## Deployment Related Medical Research Program

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<tr>
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The Congressionally Directed Medical Research Programs (CDMRP) was born from a powerful grassroots effort led by the breast cancer advocacy community that convinced Congress to appropriate funds for breast cancer research. This enabled a unique partnership among the public, Congress, and the military. In fiscal year 1993 (FY93), the CDMRP was created as an office within the U.S. Army Medical Research and Materiel Command (USAMRMC) to manage these funds. Since that time, the CDMRP has grown to encompass multiple targeted programs and has received approximately $6 billion (B) in appropriations from FY93 through FY10. Funds for the CDMRP are added by Congress to the Department of Defense (DOD) budget where support for individual research programs is allocated via specific guidance from Congress. The CDMRP manages these programs, under the auspices of USAMRMC, from receipt of funds through individual project performance to award closeout. Through FY09, approximately 9,934 awards have been made to advance health care solutions via extramural grants, contracts, and cooperative agreements.

**HISTORY**

**VISION**

To improve the health and/or mitigate injury of deployed military personnel and their family members by finding new solutions to the prevention, diagnosis, and treatment of deployment-related injuries and psychological challenges.

**BACKGROUND**

The Deployment Related Medical Research Program (DRMRP) is one of the medical research programs administered by the CDMRP. This program was established in FY08 to advance the health and welfare of deployed military personnel and their families. These funds are targeted for peer-reviewed research relating to emergent approaches and technologies using approximately $92 million (M) of the $273M appropriated in the Supplemental Appropriations Act of 2008 (Public Law 110-252) to the DOD.

In August 2008, the DRMRP released Program Announcements soliciting research proposals in response to three award mechanisms. These award mechanisms challenged the scientific and clinical communities to develop innovative ideas that will advance the delivery of emerging new approaches, technologies, and agents to the military through basic science, translational, and/or clinical research.
Hypothesis Development Award: Provides support for the initial exploration of innovative, untested, potentially groundbreaking concepts that may lead to promising new products, pharmacologic agents (drugs or biologics), behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies for deployment-related health care issues within the FY08 DRMRP topic areas.

Advanced Technology/Therapeutic Development Award: Provides support for the assessment of scientific and/or military field deployment feasibility for promising new products, pharmacologic agents (drugs or biologics), behavioral interventions, devices, clinical guidance, and/or emerging approaches and technologies. These awards are expected to yield potential deployment-related health products, approaches, or technologies positioned for human testing.

Clinical Trial Award: Supports rapid implementation of clinical trials with the potential to have a significant impact on a disease or condition addressed in one of the FY08 DRMRP topic areas. All proposed clinical trials must be responsive to the health care needs of deployed members of the Armed Forces and may address prevention, detection, diagnosis, treatment, and/or quality of life.

DRMRP Research Topic Areas

DRMRP funds for FY08 were directed toward a variety of topic areas relevant to the health and welfare of deployed military personnel and their families. As such, all research funded by the FY08 DRMRP must specifically and clearly address one of the following deployment-related topic areas:

- Blood safety and blood products
- Injury prevention
- Final development of medical devices for use in theater (including portable suction machines and electrocardiograms for theater hospitals)
- Wound infection vaccines
- Traumatic brain injury and psychological health (including post-traumatic stress disorder)
- Wound infection and healing
- Trauma treatment and rehabilitation (including face, visual/ocular, and nerve damage; dental; and auditory systems)
### DRMRP Research Gaps

Together with USAMRMC staff and lead scientists of USAMRMC Research Area Directorates, specific research gaps were identified within the specific topic areas.

