March 2024

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Impact Highlights

U.S. Army Medical Research and Development Command

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Department of Defense
U.S. Army Medical Research and Development Command
Congressionally Directed Medical Research Programs

Impact Highlights

March 2024

Congressionally Directed Medical Research Programs
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INTRODUCTION

Vision: Transforming health care through innovative and impactful research

Mission: Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service Members, their Families, Veterans, and the American public

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The Congressionally Directed Medical Research Programs (CDMRP), located within the U.S. Army Medical Research and Development Command, is a global funding organization that fosters novel approaches to congressionally targeted biomedical research areas in response to the expressed needs of its stakeholders – Service Members, Veterans, the American public, and Congress. CDMRP-managed programs are diverse but share the common goals of accelerating progress, advancing paradigm-shifting research, developing cutting-edge technologies, and identifying breakthroughs and solutions that will lead to cures, improved patient care, and enhanced quality of life.

This book highlights some examples of the successes and impacts of CDMRP-funded research in fostering exploration of innovative ideas, opening new research avenues, developing key resources and technologies, and translating promising research into clinical care. Key partners and collaborators for each effort are listed in chronological order by award, with prime awardee(s) listed first. All active CDMRP programs are represented, with brief summaries of prior programs since FY21 in Appendix A.

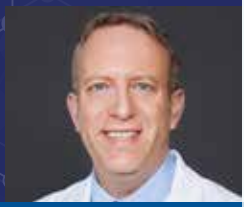
CDMRP receives annual appropriations that are disease- or condition-specific, which allows flexibility to implement targeted investment strategies each year focused on areas of highest potential impact and highest priority needs of the consumer (patients, survivors, family members, and/or caregivers) and research communities. This is accomplished through close coordination and continual development of strategic and research partnerships with the scientific and clinical communities, industry, other federal and non-federal funding organizations, and consumers — all of which are critical to enabling successful outcomes.

CDMRP maintains a passionate dedication to the mission and readily adapts to emerging priorities or congressional establishment of new programs or topics. Across all programs, CDMRP funds research to benefit people in the military health care system, to include military members, military retirees, Family members, and other beneficiaries, as well as benefiting the American public.

Since the first program appropriation in 1992, CDMRP-funded research significantly advanced knowledge, technologies, and products that are saving and improving lives:

- FDA-approved drugs and therapeutic strategies
- Diagnostic and prognostic biomarkers/tests
- Novel approaches to prevention and treatment
- Imaging technologies for clinical use
- New standards of care and clinical practice
- Biorepositories with clinical samples and data

No matter what their size and scope, all CDMRP research programs target research with the ultimate goal of impacting people and improving lives.



Lyle Ostrow, M.D., Ph.D., Amyotrophic Lateral Sclerosis Research Program (ALSRP) Programmatic Panel Chair

"ALS patients, caregivers, and advocates are involved in all aspects of ALSRP peer review, program policy, investment strategy, and research focus discussions. Through its funding mechanisms, the ALSRP prioritizes funding of novel innovative therapeutic ideas, emphasizes biomarker development, and supports the validation of therapeutic leads. More recently based on critical stakeholder input, the ALSRP has expanded into the clinical space through the Pilot Clinical Trial Award."

Maj. Toni Grimes, U.S. Army, Retired, Lupus Research Program (LRP) Consumer Peer Reviewer

"Serving on the LRP allowed me to continue doing what I have done my entire Army career, to serve my country. Through the LRP I was able to serve my lupus community and to have a voice as a lupus patient with regards to future innovative treatments, therapies, and research. It has been a true honor."

Maj. Yosef Fufa, D.N.P., U.S. Army, Alcohol and Substance Use Disorders Research Program Programmatic Panel Member

"As a behavioral health care provider, I routinely witness the negative impact of substance abuse on active-duty Service Members and Veterans alike. It has been a privilege to be a part of the team that supports the effort to combat these disorders."

ALCOHOL AND SUBSTANCE USE DISORDERS RESEARCH PROGRAM

Vision: Improve the clinical outcomes of alcohol, opioid, and other substance use disorders

Mission: To explore integrated approaches to address alcohol and substance use disorders, and reduce the number of opioid and other substance use-related deaths, through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols and enhanced quality of life for Service Members, Veterans, and the American public

Years Program Appropriated: FY10-FY19 and FY21-FY23

Total Appropriations: $56.1 million (M)

The Alcohol and Substance Use Disorders Research Program (ASUDRP) aims to bring new medications to market for the treatment of alcohol and substance use disorders. To do this, researchers conduct studies of new medications with a special emphasis on comorbidities of traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) in Service Members and Veteran populations. The program uses a translational approach, from animal models to humans, to understand the complex interaction of substance abuse with the now-common military stress comorbidities of PTSD and TBI.

Program goals include:

- New medications to treat opioid use disorder (preclinical)
- New medications to treat alcohol use disorder with co-morbid PTSD (clinical)
- New medications to treat opioid use disorder with co-morbid PTSD (clinical)

Anti-Fentanyl Vaccine and Buprenorphine Combination Therapy

IMPACT: Use of a fentanyl vaccine in high-risk populations could prevent the high rate of overdoses and deaths occurring with opioid use disorders. The vaccine also could block the effects of aerosolized fentanyl in terrorist- or combat-related attacks.

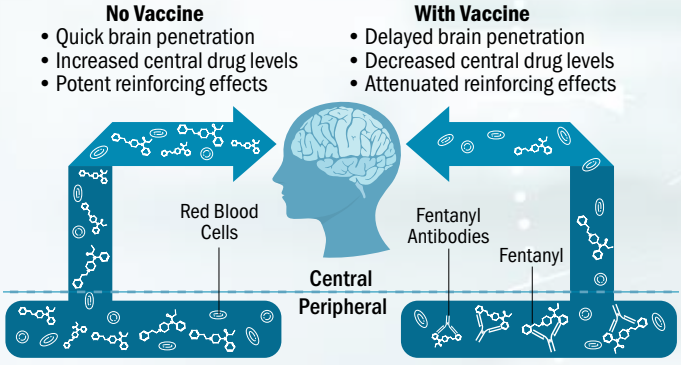
DESCRIPTION

The vaccine developed produces antibodies in the blood that attach to fentanyl. When fentanyl is ingested, this large antibody-fentanyl complex cannot get out of the bloodstream to enter the brain, heart, or other vulnerable organs to produce psychological effects, analgesia, or respiratory depression. Thus, these antibodies prevent both abuse of fentanyl and overdose.

PARTNERS/COLLABORATORS

University of Houston; Fina Biosolutions, LLC; Tulane University

AWARD NUMBER: W81XWH-18-2-0044 (Consortium Award)



This is a visual representation of how the anti-fentanyl antibodies work to bind fentanyl and prevent it from entering the brain from peripheral circulation of blood

PT150 – Cortisol Blocking Treatment

DESCRIPTION

PT150 is a glucocorticoid receptor antagonist that blocks the effects of cortisol, an endogenous stress hormone. The studies being conducted examine the efficacy, safety, and tolerability of this drug for PTSD and alcohol use disorder dual diagnosis treatment. Researchers have successfully completed a phase 1, single center, alcohol interaction study and are now conducting a phase 1, drug-drug interaction study to assess pharmacokinetic interactions between ethanol and PT150. Successful completion of the pharmacokinetic study will enable researchers to conduct the proof of concept study.

PARTNERS/COLLABORATORS

University of California San Diego; Baylor College of Medicine; POP Test Oncology, LLC

AWARD NUMBER: W81XWH-18-2-0077 (Consortium Award)

IMPACT: Proven safe, effective treatments for PTSD alone, alcohol use disorder alone, or co-occurring illness are severely limited. PT150 potentially could be safe and effective in improving PTSD and alcohol use disorder symptoms.

BXCL 501

DESCRIPTION

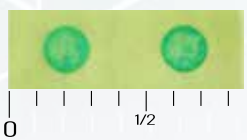
This proof of concept study examines the use of BXCL501 (dexmedetomidine [DEX] on a sublingual film) as a potentially effective therapeutic for the treatment of patients with alcohol use disorder, especially those with comorbid PTSD. DEX exerts its effects by preventing release of the neurotransmitter norepinephrine, which is responsible for stress-related agitation and hyper-arousal. Because PTSD is associated with hyper-arousal and high sympathetic nervous system activity, BXCL501 has the potential to alleviate agitation that occurs in PTSD.

PARTNERS/COLLABORATORS

VA Connecticut Healthcare System, West Haven; BioXcel Therapeutics

AWARD NUMBER: W81XWH-18-2-0044 (Consortium Award)

IMPACT: BXCL501 could be a safe and effective treatment option for alcohol use disorder and PTSD.



Green, film BXCL501 (dexmedetomidine (DEX) on a sublingual film) to be used in trial

IMPACT: Kappa opioid receptor antagonists potentially could be safe and effective in improving PTSD and alcohol use disorder symptoms.

Kappa Opioid Receptor Antagonist

DESCRIPTION

Given their general ability to mitigate the effects of stress, there is substantial interest in the development of kappa opioid receptor antagonists for indications such as alcohol use disorder and PTSD. The combination of buprenorphine and naltrexone yields a pharmacological net effect of a kappa opioid receptor antagonist. This proof of concept study evaluated the efficacy and physiological effects of buprenorphine combined with naltrexone in the treatment of comorbid alcohol use disorder and PTSD. Results are pending publication.

Measuring PTSD startle response to a loud noise

PARTNERS/COLLABORATORS

University of Alabama Birmingham School of Medicine; Yale School of Medicine; Alkermes

AWARD NUMBER: W81XWH-18-2-0077 (Consortium Award)

IMPACT: This drug combination may offer an additional safe and effective treatment option for improving opioid use disorder and PTSD symptoms.

