The proposed device may also be able to help diagnose and distinguish between TBI, PTSD, simple fatigue, and aging.

Brain Vulnerability to Repeated Blast Overpressure and Polytrauma
Joseph B. Long Ph.D., Walter Reed Army Institute of Research
FY07 Intramural TBI Investigator-Initiated Research Award $1.02M (CDMRP)
Using a preclinical rat model of blast overpressure, this study will evaluate and compare the cumulative effects of single and multiple air blast exposures on acute physiological responses, visual acuity, and neurobehavioral and histopathological outcome measures. Repeated exposures to blast overpressure of differing intensities with varied inter-blast intervals will also be used to identify a temporal window of brain vulnerability to repeated blast overpressure. Data from this study will provide a critical first step in establishing rational risk guideline.