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| **Blood Safety** | • Pathogen inactivation of platelets  
               • Pathogen inactivation of whole blood |
| **Blood Products** | Freeze-dried plasma products with the following characteristics:  
               • Human plasma derived  
               • Pathogen inactivated or pathogen free  
               • Temperature stable  
               • Lipid reduced |
| **Injury Prevention** | Biomedically valid computational models of blast-related injuries that can be used to design, build, and test:  
               • Personal protection systems, such as combat helmets and body armor  
               • Combat vehicle protection systems, such as blast-attenuating seats |
| **Final Development of Medical Devices for Use in Theater** | U.S. Food and Drug Administration (FDA)-approved, rapid detection, multiplex/multiagent, handheld systems designed to screen whole blood pre-transfusions and accurately detect bloodborne pathogens with a high degree of sensitivity and specificity for use far-forward in a wartime environment  
               • Highly portable, autonomous or semiautonomous ventilation and resuscitation systems  
               • Web-based, telemedicine modality clinical technologies |
| **Wound Infection Vaccines** | • FDA-approved vaccines to prevent sepsis caused by gram-negative bacteria  
               • FDA-approved vaccines to prevent *Staphylococcus aureus* infection; priority will be given to those vaccines that also include protection against methicillin-resistant strains  
               • Others as appropriate |
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| Traumatic Brain Injury  | • Epidemiology with emphasis on battle-induced mild traumatic brain injury (mTBI) and post-traumatic stress disorder (PTSD) analyzing the occurrence and development of symptoms including, but not limited to, repetitive injury, sleep disturbances, and cognitive and emotive symptoms (e.g., risk-taking behavior and substance abuse); effort should be directed to determining the actual incidence of mTBI on the battlefield, its effects on performance of mission, and its long-term sequelae  
• Phase II or III clinical trial(s) for pharmacological treatment of TBI including single or combination therapies  
• Impact of patient transport (e.g., ground and rotary/fixed-wing aircraft) on moderate and severe TBI, and techniques and/or therapies designed to reduce negative impact  
• A simple, quantitative, noninvasive method to diagnose mTBI that can be used for deployed troops  
• Sensors, including accelerometers and dosimeters, to measure blast and predict the occurrence of TBI  
• Efficient clinical diagnostic criteria methodologies for detecting mTBI while distinguishing it from psychological comorbidities (i.e., depression and PTSD)  
• Pain management to improve short-term outcomes and reduce the risk of long-term opioid dependence and/or abuse  
• Innovative therapies for TBI, including hyperbaric oxygen therapy and complementary and alternative medicine  
• Impact of rehabilitation strategies on neural plasticity and neurogenesis following TBI, using imaging, neurobiological, cognitive, and pharmacotherapeutic approaches so as to improve quality of life or ability to function in home and community life  
• Conclusive data on the existence and tissue-level mechanisms of nonimpact, blast-induced mTBI to support the development of effective preventive measures, diagnostic tools, and treatments |
| Wound Infection and Healing | • Improve wound healing and clinical outcomes by evaluating the role of topical nitric oxide and hyperbaric oxygen to disinfect blast wounds  
• New treatment protocols, drugs, biologics, and devices to reduce wound-related infections and accelerate wound healing  
• Approaches to prevention or treatment of bone infections  
• Methods and technologies for prevention of the formation of bacterial biofilms in wounds and colonization of orthopedic devices  