Lofexidine Combined with Buprenorphine

DESCRIPTION

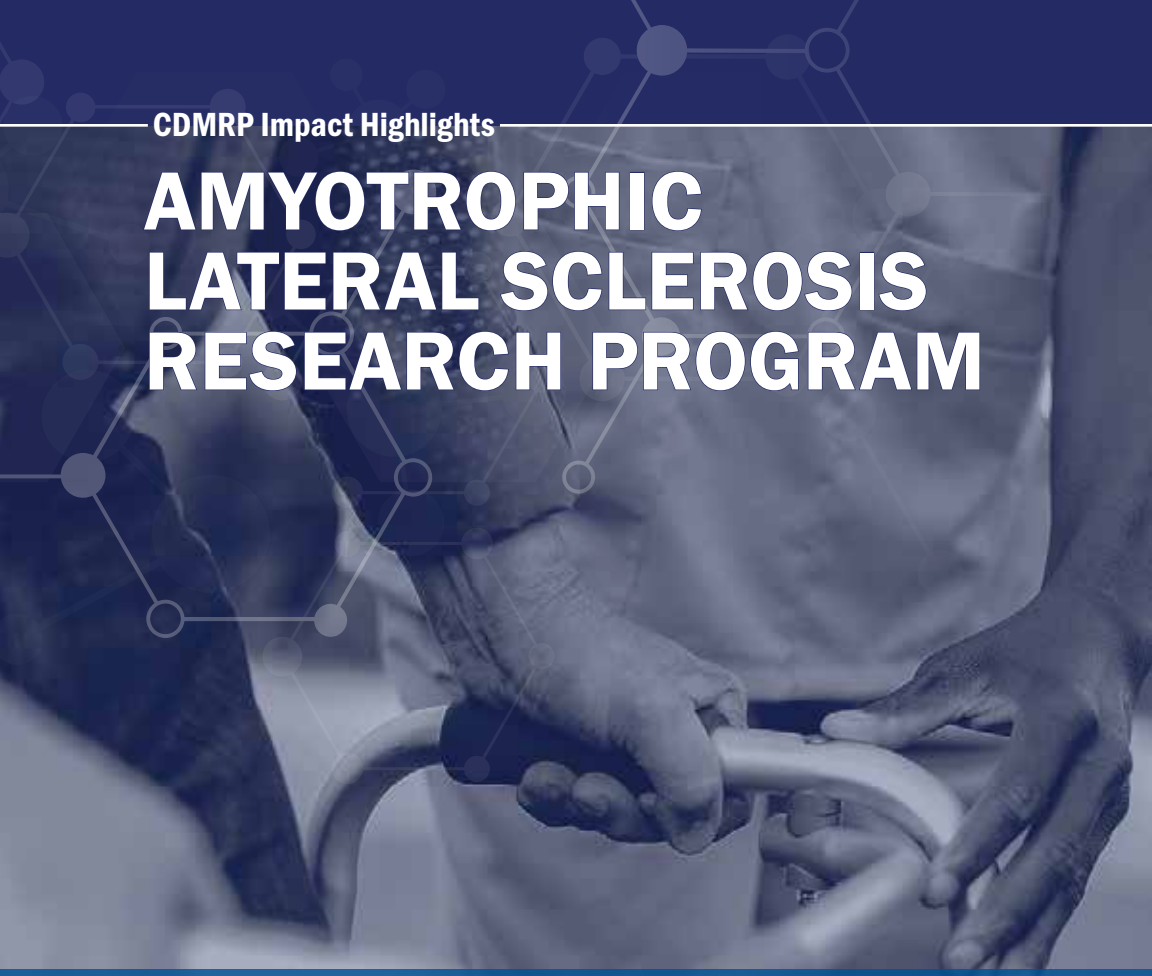
Lofexidine is approved by the FDA for opioid withdrawal, while buprenorphine is a narcotic used to treat addiction. The overall objective of this phase 2 multi-site study is to determine if lofexidine as an adjunct to buprenorphine treatment improves symptoms of both opioid use disorder and PTSD.

PARTNERS/COLLABORATORS

Baylor College of Medicine; US World Meds

AWARD NUMBER: W81XWH-18-2-0044 (Consortium Award)

AMYOTROPHIC LATERAL SCLEROSIS RESEARCH PROGRAM



Vision: Improve treatments and find cures for people with ALS

Mission: Fund impactful research to develop ALS treatments

Years Program Appropriated: FY07, FY09-FY23

Total Appropriations: $129.4M

The ALSRP is guided by a vision to improve treatment and find a cure for amyotrophic lateral sclerosis (ALS). Through its award mechanisms and funding recommendations, the ALSRP specifically supports innovative and impactful research targeting development of new therapeutics for ALS.

Combination of Riluzole + Elacridar

IMPACT: A combination drug therapy was discovered that may remove a key obstacle to treatment and provide a foundation for future drug combinations to further improve the outcomes for patients with ALS.

DESCRIPTION

The ALSRP funded the development of a combination therapy improving the action of an FDA-approved drug for ALS (riluzole). Using a mouse model of ALS, researchers established that when a protein membrane pump was blocked by the use of a known inhibiting drug, elacridar, the effectiveness of riluzole therapy was improved. Pump inhibition by chronic treatment with elacridar increased penetration of riluzole in the central nervous system, improved behavioral measures (including muscle function), and significantly extended survival of the mice. The ALSRP funded additional work into this combination approach to develop a new elacridar formulation, and perform detailed pharmacokinetics, toxicology, and large-scale good laboratory practice compound manufacturing.

PARTNERS/COLLABORATORS

Jefferson Medical College; Izumi Biosciences, Inc.

AWARD NUMBERS: W81XWH-11-1-0767, W81XWH-16-1-0072

Copper Carrier CuATSM

IMPACT: Optimizing the structure of CuATSM and its derivatives for copper delivery to damaged cells in the central nervous system could result in a novel therapeutic option and become a treatment for both SOD-familial and sporadic ALS patients.

DESCRIPTION

Use of the copper carrier CuATSM in a mouse model of ALS revealed that treated mice lived longer than untreated controls. CuATSM corrects the lack of copper ions in misfolded SOD1 proteins and may also help eliminate a chemical that interferes with mitochondrial function in ALS. The ALSRP funded the development of three novel CuATSM derivatives, all of which have low toxicity, are easily synthesized, and are effective at low dosages. The ALSRP-funded investigator has secured collaborative follow-on funding from the ALS Association and is now moving forward with submission of an Investigational New Drug application and has plans to open a trial in the U.S.

PARTNERS/COLLABORATORS

Oregon State University; Procypra Therapeutics

AWARD NUMBER: W81XWH-15-1-0289

AKV9

DESCRIPTION

The toxic buildup of proteins is a common hallmark of ALS. The ALSRP funded research to study a screening system to identify compounds that protect cells against these toxic effects. Investigators identified AKV9 as a potent inhibitor of protein aggregation, and in 2023, the FDA cleared the Investigational New Drug Application for AKV9 to treat patients with ALS.

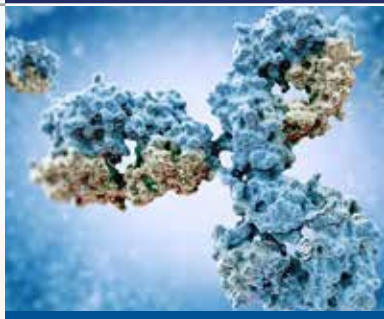
PARTNERS/COLLABORATORS

Northwestern University

AWARD NUMBER: W81XWH-10-1-0536

IMPACT: AKV9 prevents protein build-up and has been shown to improve the health of upper motor neurons via multiple mechanisms. Pilot clinical trials are coming soon.

Targeting microRNA miR-155



DESCRIPTION

miR-155 is a microRNA that promotes inflammation, and increased levels of miR-155 have been found in monocytes from ALS patient blood samples. Monocytes play a key role in ALS disease progression. Genetic manipulation of miR-155 in an ALS animal model was shown to delay disease onset and extend survival. Based on these findings, a therapeutic development company has invested in a therapeutic strategy to target miR-155 as a treatment for ALS.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital; MiRagen Therapeutics*

AWARD NUMBER: W81XWH-13-1-0181

IMPACT: miR-155 has the potential to prolong survival of ALS patients and provide a biomarker that can be used to monitor overall disease progression.

* Viridian Therapeutics, Inc. as of January 2021

Small Molecule Apilimod and Software DRVision

IMPACT: Groundbreaking data generated by an ALSRP award led to the discovery and preclinical validation of a new ALS therapeutic target and a screening platform to speed analysis of experimental samples.

DESCRIPTION

Under an ALSRP-supported award, a chemical screen revealed Apilimod, an inhibitor of a protein called PIKFYVE, as a potentially potent and broadly efficacious way to eliminate toxic proteins that cause neurodegeneration in ALS. Based on these findings, and in conjunction with the company AcuraStem Inc., a novel PIKFYVE inhibitor is now advancing into ALS clinical trials. The ALSRP-supported work additionally developed analysis software, with partner DRVision Technologies, enabling automated detection of neuron numbers and rate of neurodegeneration during large-scale screens. This software is now moving toward commercialization.

PARTNERS/COLLABORATORS

University of Southern California Keck School of Medicine; AcuraStem Inc.; DRVision Technologies

AWARD NUMBER: W81XWH-15-1-0187

Human Neural Progenitor Cells Expressing GDNF (CNS10-NPC-GDNF)

IMPACT: This treatment could increase the survival of motor neurons in ALS patients, delaying symptom progression and improving overall clinical outcomes.

DESCRIPTION

The ALSRP funded preclinical studies to deliver the growth factor GDNF to motor neurons. Delivery of GDNF, through hNPCs, enhanced motor neuron function and extended survival in ALS animal models. These results, as well as additional results outside of the ALSRP, contributed to a California Institute of Regenerative Medicine grant moving this approach into clinical trials in patients (NCT02943850).