• Evaluation of oral and topical nutritional supplements and over-the-counter products (e.g., zinc, silver, and lysine) to accelerate wound healing and enhance a patient's immune status  
• Methodologies that will predict clinical outcomes of blast-induced wound infections; approaches of interest include methodologies to assess total bacterial load in wounds and identification of critical biomarkers that predict outcomes related to wound infection |
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| **Psychological Health, Including Post-Traumatic Stress Disorder** | • Clinical trials focused on universal and selective interventions for prevention of combat deployment-related mental health and postdeployment reintegration concerns  
• Clinical trials for the treatment of combat-related psychological health problems, including PTSD and depression, and comorbid psychosocial disturbances among Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF) veterans  
• Evidence-based screening, brief interventions, and referral for treatment among service members that can be employed across levels of care, care providers, and deployment cycle with particular emphasis placed on postdeployment  
• Clinical rehabilitative-treatment trials to treat and manage combat-related persistent or chronic postconcussive symptomology, or co-occurring physical and mental health symptoms  
• Evidence-based interventions to provide “care for the caregiver,” focusing on reducing physical and psychological stress among primary care providers, nurses, mental health providers, and chaplains involved in the care of OIF/OEF service members  
• The impact of military life on quality-of-life/health indices among spouses, partners, caregivers, and/or co-resident family members |
| **Trauma Treatment and Rehabilitation, Including Nonsurgical Orthopedic Conditions** | • Prosthetics  
• Prevention and rehabilitation strategies designed to minimize bone loss and prevent heterotopic ossification following amputation  
• Assessment tools that incorporate simultaneous physical and cognitive demands for use in monitoring clinical performance outcomes and return-to-duty status  
• Comparison of the effect of known resuscitation adjuncts, drugs, and biologics via a realistic animal model of hemorrhage and tissue injury with the goal of getting a lifesaving, noncoagulopathic drug into clinical trials and through FDA certification quickly  
• Characterization of oral, maxillofacial, and craniofacial injuries, including treatment needs, prosthetic replacements required, treatment costs, and long-term patient morbidity from combat injuries, and biocompatible craniofacial implants for use in craniofacial reconstruction due to combat trauma  
• Characterization of physical, mechanical, and aesthetic properties of human skin in the subject population ages 17–45  
• Treatments and techniques to prevent and treat penetrating eye injuries  
• Novel rehabilitation techniques, including virtual reality, nonsurgical treatment of extremity injuries (e.g., novel physical therapy techniques), for the mental and physical rehabilitation of those other than amputees to facilitate recovery and return to duty  
• Novel approaches for repair and treatment of nerve damage, including nerve regeneration and nerve grafting  
• Surgical and nonsurgical approaches to the treatment of combat-related middle and inner ear trauma, including reconstruction, replacement, or augmentation of hearing structures |
Proposal review for all submissions was conducted using a modified version of the USAMRMC two-tier review model recommended by the Institute of Medicine. This two-tier review model has received high praise from the scientific community, advocacy groups, and Congress. The first tier was the scientific peer review of proposals against established criteria for determining scientific merit. For the DRMRP there was also a separate military relevance review of proposals against criteria for determining the relevance of the proposed research study to the military community. The results of these two review sessions were aligned by the Joint Program Alignment Peer Review Panel.

The combined results of these peer review processes were passed along to the Joint Senior Leadership Integration Panel (JSLIP) for the second tier of review, programmatic review. The JSLIP compared proposals to each other and recommended proposals for funding based on the recommendations of the peer review panels, responsiveness to the DRMRP topic areas and research gaps, programmatic relevance, adherence to the intent of the award mechanism, and program portfolio balance. Following programmatic review, those proposals that best fulfill these criteria and most effectively address the unique focus and goals of the program were recommended for funding to the final approval authority, the Deputy Assistant Secretary of Defense for Force Health Protection and Readiness.
Consumer Advocates Role in the DRMRP

Consumer advocates for the DRMRP represent the voice and vision of deployed military personnel. Individuals or family members of individuals who have experienced or are experiencing trauma and/or injuries related to deployment participate as consumer advocates in practically every aspect of program execution. In addition, medics who administer care on the front lines participated in the scientific and military relevance review of proposals to lend their perspective. They work collaboratively with leading scientists and clinicians in evaluating proposed research and recommending proposals for funding.

A Consumer’s Perspective...

Wounded Warrior, Heart of a Champion: Melissa Stockwell

On April 13, 2004, 1st Lieutenant Melissa Stockwell’s life changed forever. Deployed to Iraq 3 weeks earlier, she was working as a transportation officer leading supply convoys from one point to the next. On that fateful day, Melissa was traveling on a routine convoy through central Baghdad when her Humvee was hit by a roadside bomb. The bomb, and subsequent injuries, resulted in amputation of her left leg above the knee during emergency, lifesaving surgery at the American hospital in Baghdad. She was soon transported home from Iraq for treatment at the Walter Reed Army Medical Center. Melissa spent the next year recovering from infections, regaining her strength, learning to walk with a prosthetic leg, and becoming independent again. A positive, motivated attitude helped her to resume a normal life and to dream of even greater things. Once she began walking with a prosthetic leg, her lifelong passion for sports and the thrill of competition drove her to get back in the game. With the help of the Wounded Warrior Project, Disabled Sports USA, and Achilles, it was not long before she was skiing the mountains of Breckenridge, Colorado, and running in the NYC marathon. “I really learned that losing a leg didn’t have to stop me from doing anything I wanted to do with my life. In the year after my injury, I had already done more with one leg than I ever would have imagined doing with two legs.”
In April 2005, Melissa medically retired from the U.S. Army, earning a Purple Heart Award and a Bronze Star Medal. She decided to return to school to become a prosthetist, learning how to fit other amputees with artificial limbs. Throughout her recovery, her love of sports never wavered. Soon after school started, she learned about the Paralympics, the international competition for athletes with physical disabilities. This was a venue for her to not only compete on the second largest athletic stage in the world (second only to the Olympics), but one in which she could once again proudly wear the uniform of her country. With the support of her family and friends, her hard work and dedication to practicing endless laps in the pool helped her to achieve her dream of making the 2008 U.S. Paralympic swim team. “Competing in Beijing was one of the most incredible things I have ever done and [I] will take my experiences there with me wherever I go.”

After the Beijing Paralympics, Melissa returned home to Chicago to resume her training as a prosthetist and to continue her athletic goals. Soon after she returned, she learned of the CDMRP and took part in her first session as a consumer advocate for the DRMRP. “It was here where I was able to vote on the services and programs that I felt were most important to the returning veterans. I was able to influence where the financial resources would go and what programs the government would support dealing with deployments, prosthetic research, and more. It is my hope that people like me could benefit along with all the other returning wounded soldiers. My experience as a consumer advocate was great and I would highly recommend it. I left with a feeling of satisfaction that I made a difference and hoped that others would reap the rewards of the work we all put in and benefit from the choices we had made.” Melissa currently serves on the board of directors of the Wounded Warrior Project and loves the feeling of giving back to the organization that helped her on her road to recovery. She also continues to mentor newly injured veterans, hoping that her experiences and knowledge of the recovery process will help them toward a successful future.

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Psychological Health

Reaching Out to Military Personnel with Substance Abuse Disorders
Denise Walker, Ph.D., University of Washington, Seattle, Washington

Substance abuse disorders occur at disproportionately higher levels in military populations. However, surveys have shown that many active duty personnel who are suffering from alcohol or drug abuse dependence do not seek help. Therefore, increasing self-referrals to treatment is a high priority. Dr. Denise Walker was awarded an FY08 DRMRP Clinical Trial Award to develop and assess a brief telephone-delivered motivational enhancement therapy (MET) called “The Warrior Check-Up.” The intervention is designed to confidentially support soldiers who are concerned about their drinking or drug use, but are not in treatment, in taking stock of their experiences, considering their options, and either entering treatment or self-initiating change. The focus of the project’s first year was conducting focus groups for the purpose of adapting the intervention to fit within the military culture. In the project’s second year, a randomized clinical trial of the MET intervention began recruiting 240 participants from Joint Base Lewis-McChord. If successful, the Warrior Check-Up will offer a new means of reaching untreated deployed soldiers misusing alcohol and/or drugs and motivating them to address their dependence.
Traumatic Brain Injury