PARTNERS/COLLABORATORS

Cedars-Sinai Medical Center; California Institute of Regenerative Medicine

AWARD NUMBER: W81XWH-14-1-0189

FDA-Approved Neuroleptic Drug Pimozide

DESCRIPTION

The ALSRP funded large-scale screens of thousands of FDA-approved drugs to identify chemical modifiers of TDP-43 in preclinical models of ALS. A class of neuroleptics was identified, with pimozide being the most potent compound, as confirmed in all models tested. A national clinical trial has started in Canada (funded by ALS Canada and Brain Canada) to determine the potential for pimozide as a therapeutic (NCT03272503).

PARTNERS/COLLABORATORS

University of Montreal

AWARD NUMBER: W81XWH-11-1-0573

IMPACT: Extending on the findings funded by ALSRP, the Canadian team found that Pimozide may be able to prevent the progression of ALS.

Tegoprubart

DESCRIPTION

Evidence suggests that some aspects of disease onset and progression in ALS are regulated by immune cells. The ALSRP funded pharmacokinetic and toxicology studies using a novel antibody, Tegoprubart, that is designed to block the protein activity of CD40L, a key player in immune response activation. These preclinical studies supported IND-enabling pharmacokinetics and toxicology studies of the humanized anti-CD40L antibody (formerly AT-1501), which showed significant therapeutic benefit in an ALS mouse model, as evidenced by prolonged weight maintenance, delayed onset of neurological disease, and extended survival. Results led to testing Tegoprubart in human clinical trials by Anelixis Therapeutics, Inc., and in 2020 the FDA granted Tegoprubart orphan drug designation.

PARTNERS/COLLABORATORS

ALS Therapy Development Institute; Anelixis Therapeutics, Inc.

AWARD NUMBER: W81XWH-17-1-0057

IMPACT: If the ongoing clinical trials are successful, Tegoprubart will become a new treatment option to slow disease progression and extend lives for people living with ALS.

IMPACT: Prosetin, a therapeutic to prevent motor neuron toxicity in ALS, enters clinical trials, strengthened by early support from the ALSRP.

Prosetin

DESCRIPTION

The ALSRP funded the development of a potent and selective inhibitor of endoplasmic reticulum stress in a cellular model of ALS. This research created prosetin, a brain penetrant kinase inhibitor of pathologies observed in both familial and sporadic forms of ALS. Compared to currently available therapeutics, prosetin is a prime candidate for broad and sustained treatment. Prosetin received orphan drug designation from the FDA. In 2022, the first-in-human phase 1 clinical trials were initiated in healthy volunteers and ALS patients.

PARTNERS/COLLABORATORS

Columbia University; Project ALS Therapeutics Core

AWARD NUMBER: W81XWH-21-1-0370

IMPACT: Successful development of RASRx1902 has the potential to improve the treatment, quality of life, and long-term outlook for individuals affected by ALS.

RASRx1902

DESCRIPTION

RASRx1902 is an investigational oral drug that has been shown to reduce inflammation and oxidative stress, improve cognitive function, and stimulate muscle regeneration in Duchenne muscular dystrophy. Since these factors are known to be involved in ALS, the ALSRP supported investigations re-purposing this compound to decrease neurological deficits and increase lifespan of ALS models. In 2017, the FDA granted orphan drug designation to RASRx1902, clearing its path to potential therapeutic use.

PARTNERS/COLLABORATORS

The University of Arizona Health Sciences Center for Innovation in Brain Science

AWARD NUMBER: W81XWH-19-1-0471

AUTISM RESEARCH PROGRAM

Vision: Improve the lives of individuals with autism spectrum disorders now and in their future

Mission: Promote innovative research that advances the understanding of autism spectrum disorder and leads to improved outcomes for Service Members, their Families, and the American public

Years Program Appropriated: FY07-FY23

Total Appropriations: $149.4M

The ARP's mission is to promote innovative research that advances the understanding of autism spectrum disorders and leads to improved outcomes for Service Members, their Families, and the American public. The ARP developed its overall strategic goals, which include: (1) understand causes, mechanisms, and signs of autism spectrum disorders, (2) advance effective treatments and interventions for autism, (3) address the needs of persons with autism into adulthood, and (4) support those caring for the autism community.

IMPACT: Once the NIH pivotal trial is completed, cognitive enhancement therapy could become a reimbursable and standardized therapy for adults with autism spectrum disorder.

Cognitive Enhancement Therapy for Adults with Autism Spectrum Disorder

DESCRIPTION

Cognitive enhancement therapy has been successful in helping people with schizophrenia improve cognitive development and social functioning. Only a few interventions currently exist for the adult population, none of which effectively target both the social and non-social cognitive impairments that can influence major domains of functioning, including employment. Cognitive enhancement therapy was found to be highly efficacious in enhancing neurocognitive function, specifically attention and processing speed in autism spectrum disorder adults. These improvements demonstrated a substantial effect on employability in these adults. The investigators have been funded by the National Institutes of Mental Health to conduct a large-scale clinical trial to evaluate the use of cognitive enhancement therapy in adults with autism spectrum disorder.

PARTNERS/COLLABORATORS

University of Pittsburgh

AWARD NUMBERS: W81XWH-11-1-0665, NIMH R01 MH106450

Google Glass with Empowered Brain

IMPACT: The Empowered Brain technology has already been implemented in classrooms to improve the social and emotional behavior of students with autism spectrum disorder.

DESCRIPTION

Empowered Brain is an augmented reality and virtual reality software technology that is aimed at improving the symptoms of social interaction disorders often seen in those with autism spectrum disorder. With Empowered Brain, individuals look through Google Glass, which incorporates virtual reality displays to provide users with experiences that will help them cope with real-life situations. Empowered Brain technology proved both feasible and efficacious in improving symptoms of autism spectrum disorder, including social withdrawal, irritability, and hyperactivity in students with autism. Educators who have incorporated the technology in their classroom reported that students' attention was significantly increased and there was improved development of student-teacher relationships. The research team is currently working with one of the largest public school districts in Massachusetts to implement the technology in their job placement effort.

PARTNERS/COLLABORATORS

Brain Power LLC

AWARD NUMBER: W81XWH-17-1-0449

PS+ASD for Adult Military Dependents with Autism Spectrum Disorder

IMPACT: The PS+ASD program was found to be extremely successful at helping young adults with autism spectrum disorder obtain employment and transition into independence.

DESCRIPTION

Project SEARCH plus Autism Spectrum Disorder Supports (PS+ASD) is an employment-based training program for improving social communication, behavior, and employment outcomes for transition-aged youth with autism spectrum disorder. The training support system consists of intensive applied behavioral analysis, assistance from an on-site behavior and autism specialist, and staff training. The training program works with young adults with autism from military Families who are in their last year of high school; the students are immersed in large community businesses with real-world work environments. Participants in the PS+ASD program showed improved independence, social responsiveness, self-management, work skills, and quality of life. Over 76% of the internship participants gained competitive integrated employment.

PARTNERS/COLLABORATORS

Virginia Commonwealth University

AWARD NUMBER: W81XWH-16-1-0707

ImPACT Online Program

DESCRIPTION

Although parent training is considered an essential component of early intervention programs for children with autism spectrum disorders, many families have difficulty accessing such training programs. Web-based distance learning programs have great potential for increasing access to families. This project developed a highly innovative, web-based, distance learning program called Improving Parents as Communication Teachers (ImPACT). ImPACT uses effective adult learning tools to help parents learn the intervention techniques and to integrate them into daily interactions with their child. Results showed that internet-based instruction is a feasible method for training parents on evidence-based intervention strategies. The project received follow-on funding from the Health Resources and Services Administration for an efficacy study.

PARTNERS/COLLABORATORS

Michigan State University

AWARD NUMBER: W81XWH-10-1-0586

IMPACT: This type of online training could allow greater dissemination of interventions to underserved populations. The ImPACT program has now been adapted to ImPACT for Toddlers, a program to coach parents and caregivers of 12- to 24-month-olds (http://www.project-impact.org).

IMPACT: The MAXout treatment manual will be disseminated freely to the public.

MAXout for Social-Communication

DESCRIPTION

Individuals with autism spectrum disorder exhibit social-communication impairments that impede their daily living. This project aimed to develop a comprehensive outpatient psychosocial treatment, MAXout, and evaluate its efficacy on improving autism symptoms and social-communicative function of 7- to 12-year-olds with autism spectrum disorder in a randomized controlled trial. MAXout is an 18-week treatment program targeting social and social-communication skills, face-emotion recognition, nonliteral language skills, and interest expansion. Results showed that MAXout significantly reduced autism spectrum disorder symptoms and improved social skills and behavior symptoms. These treatment effects were well maintained at post-treatment follow-up.

In a newly funded follow-on project, the research team is testing the feasibility and efficacy of an after-school social intervention delivered by paraprofessionals for children with high-functioning autism spectrum disorder. This study will train paraprofessionals in implementing the intervention, after which it will be delivered to elementary-aged children as part of the existing after school program.

PARTNERS/COLLABORATORS

Canisius College*

AWARD NUMBERS: W81XWH-15-1-0195, W81XWH-22-1-0688

* Canisius University as of August 2023

BONE MARROW FAILURE RESEARCH PROGRAM

Vision: To understand and cure bone marrow failure diseases

Mission: To encourage and support innovative research that is committed to advancing the understanding and treatment of inherited and acquired bone marrow failure diseases, thereby improving the health of affected Service Members, Veterans, and the general public, with the ultimate goals of prevention and cure

Years Program Appropriated: FY08-FY23

Total Appropriations: $64.05M

The Bone Marrow Failure Research Program (BMFRP) encourages and supports innovative research that is committed to advancing the understanding and treatment of inherited and acquired bone marrow failure diseases, thereby improving the health of affected Service Members, Veterans, and the general public, with the ultimate goals of prevention and cure. The pathology of bone marrow failure is complex. It is complicated by the diverse syndromes that contribute to it, which vary in etiology, age of onset, symptoms, and severity. There are many unanswered bone marrow failure research questions; thus, the strategy of the BMFRP is to retain a broad set of research priorities. Current emphasis is placed on projects that improve our understanding of the causes and progression of bone marrow failure diseases and those that discover effective treatments and cures.

IMPACT: Clinical trial results of H3B-8800 demonstrated the potential of a safe, novel therapeutic for improved care/treatment of different cancers.

H3B-8800

DESCRIPTION

H3B-8800 is an orally administered small molecule that binds to a complex of seven proteins responsible for mRNA processing that is commonly mutated in myelodysplastic syndromes, acute myeloid leukemia, and chronic myelomonocytic leukemia. The BMFRP supported preclinical mouse model studies of H3B-8800 and related molecules that displayed preferential killing of cancer cells harboring relevant mutations. H3B-8800 has since been evaluated in a phase 1 clinical trial (NCT02841540), demonstrating safety, even with prolonged dosing, for patients with these conditions. H3B-8800 may also have benefits in chronic lymphocytic leukemia and displays synergism with venetoclax, which is used to treat adults with chronic lymphocytic leukemia, small lymphocytic lymphoma, or acute myeloid leukemia.[1]

PARTNERS/COLLABORATORS

Sloan Kettering Institute for Cancer Research;
Fred Hutchinson Cancer Research Center

AWARD NUMBER: W81XWH-16-1-0059

[1] López-Oreja I, Gohr A, et al. 2023. SF3B1 mutation-mediated sensitization to H3B-8800 splicing inhibitor in chronic lymphocytic leukemia. *Life Science Alliance* 6(11):e202301955.

Exogenous RvE1

DESCRIPTION

Macrophages may be key targets for mitigating bone marrow failure diseases. Data from BMFRP-funded research demonstrated that impaired macrophage activity resulted in unsuccessful resolution of inflammation leading to bone marrow failure in severe aplastic anemia.[2] More recent findings in mouse models of severe aplastic anemia, also supported by BMFRP, identified that treatment with a small pro-resolving lipid mediator called Resolvin E1 improves the ability of macrophages to resolve inflammation and has therapeutic benefits to alleviate disease symptoms. Follow-on funding from BMFRP will address the precise mechanisms of Resolvin E1 protection.

PARTNERS/COLLABORATORS

Albany Medical College

AWARD NUMBER: W81XWH-20-1-0314

IMPACT: Promoting the ability of macrophages to resolve inflammation has the potential to provide protection and alleviate bone marrow failure symptoms of severe aplastic anemia.

[2] Seyfried AN, McCabe A, et al. 2021. CCR5 maintains macrophages in the bone marrow and drives hematopoietic failure in a mouse model of severe aplastic anemia. *Leukemia* 35(11):3139-3151.

Hematopoietic Stem and Progenitor Cell Immune Privilege Site

IMPACT: This scientific advancement identified new opportunities to improve care for bone marrow diseases.

DESCRIPTION

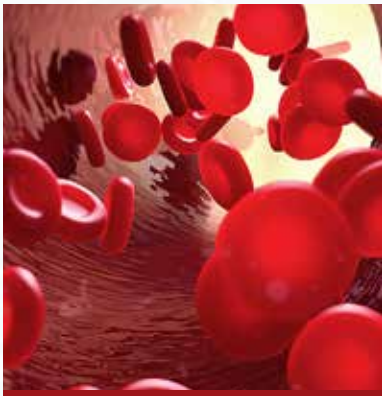
Hematopoietic stem and progenitor cells are an important part of the bone marrow that differentiate to produce blood cells in a process known as hematopoiesis. To sustain an appropriate population, these cells must also expand and replicate. The stem cell niche, a special compartment of the bone marrow where hematopoietic stem and progenitor cells conduct this process of self-renewal, was identified as an immune privilege site in bone marrow where regulatory T cells are immune-suppressive and shield hematopoietic stem and progenitor cells from immune rejection. This finding could pave the way for allogeneic transplant in unconditioned hosts and benefit a larger patient pool for bone marrow transplant, ultimately leading to better treatment of bone marrow disorders.

PARTNERS/COLLABORATORS

Massachusetts General Hospital

AWARD NUMBER: W81XWH-10-1-0217

Metformin Therapy for Fanconi Anemia



DESCRIPTION

Metformin is an orally administered FDA-approved therapy for type 2 diabetes. The BMFRP-funded research showed that Metformin increased blood production and reduced cancer formation in animal models of Fanconi Anemia, a rare inherited disease with bone marrow failure and increased risk of cancer. This research suggests repurposing Metformin as a treatment for the disease. Based on these findings, Boston Children's Hospital initiated a pilot phase 2 clinical trial (NCT03398824) to assess safety and tolerability in nondiabetic patients with Fanconi Anemia.

PARTNERS/COLLABORATORS

Oregon Health and Science University, Portland

AWARD NUMBER: W81XWH-16-1-0300

IMPACT: Results from this research contributed to a phase 2 clinical trial to assess using Metformin, an FDA-approved diabetes therapeutic, as a new therapy for patients with Fanconi Anemia.

Matt Pearl, BMFRP Consumer Peer Reviewer

"I have a rare disease called Fanconi anemia. At 9 years old, I received my life-saving bone marrow transplant in 2006. Survival rates were only 50% then. Now, thanks to research, an unrelated transplant is over 90% successful. I am grateful for the research the BMFRP has done, is doing, and will continue to do. I witnessed their impact firsthand. I can help others and make a difference with my life thanks to research like this. Others should have that chance, too! Thank you!"."

Leslie Falduto, BCRP Consumer Peer Reviewer

"The DOD BCRP plays a huge role in change for breast cancer by looking at the community as a whole, from early to late-stage breast cancer. When it comes to advancing treatment for breast cancer, all stages are important."

BREAST CANCER RESEARCH PROGRAM

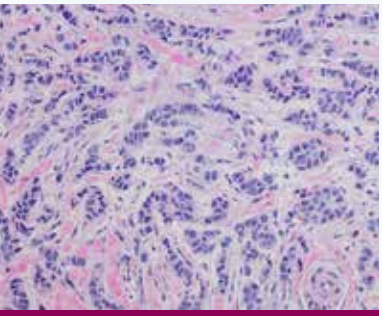
Vision: A world without breast cancer

Mission: To end breast cancer for Service Members, Veterans, and the general public by funding innovative, high-impact research through a partnership of scientists and consumers

Years Program Appropriated: FY92-FY23

Total Appropriations: $4.241 billion (B)

The Breast Cancer Research Program's (BCRP) mission is to end breast cancer for Service Members, Veterans, and the general public by funding innovative, high-impact research through a partnership of scientists and consumers. The BCRP recognizes that many overarching questions remain unanswered in breast cancer, and funding must be invested in critical areas of research to make breakthroughs that will save lives and lead to eradication of this disease. To meet this urgent need, the BCRP requires all applications to address overarching challenges that focus on the goals of primary prevention and risk, identifying what drives breast cancer progression, revolutionizing treatment regimens, and improving prognosis by preventing recurrence and eliminating mortality associated with metastasis.



IMPACT: Herceptin revolutionized breast cancer treatment and the field of targeted therapeutics and is now part of standard of care treatment regimens for HER2+ early-stage and metastatic breast cancers.

Herceptin®

DESCRIPTION

Herceptin (trastuzumab) is a monoclonal antibody that targets the human epidermal growth factor receptor 2 (HER2). HER2-positive (HER2+) breast cancer accounts for approximately 15% to 20% of all breast cancers. The BCRP was instrumental in supporting the preliminary studies needed to test the efficacy of Herceptin, which later led to clinical trials and ultimately, FDA approval.

"I am alive today because of a research grant funded by the DOD BCRP to Dr. Dennis Slamon. That groundbreaking research led to the development of my personal miracle drug: Herceptin."
Beth Emery, BCRP Consumer Reviewer, National Breast Cancer Coalition Team Leader

PARTNERS/COLLABORATORS

University of California, Los Angeles

AWARD NUMBER: DAMD17-94-J-4118

IMPACT: The American Society of Clinical Oncology published updated guidelines on adjuvant hormonal therapy recommending all women diagnosed with hormone receptor-positive (HR+) breast cancer be offered the option of taking hormonal therapy for 10 years.

Long-Term (10 Years) Tamoxifen Treatment for Estrogen Receptor-Positive Breast Cancer

DESCRIPTION

Adjuvant tamoxifen is the first-line treatment for estrogen receptor-positive breast cancer in premenopausal women. BCRP funds supported initiation of the phase 3 ATLAS (Adjuvant Tamoxifen Longer Against Shorter) clinical trial which showed that the risk of recurrence or death from breast cancer was reduced in women who took tamoxifen for 10 years, compared to those who took it for 5 years (the previous standard of care).

PARTNERS/COLLABORATORS

University of Oxford

AWARD NUMBER: DAMD17-94-J-4422

Cyclin-Dependent Kinase Inhibitors – Ibrance®, Verzenio®, Kisqali®

DESCRIPTION

Ibrance (palbociclib), Verzenio (abemaciclib), and Kisqali (ribociclib) are drugs that inhibit the cyclin-dependent kinases, which play a key role in the uncontrolled proliferation of cancer cells. The BCRP funded preliminary laboratory studies that provided support for subsequent clinical trials combining Ibrance with letrozole. BCRP-funded preclinical studies also contributed to development of other cyclin-dependent kinase inhibitors, including Verzenio and Kisqali.