Developing Diagnostics for the Rapid Assessment of Traumatic Brain Injury

Calvin Goforth, Ph.D., SFC Fluidics, LLC, Fayetteville, Arkansas

TBI, which affects millions of civilians and military personnel, is typically diagnosed using a battery of neurologic exams along with an imaging modality, such as computed tomography (CT). However, TBI diagnosis using these current methods can be unreliable, and CT may lack the sensitivity necessary to diagnose mild injuries. Recent investigations demonstrate that in response to a head injury, a number of protein biomarkers exclusive to head injury are released into the blood stream, the quantities of which are directly proportional to the severity of injury. Although diagnostic protocols for determining the quantities of TBI biomarkers in the blood exist, time and logistical constraints limit their utility in rapidly diagnosing and triaging injured soldiers in the field. Thus, with funding from an FY08 DRMRP Advanced Technology/Therapeutic Development Award, SFC Fluidics is developing a portable and field-deployable handheld device capable of measuring biomarker quantities using a finger-prick blood sample to assess the presence and magnitude of a TBI. Thus far, the SFC Fluidics team has optimized the detection of the TBI biomarkers, S100beta and glial fibrillary acidic protein (GFAP), with a portable benchtop instrument. In addition, SFC Fluidics has developed an intermediate-sized handheld prototype to identify and troubleshoot potential technical and quality control issues before completing the final prototype. Ultimately, it is anticipated that this deployable handheld device will assist in providing a rapid diagnosis with respect to the presence and seriousness of TBI in soldiers in the field.
Protecting the Brain from Repetitive Mild Traumatic Brain Injuries
Andre Obenaus, Ph.D., Loma Linda University, Loma Linda, California

Repetitive mild traumatic brain injuries (rmTBIs) result in cumulative brain damage, leading to lingering symptoms that may interfere with social and occupational duties. Cellular metabolic perturbations due to excitotoxicity are likely involved in the pathological processes within the traumatized brain tissues and may be an important mechanism underlying functional disturbances. Hyperbaric oxygen (HBO) therapy improves cellular oxygen uptake and minimizes injury from subsequent trauma, proving itself as a potential neuroprotective treatment. Used in conjunction with intranasal nicotinamide, Dr. Andre Obenaus, recipient of an FY08 DRMRP Hypothesis Development Award, is assessing whether HBO therapy, either prophylactically or therapeutically, can improve physiological outcomes following rmTBI.

In collaboration with Dr. Lei Huang, Dr. Obenaus has developed a rat model of rmTBI by injuring the brain twice in the same location either 3 or 7 days after the initial impact. Magnetic resonance imaging showed that at 24 hours and 14 days post injury, animals that had incurred rmTBI 3 days apart had an increased presence of edema compared to animals that had incurred rmTBI 7 days apart. Rats with rmTBI 7 days apart showed little or no edema and only mild bleeding at the injury site compared to the animals with rmTBI 3 days apart. Thus, the brain appears to exhibit heightened vulnerability to a second mild traumatic insult up to 3 days after an initial mTBI event. Three months after the initial injury, an accelerated water maze paradigm with higher cognitive demands revealed learning deficits in the rmTBI 3-day-apart group, which suggests that cognitive impairments may develop slowly after rmTBI. HBO pretreatment of 1 hour per day for 3 days prior to rmTBI reduced the initial amount of edema and resulted in no sign of tissue injury at 24 hours after the second episode of an rmTBI incurred 3 days apart. Decreased edema levels and lesion volume persisted to 14 days post-initial injury in HBO-treated animals. HBO pretreatment also reduced the amount of extravascular blood within the double-impacted brain compared to nontreated rmTBI animals. These findings demonstrate the efficacy of HBO pretreatment in rescuing brain tissues at risk following rmTBI. While still ongoing, it is anticipated that the results of this study will provide the framework for future investigations that will assess the neuroprotective benefits of HBO treatment for combat personnel and civilians afflicted with rmTBI.
Trauma Treatment and Rehabilitation