"The same month the CDK4/6 inhibitor [ademaciclib] got approval, I was diagnosed with metastatic breast cancer. Words can't express the gratitude I have of living each day."
Patti Kellerhouse, BCRP Consumer Reviewer

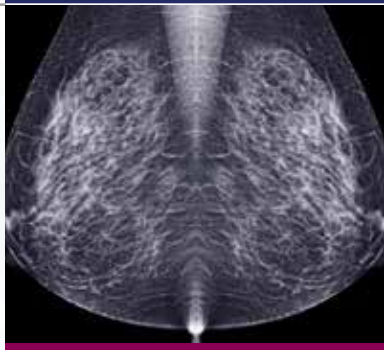
PARTNERS/COLLABORATORS

University of California, Los Angeles

AWARD NUMBER: W81XWH-11-1-0104

IMPACT: Ibrance, Verzenio, and Kisqali are approved by the FDA for the treatment of advanced or metastatic HR+, HER2-negative (HER2-) breast cancer. Verzenio is also approved for adjuvant treatment of some patients with high-risk early-stage HR+, HER2- breast cancer.

Digital Mammography and Digital Breast Tomosynthesis



DESCRIPTION

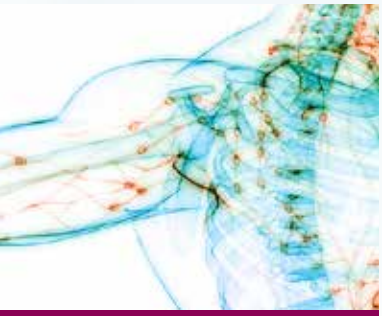
Digital mammography allows for an expanded detection range of X-ray signals than standard film mammography. A BCRP-supported study demonstrated that digital mammography is superior to film mammography in detecting breast cancer in women with dense breast tissue, leading to a change in clinical practice. The BCRP also supported the development and clinical evaluation of digital breast tomosynthesis, a tool that offers an additional 3D view to capture images for improved sensitivity.

PARTNERS/COLLABORATORS

University of Iowa; Massachusetts General Hospital

AWARD NUMBERS: DAMD17-99-1-9001, DAMD17-98-1-8309

IMPACT: Digital mammography is now used in clinical practice, and tomosynthesis systems are FDA-approved and commercialized.



Sentinel Lymph Node Biopsy

IMPACT: The sentinel lymph node biopsy diagnostic/prognostic technique, which is now standard of care, enables clinicians to determine tumor staging and whether more-extensive lymph node surgery is necessary.

DESCRIPTION

The previous standard for detecting breast cancer invasion into the lymph nodes was to remove the majority of axillary lymph nodes and search for cancer cells. In a significant proportion of women, this causes lymphedema of the arm, a condition that compromises functionality and quality of life. In a sentinel lymph node biopsy, lymph node removal is limited to only the first few nodes that receive lymph drainage from the breast. The BCRP provided funding for multicenter clinical trials to validate lymph node mapping and sentinel lymph node biopsy as an accurate method to predict the presence of disease in the axillary lymph nodes.

PARTNERS/COLLABORATORS

East Carolina University; University of South Florida

AWARD NUMBERS: DAMD17-98-1-8079, DAMD17-00-1-0239, DAMD17-97-1-7209

Molecular Breast Imaging

IMPACT: Molecular breast imaging is an FDA-approved, commercially available technology.

DESCRIPTION

Molecular breast imaging is a nuclear medicine technique that uses high-resolution gamma cameras to detect the functional uptake of a radiotracer in the breast. Following a Mayo Clinic study that demonstrated molecular breast imaging to be more sensitive than conventional mammograms for detecting breast cancer in women with dense breast tissue, the BCRP funded work to evaluate the concordance of molecular breast imaging with magnetic resonance imaging of the breast, to investigate the effects of fluctuating hormonal levels on appearance and to develop important quantitative analysis software for molecular breast imaging.

PARTNERS/COLLABORATORS

Mayo Clinic

AWARD NUMBER: W81XWH-07-1-0548

Prone Radiotherapy Treatment to Reduce Harmful Radiation to the Heart and Lung

DESCRIPTION

With BCRP support, clinical trials were conducted to assess the efficacy of an accelerated, hypofractionated whole-breast radiation therapy designed to minimize the length of radiotherapy required after partial mastectomy in patients with ductal carcinoma in situ. In this method, patients are treated on a specially designed table in the prone position rather than in the supine position, greatly reducing unnecessary radiation exposure of the heart and lungs.

PARTNERS/COLLABORATORS

New York University School of Medicine*

AWARD NUMBER: DAMD17-01-1-0345

IMPACT: Prone radiotherapy is poised to become a standard choice in breast radiotherapy. Current clinical trials and long-term follow-up will continue to examine this radiotherapy approach for efficacy and toxicity.

* Renamed New York University Grossman School of Medicine in November 2021

IMPACT: The BRCA2 617delT mutation is now part of a commercialized test for BRCA1/BRCA2 gene mutations in this risk group.

BRCA2 617delT Mutation

DESCRIPTION

Breast cancer and ovarian cancer risks are greater in individuals with mutations in the BRCA1 and BRCA2 tumor suppressor genes. The likelihood of BRCA1 or BRCA2 mutations is higher in certain populations, including individuals of Ashkenazi Jewish descent. BCRP funding contributed to the discovery of the BRCA2 617delT mutation, one of the three founder BRCA1/2 mutations that occur in Ashkenazi Jews.

PARTNERS/COLLABORATORS

University of Utah

AWARD NUMBER: DAMD17-94-J-4260

IMPACT: The OncoVue, which is commercially available, can identify high-risk patients and enable clinicians to individualize breast cancer screening and monitoring.

OncoVue®

DESCRIPTION

Risk association studies funded by the BCRP formed the foundation for a breast cancer risk assessment test. Single nucleotide polymorphisms are DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered. OncoVue is the first genetic-based breast cancer risk test that incorporates a woman's sequence variations with her personal history to estimate her risk for breast cancer.

PARTNERS/COLLABORATORS

Oklahoma Medical Research Foundation

AWARD NUMBER: DAMD17-01-1-0358

PALB2 Gene Mutations

DESCRIPTION

BCRP funding contributed to the discovery of PALB2, a BRCA2 binding protein. PALB2 and BRCA2 work together to mend broken strands of DNA, which helps to maintain the rate of cell growth. While BRCA1 and BRCA2 gene mutations are high-risk factors for breast cancer, these mutations do not account for all familial breast cancers. Identification of mutations in the PALB2 gene indicates an approximate two-fold increase in breast cancer susceptibility due to its inability to interact with BRCA2.

PARTNERS/COLLABORATORS

Dana-Farber Cancer Institute

AWARD NUMBER: DAMD17-02-1-0360

IMPACT: A commercialized PALB2 genetic test is available for those with familial breast cancer.

PTEN Gene

DESCRIPTION

BCRP funding contributed to the original discovery of the PTEN (phosphatase and tensin homolog) gene. In normal cells, PTEN functions as a tumor suppressor protein that helps regulate cell division and growth. PTEN is one of the most frequently mutated genes in several cancers, and PTEN mutations have been shown to be predictive of aggressive cancer. PTEN mutations also occur in a group of genetic syndromes that are characterized by malignant and benign tumors.

PARTNERS/COLLABORATORS

Cold Spring Harbor Laboratory

AWARD NUMBER: DAMD17-94-J-4247

IMPACT: A PTEN test is commercially available to confirm mutations in this gene for clinical and prenatal diagnoses and identification of at-risk family members.

Breast Cancer Index™ for Predicting Disease Recurrence

DESCRIPTION

Women with estrogen receptor-positive breast cancer have an increased risk of relapse many years after their initial diagnosis. To identify women with an increased risk of disease recurrence, research was conducted with BCRP support to validate biomarkers that correlate with relapse-free survival and tumor grade. Ultimately, this led to a risk assessment test termed the Breast Cancer Index.

PARTNERS/COLLABORATORS

Massachusetts General Hospital

AWARD NUMBERS: W81XWH-04-1-0606, W81XWH-10-1-0444

IMPACT: The Breast Cancer Index test, which is commercially available, provides a quantitative assessment of the likelihood of recurrence and benefit from extended endocrine therapy. In 2023, the Defense Health Agency expanded a genetic testing pilot program to include the Biotheranostics Breast Cancer Index, making it available for Service Members and their Families through TRICARE.

CHRONIC PAIN MANAGEMENT RESEARCH PROGRAM

Vision: Improving the medical readiness of Service Members, as well as the quality of life and level of function of all Americans, with or at risk for developing chronic pain

Mission: To support and promote innovative, high-impact research to prevent the development and improve the management of chronic pain in Service Members, Veterans, and beneficiaries

Years Program Appropriated: FY19-FY23

Total Appropriations: $70M

Chronic pain management is a major public health concern for civilian and military populations, affecting millions in the U.S. at an estimated annual cost in personal and health system expenditures of $560-$635 billion. The problem is magnified by the current opioid crisis, which has been exacerbated by the use of addictive narcotics to manage chronic pain. Chronic pain is defined as a pain that occurs on at least half the days for 6 months or more and that can be caused by issues including, but not limited to: combat- and training-related physical or mental stress and trauma, migraines and chronic headaches, traumatic brain injury, arthritis, muscular-skeletal conditions, neurological disease, tick- and vector-borne disease, other insect-transmitted or tropical disease, and cancer. The Chronic Pain Management Research Program (CPMRP) supports research in the fields of: pain chronification, the development of novel non-opioid therapies, and the implementation and comparative effectiveness of evidence-based efficacious interventions to manage chronic pain.