Optimizing Biomechanical Analysis to Improve Running-Specific Prostheses

Jae Kun Shim, Ph.D., University of Maryland, College Park, Maryland

Running is an ingrained part of military culture and a functional goal for many military amputees. Previous studies modeling amputee running have used erroneous methodology that has not been validated. This has likely resulted in large errors in biomechanical and kinetic calculations that are used in the design of prostheses. Furthermore, these studies have mostly been conducted in prostheses designed for walking and standing, rather than running. Dr. Jae Kun Shim received an FY08 DRMRP Hypothesis Development Award to develop and validate a new model for running-specific prostheses that could lead to improvements in current prosthetic designs. Motion analysis will be conducted using a four-camera motion capture system that will collect three-dimensional positional data of reflective markers placed along the running-specific prostheses. Forces will be applied to simulate running. Inverse dynamics analysis will be conducted to provide a precise estimate of the joint kinetics and energetics experienced while an amputee is running. From these data, optimal reflective marker sets that yield the smallest error will be identified. Dr. Shim is hopeful that the knowledge acquired from this study will benefit amputees by informing the future design of improved prostheses for running.

Sealing Penetrating Eye Injuries Using Photoactivated Bonding

Irene E. Kochevar, Ph.D., and Col Anthony J. Johnson, M.D., Massachusetts General Hospital, Boston, Massachusetts

Penetrating eye injuries from improvised explosive devices are not uncommon in the current military conflicts. Lacerations to the cornea and sclera require immediate, waterproof closure to stabilize the wound and prevent endophthalmitis (infection of the intraocular cavity), which can cause permanent loss of vision or loss of the eye itself. Eye lacerations are generally treated with sutures or cyanoacrylate glue as a temporary stabilization technique when surgery is not immediately possible. While these methods are useful, applying sutures is a lengthy surgical procedure requiring a skilled ophthalmologist, and cyanoacrylate glue requires subsequent surgical intervention and can cause damage to the adjacent tissue during removal.

Dr. Irene Kochevar and Col Anthony Johnson, recipients of an FY08 DRMRP Advanced Technology/Therapeutic Development Award, aim to assess an advanced technology called Photochemical Tissue Bonding (PTB) as a potential alternative for sutures or cyanoacrylate glue for treating ocular lacerations. In PTB, a green laser activates the immediate formation of molecular bridges between a layer of amniotic membrane and the surface of the eye without collateral damage, and the eye can heal without further intervention. Importantly, PTB may be quickly administered by physicians without extensive ophthalmologic training due to its simplicity, and it may more effectively preserve the vision of wounded warriors in combat. Dr. Kochevar and Col Johnson have begun optimizing PTB for treating penetrating eye injuries in an animal model, and they expect that PTB will result in improved treatment outcomes compared to conventional methods.
Scaffold-Guided Bone Regeneration for Craniofacial Reconstruction


Severe impact injuries to the head and face from combat trauma often require reconstructive surgeries to restore and rebuild lost skeletal structures. Currently, these procedures involve the use of metallic implants or transplantation of tissue from donors or from other parts of the patient’s own body, which fall short of the ideal. Limitations include a shortage of tissue supply, donor site morbidity, poor integration with the host tissue, and host rejection. Dr. Hyun-Duck Nah-Cederquist, recipient of an FY08 DRMRP Hypothesis Development Award, is developing a biocompatible bone scaffold that can guide and stimulate host bone tissue regeneration. The scaffolds will be built of biodegradable and osteo-inductive PCL-bTCP or PLGA-bTCP copolymers that will serve as a temporary platform to guide and stimulate host bone tissue regeneration. Bone is highly vascularized, and its viability critically depends on nutrients and oxygen delivered by blood vessels. Therefore, rapid induction of vasculogenesis/angiogenesis is essential for the three-dimensional scaffold-guided reconstruction of large bone volumes. To aid this process, scaffolds will incorporate microspheres carrying a combination of angiogenic factors (FGF-2 and VEGF) that will be released at the transplantation site to encourage vascularization. Furthermore, the microspheres will sustainably release BMP-2, an osteogenic factor that will promote bone formation. Dr. Nah-Cederquist is currently validating the growth factor loaded scaffolds in a mouse model. If effective, the scaffolds will be tested for the repair of human-sized large bone deficits in a larger model system. The researchers are hopeful that this bone regeneration strategy will someday benefit soldiers needing craniofacial reconstruction.
Blood Safety