Psychologically Informed Physical Therapy (PiPT)

IMPACT: The study may pave the way for PiPT implementation in military treatment facilities and health care settings, providing improved care and facilitating return to Service.

DESCRIPTION

PiPT is a treatment modality in which physical therapists have been trained to identify and address psychological factors that increase the likelihood of disability in patients. The feasibility of using PiPT to reduce disabilities related to musculoskeletal disorders has been demonstrated in pilot studies conducted onboard a U.S. Navy aircraft carrier. The CPMRP is supporting a hybrid effectiveness-implementation study to identify optimal conditions to use PiPT in shore-based health care settings for active-duty Service Members and measure their effectiveness in reducing musculoskeletal disorder-related pain chronicity when compared to standard-of-care physical therapy.

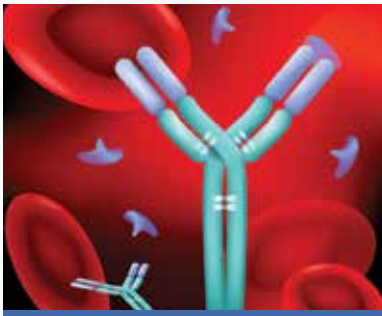
PARTNERS/COLLABORATORS

New York University School of Medicine;* Naval Medical Center Portsmouth

AWARD NUMBER: W81XWH-20-2-0036

* Renamed New York University Grossman School of Medicine in November 2021

Brain-Penetrant P2X4 Receptor Antibody Fragment Therapies



DESCRIPTION

P2X4 is a fast-acting receptor that is activated and upregulated in response to nerve injury. Preclinical evaluation of P2X4 receptor-targeting antibody fragments has demonstrated their efficacy as analgesics and in the reduction of anxiety-related behaviors associated with chronic pain. The CPMRP is funding studies designed to optimize P2X4 receptor therapies along with preclinical evaluation of the lead candidate for safety, toxicity, biodistribution, and pharmacokinetics to facilitate translation to clinical evaluation.

PARTNERS/COLLABORATORS

University of New Mexico Health Sciences Center

AWARD NUMBER: W81XWH-20-1-0930

IMPACT: Availability of novel and effective non-opioid treatment alternatives will reduce reliance on addictive therapeutics for chronic pain management.

Mechanism of Osteoarthritis Pain via a Tissue Chip Model System

DESCRIPTION

The CPMRP is supporting an effort to improve the tissue chip microJoint, a model system of the knee joint comprised of cartilage, bone, synovium, and fat pad, by introducing neural cells. Mechanical stimulation of the updated model system will be used to replicate the onset and progression of osteoarthritis. Intracellular signaling and the remodeling of the tissue and sensory neurons will be monitored to identify biomarkers associated with the transition from acute to chronic pain. Once identified, the mediators responsible for chronic pain development can be targeted to prevent the development of osteoarthritis.

PARTNERS/COLLABORATORS

University of Pittsburgh

AWARD NUMBER: W81XWH-20-1-0902

IMPACT: The development of an advanced system that can model the conditions contributing to the development of osteoarthritis may help identify potential therapeutic targets for treatment.

NIH-DOD-VA Interagency Collaboration

IMPACT: Improved coordination between government agencies enables the CPMRP to leverage the distinct knowledge and resources of the respective departments to offer innovative and collaborative opportunities while preventing redundant efforts and maximizing federal investments to develop new solutions for chronic pain management.

DESCRIPTION

The CPMRP leverages existing interagency partnerships that were established as part of the ongoing NIH-DOD-VA Pain Management Collaboratory (PMC). Representatives from the PMC-sponsoring agencies, funded investigators, and supporting working groups and committees have been incorporated into CPMRP efforts to maximize visibility and coordination of various initiatives throughout the government that address pain management. The CPMRP team manages four pragmatic clinical trials funded through the PMC by the DOD Joint Program Committees and actively participates in PMC meetings. The FY23 program cycle for the CPMRP expanded the level of interagency collaboration with a funding opportunity called the Pain Management Collaborative Clinical Research Award. This award mechanism seeks to fund a large-scale, multi-centered pragmatic clinical trial of evidence-based, non-drug-based or multimodal approaches to pain management in the Military and Veteran-related health care systems. Award recipients are expected to be active collaborators within the interagency PMC effort.

PARTNERS/COLLABORATORS

NIH National Center for Complementary and Integrative Health; Department of Veterans Affairs; Defense and Veterans Center for Integrative Pain Management; University of Texas Health Science Center at San Antonio; Brooke Army Medical Center; Yale University; Uniformed Services University of the Health Sciences

AWARD NUMBER: N/A

COMBAT READINESS–MEDICAL RESEARCH PROGRAM

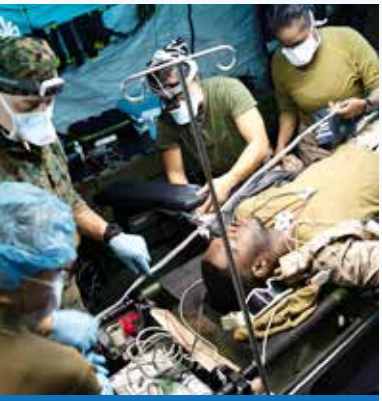
Vision: To increase survivability and readiness of the Warfighter

Mission: Develop innovative high-impact solutions to increase medical readiness, diagnose and treat life threatening injuries, reduce morbidity and mortality, and promote positive long-term outcomes for the Warfighter

Years Program Appropriated: FY19-FY23

Total Appropriations: $50M

The Combat Readiness–Medical Research Program (CRRP) was established in FY19 to pursue military-relevant advanced technology and therapeutic research related to forward-deployable solutions that can promptly address life-threatening injuries, medical threats, and treatments for Service Members in battlefield settings. The congressional language for the CRRP encompasses research that would enable the Warfighter to better respond to serious injury and mitigate the long-term effects of battlefield trauma in remote and austere environments, as well as solutions that can translate to prolonged prehospital civilian trauma care in complex environments of disrupted communication and delayed medical evacuation. CRRP Topic Areas vary each fiscal year in response to congressional direction.



ClotChip,™ a Field-Deployable Dielectric Coagulometer for Point-of-Care Assessment of Trauma-Induced Coagulopathy

IMPACT: Early detection of blood clotting problems in injured patients in both combat and civilian trauma settings may improve trauma care by helping clinicians make earlier decisions on the best types of blood products needed, thus potentially increasing survivability.

DESCRIPTION

ClotChip is a sensor device that can be used to rapidly assess a patient's bleeding risk by measuring clotting ability following injury. This funded effort seeks to evaluate performance of the current commercial-ready ClotChip device under environmental conditions similar to various military environments (extreme temperature, high vibration, etc.), as well as develop and perform initial validation of a ruggedized prototype that would be suitable for use closer to the point of injury and in extreme fielding conditions. This work complements the strategic research goals and investments of the Combat Casualty Care Research Program.

PARTNERS/COLLABORATORS

Case Western Reserve University; XaTek, Inc.; Naval Medical Center Portsmouth

AWARD NUMBER: W81XWH-20-C-0120

Combat-Ready Exposure Device (CRED) for Detection of Heavy Metals

DESCRIPTION

CRED is a portable device for the detection of lead and other heavy metals in human blood and tissue. This research effort is focused on refining and validating the CRED prototype in order to combine validated metrics of human-absorbed heavy metal doses with portability for monitoring both acute and chronic heavy metal exposures in field settings and military training and combat environments (e.g., from ammunition and munitions, burn pits, and particulate matter from improvised explosive devices). This project is synergistic with the Military Operational Medicine Research Program's efforts to detect, monitor, and assess environmental and occupational exposure to toxic contaminants.

PARTNERS/COLLABORATORS

Henry M. Jackson Foundation; U.S. Army Research Institute of Environmental Medicine; Harvard T.H. Chan School of Public Health

AWARD NUMBER: W81XWH-20-2-0037

IMPACT: A wearable sensor to detect and monitor exposures to toxic levels of heavy metals in the body could lessen short- and long-term neurological and physiological effects, as well as improve military performance and force readiness.

Scalable Peptide Therapy to Limit Burn Conversion and Speed Wound Closure

IMPACT: Development of therapeutic approaches that can promote tissue healing as well as prevent catastrophic secondary wound complications following burn injury may significantly reduce the long-term effects associated with serious burn injury.

DESCRIPTION

cNP8 is a novel small biologic molecule for treating burn wounds that limits burn injury progression, shortens healing time, and reduces scarring of acute, deep burns. cNP8 promotes tissue healing and regeneration while limiting conversion of burn injuries to more serious deep tissue wounds. This funded study resulted in a successful FDA Investigational New Drug Application and NeoMatrix Therapeutics received follow-on DOD funding from the Combat Casualty Care Research Program for the phase 1 clinical trial. This work addresses the critical need for battlefield wound healing and prevention of injury progression.

PARTNERS/COLLABORATORS

NeoMatrix Therapeutics, Inc.

AWARD NUMBER: W81XWH-20-1-0874

DUCHENNE MUSCULAR DYSTROPHY RESEARCH PROGRAM

Vision: To preserve and improve the function and quality of life, and to extend the life span of all individuals with Duchenne

Mission: To support discovery and development of therapeutics for Duchenne muscular dystrophy at all stages of the disease for the benefit of military Families and the general public

Years Program Appropriated: FY11-FY23

Total Appropriations: $69.6M

The initial research programs for Duchenne muscular dystrophy and muscle diseases began in 2003 and were institution-based at Children's National Medical Center and the University of Pittsburgh. The success of these early programs during the mid- to late-2000s led to initiation of the Duchenne Muscular Dystrophy Research Program (DMDRP). The DMDRP acknowledges there are a broad range of unanswered questions that are critical to treating Duchenne muscular dystrophy patients, improving their quality of life, and developing a cure. To make its biggest impact for the Duchenne research field and patient communities, the DMDRP focuses its funding on developing or improving treatments and clinical trial readiness. To support these priorities, all applications are required to address challenges that focus on development of safe and effective macromolecular and cellular therapies, assessment of clinical trial tools and outcome measures, preclinical translational research to support therapeutic development, or research to improve clinical care and quality of life.