A Transportable Pathogen Reduction System for Treatment of Whole Blood

Raymond Goodrich, Ph.D., CaridianBCT Biotechnologies, Lakewood, Colorado

During combat, fresh whole blood (FWB) is used to treat life-threatening blood loss resulting from traumatic injuries when screened blood components are unavailable. While FWB may be critical in saving the lives of injured warriors, it is often transfused without any donor screening nor standard viral testing. Additionally, FWB is used without leukoreduction, which introduces a large number of viable white blood cells into severely injured patients, potentially increasing the rate of infections among other serious immunological complications.

Dr. Raymond Goodrich and his research group, recipients of an FY08 DRMRP Advanced Technology/Therapeutic Development Award, aim to develop a portable, disposable device for pathogen reduction in FWB that will minimize the risk of infectious disease transmission as well as potential adverse immunological effects of bypassing leukoreduction. With the award, Dr. Goodrich and his team are developing a prototype for the device (named the Mirasol System for Whole Blood) that uses riboflavin (vitamin B2) and UV light to rapidly inactivate pathogens and leukocytes in whole blood. Validation and optimization studies are being conducted for the device’s effectiveness against pathogens including bacteria, viruses, and parasites. Dr. Goodrich plans on assessing the quality and safety of FWB for use in patients following Mirasol System treatment under various storage conditions. When completed, the Mirasol System will undergo operational testing in simulated combat environments.
Blood Products

Pharmacologic and Hemostatic Resuscitation Protocol for the Treatment of Polytrauma

Hasan B. Alam, M.D., Massachusetts General Hospital, Boston, Massachusetts

Extensive hemorrhage causes systemic shock and cellular damage by reducing the available oxygen to the cells in the body. Conventional resuscitation methods may worsen the damage by causing the body to produce reactive oxygen species (free radicals) that not only directly cause cellular injury but also prime and activate various inflammatory cells that increase the rate of apoptosis. Although hemorrhage is one the leading causes of preventable deaths in both civilian and combat trauma, there are no available treatments that can attenuate the cellular damage that results from severe blood loss. Moreover, coagulopathy, abnormalities in blood clot formation associated with hemorrhages and TBI, is linked to greater mortality in trauma patients. The standard treatment for coagulopathy is blood component transfusion; however, blood components have limited availability in the battlefield and require refrigerated storage and transportation.

Previously, Dr. Hasan Alam demonstrated that histone deacetylase inhibitors (HDACI), several of which are already approved for clinical use, attenuate organ damage and improve early patient survival after lethal hemorrhage by activating the transcription of genes involved in cellular protective pathways. With his FY08 DRMRP Advanced Technology/Therapeutic Development Award, Dr. Alam is seeking to develop a Pharmacologic and Hemostatic Resuscitation (PHR) protocol, which includes the administration of HDACI and plasma. Dr. Alam hypothesizes that the early administration of PHR will minimize coagulopathy, cellular injury, and damage to cognitive functions and thus improve the overall survival of trauma victims after significant blood loss and/or TBI. Additionally, Dr. Alam is developing freeze-dried plasma that can be stored at ambient temperature and prepared quickly in the field.
Injury Prevention

Understanding Blast-Related Injuries
Andrew Merkle, M.S., Johns Hopkins Applied Physics Laboratory
Laurel, Maryland

Explosive munitions and other improvised explosive devices continue to present a substantial threat to military and civilian personnel. Exposure to these blasts can cause acute injuries that can be prevented. However, the mechanism of these injuries is not well understood. Mr. Andrew Merkle, recipient of an FY08 DRMRP Advanced Technology/Therapeutic Development Award, is developing biomedically validated human models capable of simulating and predicting blast-induced injury in multiple scenarios. Mr. Merkle and his transdisciplinary team of engineers, scientists, and medical personnel will identify the decisive mechanism through which the blast interacts with the human body and causes injury. These parameters will be used to develop computational models to simulate the blast in open field, enclosed, and vehicle-mounted scenarios. Head, neck, and thoracic models will be exposed to simulated blast conditions, and biomechanical measurements will be obtained and evaluated. These data will be combined with real-world data to allow developers to design, test, and evaluate personal and vehicle protection systems. Together, this work will help reduce the frequency and severity of these types of injuries.

Biomedically Validated Human Computational Models for Blast Injury Prevention (CoM BIP)

Biomedically validated computational models of the human body for use in the understanding mitigation of injury due to dynamic loading events.
Wound Infection and Healing

Targeted Prevention and Treatment of Bacterial Biofilm Infections of Severe Burns and Wounds

Jerry A. Nick, M.D., National Jewish Health, Denver, Colorado

Recurrent infection of severe wounds, specifically burns, contributes to deployment-related morbidity and mortality. The bacterium *Pseudomonas aeruginosa*—the most important cause of wound and burn infections—can form a self-encased community called a “biofilm,” thereby making conventional treatments difficult. At the site of injury, further tissue damage and increased ability of *P. aeruginosa* to form biofilms can occur due to an excessive number of white blood cells (neutrophils) surrounding the wound. In an effort to limit neutrophil influx and the ability of *P. aeruginosa* to form biofilms, Dr. Jerry Nick, recipient of an FY08 DRMRP Hypothesis Development Award, is testing the effectiveness of a novel dual therapeutic approach combining the anti-inflammatory N2 peptide with the antibiotic azithromycin for the treatment and prevention of post-burn *P. aeruginosa* wound infection. Thus far, Dr. Nick has demonstrated a decrease in wound severity and early *P. aeruginosa* wound infection by briefly stopping the influx of neutrophils to the site of thermal injury. Dr. Nick anticipates that the addition of azithromycin will substantially improve the post-burn *P. aeruginosa* wound infection, which suggests that early aggressive treatment is essential to preventing *P. aeruginosa* biofilm formation. Ultimately, it is anticipated that data generated from this study will assist in the development of novel treatment strategies to prevent secondary infection by *P. aeruginosa* due to severe wounds and burns occurring in combat.
Wound Infection Vaccines

A Candidate S. aureus Vaccine to Prevent Skin and Soft Tissue and Wound Infections

Michael Landrum M.D., Infectious Disease Clinical Research Program (IDCRP), Uniformed Services University of the Health Sciences, Bethesda, Maryland

Staphylococcus aureus is a leading cause of infections impacting all stages of military deployment from skin and soft tissue infections during deployment and training to wound infections in casualties in theater. Furthermore, newly emerging antibiotic-resistant strains of S. aureus in both the civilian community and military settings highlight the need for an effective way to prevent these infections. To date, vaccines that have been developed against S. aureus have not been effective. Dr. Michael Landrum, recipient of an FY08 DRMRP Clinical Trial Award and IDCRP principal investigator, hypothesizes that the inclusion of two toxoids in a multivalent S. aureus vaccine, may induce a broader immune response and therefore be more effective at preventing S. aureus infection. The two toxoids are a recombinant nontoxic form of staphylococcal alpha-toxin (rAT) and a recombinant subunit of Panton Valentine leukocidin (PVL) toxin that were developed by Nabi Biopharmaceuticals. To determine the safety and immunogenicity of these antigens, Dr. Landrum is conducting a 12-month, double-blind, randomized, Phase I–II dose escalation study. Participating in this study are 176 patients recruited from Brooke Army Medical Center or Naval Medical Center Portsmouth. If successful, this study will facilitate progression toward a new staphylococcal vaccine that may benefit active duty military members at risk for these infections.
For more information, visit:
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