Exondys 51® (Eteplirsen) and Viltepso® (Vitolarsen)

IMPACT: These exon-skipping drugs are currently available as potential treatments for the over 20% of patients with Duchenne muscular dystrophy who have a mutation amenable to exon 51 skipping (13%) or exon 53 skipping (8%).

DESCRIPTION

Duchenne muscular dystrophy is a genetic disease characterized by progressive muscle weakness and degeneration of skeletal and cardiac muscles. There is no cure for Duchenne, and young men with this disease rarely live beyond their early 30s. Duchenne muscular dystrophy is caused by mutations in the dystrophin gene that lead to an absence of dystophin in muscle cells. One treatment approach is to induce dystophin production by skipping over the mutation(s) in the genetic code (exon skipping), which can lead to production of a truncated form of dystrophin that is functional. Expression of a functional form of dystrophin will provide clinical benefit by helping to maintain muscle function. The DMDRP supported preclinical studies optimizing sequences for exon 51- and 53-skipping drugs, proof-of-concept studies in large animal models, and Good Laboratory Practice toxicology studies. The continued development of exon 51- and 53-skipping drugs by industry, the federal government, and non-government organizations led to accelerated FDA approval of Exondys 51 and Viltepso.

PARTNERS/COLLABORATORS

Children's National Medical Center (Muscle Research Consortium; Cooperative International Neuromuscular Research Group)

AWARD NUMBERS: W81XWH-09-1-0599, W81XWH-09-1-0215, W81XWH-11-1-0419

Agamree 51® (Vamorolone)

DESCRIPTION

The current standard of care for Duchenne muscular dystrophy is the use of anti-inflammatory corticosteroids to prolong muscle function, but they drive significant adverse side effects. The CDMRP supported preclinical studies on the development, safety, and efficacy evaluation of a non-hormonal steroid drug, VBP15, also called vamorolone, which demonstrated decreased muscle inflammation and reduced side effects observed with other corticosteroid-based treatments. Investigators submitted a New Drug Application after completion of a phase 2b study in boys with Duchenne that demonstrated efficacy similar to corticosteroids, and safety outcomes indicated a benign safety profile. The FDA accepted the application and approved Agamree 51 (vamorolone) for the treatment of Duchenne muscular dystrophy.

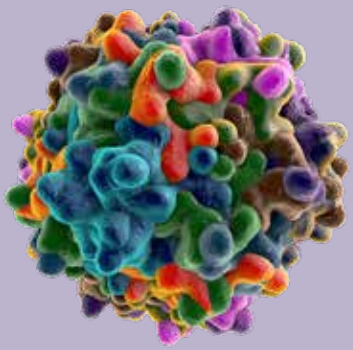
IMPACT: FDA approval of vamorolone in October 2023 addresses a clear unmet medical need by offering individuals with Duchenne muscular dystrophy a new option to improve quality of life and preventing long-term complications.

PARTNERS/COLLABORATORS

Children's National Medical Center

AWARD NUMBERS: W81XWH-05-1-0616, W81XWH-09-1-0218, W81XWH-11-1-0754

Vamorolone Shifts Balance of Efficacy/Safety of Corticosteroids



Micro-Dystrophin Gene Therapy

IMPACT: This gene therapy approach, if successful, will offer a treatment for maintaining muscle function long-term and improving the quality of life for individuals with Duchenne muscular dystrophy.

DESCRIPTION

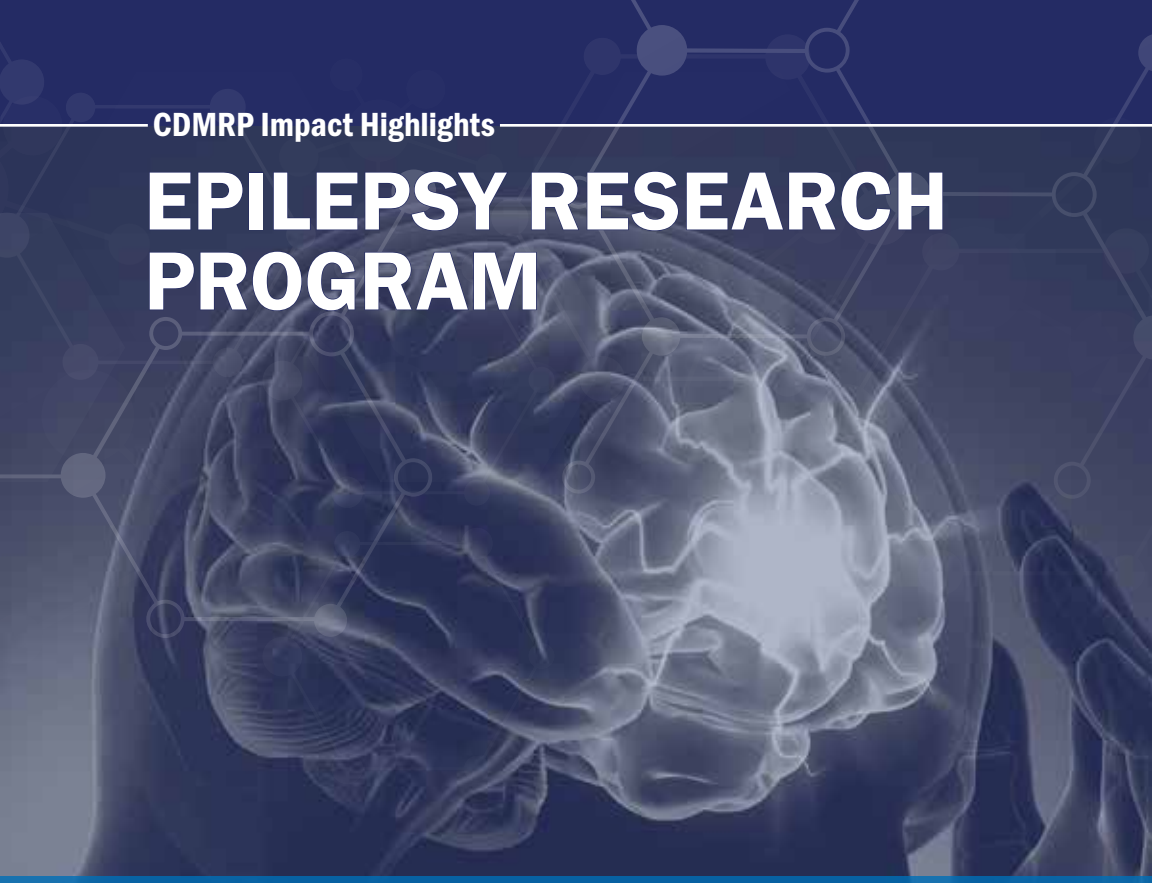
The anti-inflammatory corticosteroids currently used to prolong muscle function in Duchenne muscular dystrophy have significant adverse side effects, and muscle function is prolonged only temporarily. Efforts to develop long-term treatments and even a cure are focused on correcting the genetic mutations in the dystrophin gene that cause the disease. A very promising treatment approach is gene therapy using a micro-dystrophin gene that produces functional dystrophin. The DMDRP supported independent preclinical studies on adeno-associated virus vector optimization, production, and delivery methods for gene therapy that demonstrated improved cardiorespiratory function and persistent micro-dystrophin expression in large animal models for at least two years. The combined results from these two studies led to a collaboration with Solid Biosciences for a clinical trial (NCT03368742) evaluating micro-dystrophin gene transfer (SGT-001) in adolescents and children with Duchenne. Updated data from this ongoing trial demonstrates motor and pulmonary function stabilization or improvement in participants treated with SGT-001.

PARTNERS/COLLABORATORS

University of Florida; University of Missouri; Texas A&M University

AWARD NUMBERS: W81XWH-13-1-0283, W81XWH-14-1-0302

EPILEPSY RESEARCH PROGRAM



Vision: A time when post-traumatic epilepsy is prevented or optimally managed

Mission: To understand the mechanisms of post-traumatic epilepsy and associated comorbidities to improve quality of life, especially in Service Members, Veterans, and caregivers

Years Program Appropriated: FY15-FY23

Total Appropriations: $73.5M

The Epilepsy Research Program (ERP) was initiated in 2015 to develop an understanding of the magnitude of post-traumatic epilepsy within the military and to expand research into the basic mechanisms by which traumatic brain injury (TBI) leads to epilepsy. The ERP challenges the research community to investigate topics related to epileptogenesis for the identification of mechanisms by which brain injury produces epilepsy; study the prevention of post-traumatic epilepsy and concomitant comorbidities; and develop innovative research tools or biomarkers to better detect, diagnose, or predict the development of post-traumatic epilepsy. To address these challenges, ERP solicits research pertaining to post-traumatic epilepsy that (1) identifies biomarkers or mechanisms, (2) executes epidemiological characterization following TBI, (3) studies its evolution, or (4) develops or tests tools intended to better inform or improve upon research and care.

Blocking Innate Immune Response After Mild TBI May Prevent Long-Term Consequences of Injury

IMPACT: Inhibiting the complement immune pathway after TBI decreases neuroinflammation and is a potential preventative therapy for post-traumatic epilepsy.

DESCRIPTION

Two separate ERP-funded research teams demonstrated that inhibiting the complement immunological pathway prevents secondary brain damage, chronic neuronal inflammation, and the emergence of epileptic activities in animal models of mild TBI. This research suggests that the complement pathway has potential to be a target for future post-traumatic epilepsy therapies.

PARTNERS/COLLABORATORS

J. David Gladstone Institutes; University of Queensland

AWARD NUMBERS: W81XWH-16-1-0576, W81XWH-17-1-0670

Quality of Life for Military Populations with Post-Traumatic Epilepsy

IMPACT: Understanding the unique health care needs of Veterans with post-traumatic epilepsy can help provide more effective interventions to this population and reduce the impact of epilepsy on patients, their Families, and care partners.

DESCRIPTION

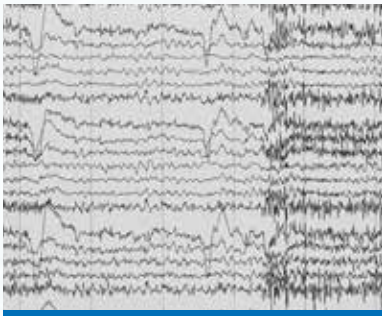
The ERP supported a comprehensive effort to compile epidemiological data needed to better understand and improve patient management for post-traumatic epilepsy. This novel study compared patient history to severity of TBI diagnoses in a post-9/11 Veteran cohort, a population with high mild-TBI incidence. Initial findings reinforce the ideas that persons living with both epilepsy and TBI have worse physical function and report lower quality of life than those with either epilepsy or TBI alone.

PARTNERS/COLLABORATORS

Biomedical Research Foundation of South Texas; South Texas Veterans Health Care System

AWARD NUMBER: W81XWH-16-2-0046

Large Animal Models of Post-Traumatic Epilepsy



DESCRIPTION

During the time between TBI and the development of post-traumatic epilepsy, the brain undergoes changes that make it prone to seizures, a process known as epileptogenesis. The most common models rely on rodents. While these models replicate some of the hallmarks of epilepsy, they may not adequately model the complex focal and diffuse brain injuries typically seen in post-traumatic epilepsy patients. In contrast, the swine brain more closely resembles human neuroanatomy. Evaluation of this animal model demonstrates some novel brain circuitry alterations, electrophysiological markers, and blood biomarkers that may be more clinically relevant and lead to a much deeper understanding of the fundamental mechanisms of epileptogenesis.

IMPACT: Better understanding of the changes in the brain after TBI that make it more prone to seizures could potentially lead to new and better clinical interventions.

PARTNERS/COLLABORATORS

University of Pennsylvania; CURE Epilepsy; Department of Neuropathology, Queen Elizabeth University Hospital

AWARD NUMBERS: W81XWH-20-1-0838, W81XWH-16-1-0675, W81XWH-20-1-0901, W81XWH-15-2-0069 (JPC-6 Funded Subaim)

Sodium Butyrate

DESCRIPTION

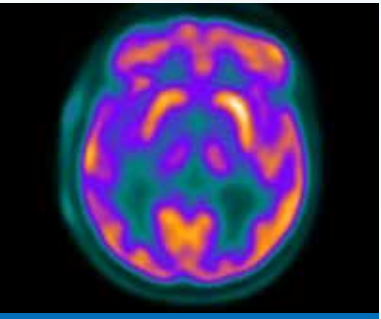
Histone deacetylases are proteins that control gene expression. In TBI, these proteins drastically increase in number. This study evaluated whether sodium butyrate could inhibit histone deacetylases function and found that sodium butyrate not only inhibited function, but also decreased events associated with post-traumatic epilepsy. Research is currently in animals only.

IMPACT: Moderating gene expression using sodium butyrate is a potential therapy for post-traumatic epilepsy.

PARTNERS/COLLABORATORS

Texas A&M Health Sciences Center, College of Medicine and Center for Epigenetics

AWARD NUMBER: W81XWH-16-1-0660



Repetitive Mild TBIs Contribute to Worsening Neurological Complications

IMPACT: The physiological and behavioral consequences of repetitive mild traumatic brain injuries (concussions) can have an additive effect, resulting in similar damage to that of a single moderate or severe brain injury.

DESCRIPTION

Blood brain barrier damage, inflammation, behavioral decline, and brain cell swelling increases in animals who experience multiple mild traumatic brain injuries. New neuroimaging techniques demonstrate that in some animal models, just three mild TBIs can result in similar blood brain barrier damage to that of a single moderate injury. Given the high prevalence of concussion in the general population, and even more concerning, the prevalence of multiple concussions, understanding the different molecular and physiological consequences of single versus multiple brain injuries is critical to determining who may be at risk of developing post-traumatic epilepsy and to the development of targeted therapies to prevent epileptogenesis.

PARTNERS/COLLABORATORS

Tufts University School of Medicine; University of Virginia School of Medicine; Massachusetts General Hospital

AWARD NUMBER: W81XWH-17-1-0531

HEARING RESTORATION RESEARCH PROGRAM

Vision: Reduce the burden of hearing loss on Service Members, Veterans, and the American public

Mission: Deliver groundbreaking research and solutions for hearing restoration by advancing the understanding, diagnosis, repair, and regeneration of the auditory system

Years Program Appropriated: FY17-FY23

Total Appropriations: $65M

The Hearing Restoration Research Program (HRRP) pursues the treatment of auditory system injuries and the restoration of hearing. Currently, no drug has been approved by the FDA to treat hearing loss associated with sensory, neural, synaptic, or central auditory dysfunction. Significant progress has been made in the understanding of hearing loss and regeneration mechanisms in animal models. However, the unique anatomical features of the inner ear severely hinder the clinical validation of preclinical findings, the translation of preclinical findings into clinical applications, and advancements in diagnostics that allow patients to be matched to appropriate interventions and outcome measurements. The HRRP challenges the science community to design innovative studies to overcome the major obstacles in clinical translation and advancements in diagnostics.

Miniature µOCT Intracochlear Imaging Probe

IMPACT: Developing a key technology, the miniature intracochlear imaging probe will revolutionize the diagnosis and treatment of sensorineural hearing loss.

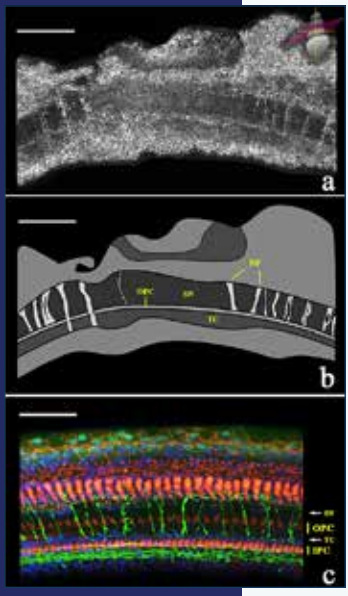
DESCRIPTION

The lack of capability to examine cochlear pathology at the cellular level severely hinders efforts to understand, diagnose, and develop treatment for sensorineural hearing loss, one of the most common war-induced injuries among American military personnel. With 1-micrometer resolution, the miniature µOCT intracochlear imaging probe can resolve intracochlear cells and auditory nerve fibers and reveal cochlear microstructure. Its successful development will make a breakthrough in the diagnosis of cellular-level cochlear pathology, enabling precision medicine in the treatment of sensorineural hearing loss.

PARTNERS/COLLABORATORS

Massachusetts Eye and Ear Infirmary, Harvard Medical School

AWARD NUMBER: W81XWH-20-1-0855

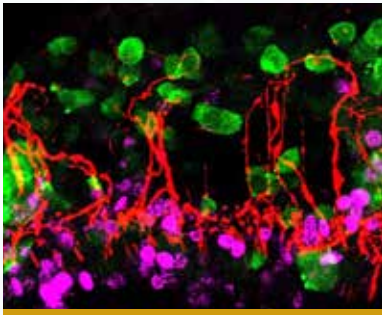


µOCT image of nerve fiber bundles traversing the tunnel of Corti and space of Nuel to innervate outer hair cells (500 µm × 500 µm).

(a) Volumetric reconstruction of maximum-projected µOCT image stack, depicting bundles of nerve fibers traversing the organ of Corti towards the outer hair cell region. The schematic in the top right-hand corner shows the orientation of the virtual sectioning plane. Scale = 150 µm. (b) Schematic representation of the microanatomy in the top panel, with bundles of nerve fibers (NF) crossing the tunnel of Corti (TC) and/or the space of Nuel (SN). OPC = outer pillar cells. Scale = 150 µm. (c) For reference, a confocal laser scanning microscopy image of the guinea pig organ of Corti. Rhodamine phalloidin (red) marks outer and inner pillar cells (OPC and IPC, respectively), Hoechst stain (blue) marks cell nuclei, and neurofilament-H (green) marks neuronal fibers. Scale = 50 µm.

Figure: Iyer, J. S. et al. Micro-optical coherence tomography of the mammalian cochlea. Sci. Rep. 6, 33288; doi: 10.1038/srep33288 (2016).

Cell Reprogramming in the Mature Mammalian Inner Ear



DESCRIPTION

The adult mammalian inner ear contains auditory cells that lack the capacity to divide or regenerate. This research began as a proof-of-principle study on the potential of "reprogramming" as a strategy to make new auditory cells in the inner ear. The team demonstrated cochlear hair cell regeneration by inducing co-activation of two genes involved in the pathway. Their success allowed for the development of drug-like cocktails that would use this pathway to reprogram existing cells to become new hair cells. Additionally, they improved efficacy of these regenerative therapeutics. This work produced two significant publications and a patent application, which led to two more awards funded by HRRP and the Military Operational Medicine Research Program.

PARTNERS/COLLABORATORS

Massachusetts Eye and Ear Infirmary, Harvard Medical School

AWARD NUMBERS: W81XWH-18-1-0331, W81XWH-21-1-0957, DMRDP HT9425-23-2-0031

IMPACT: Research results include significant advancement in the preclinical development of a novel strategy for auditory hair cell regeneration and hearing restoration.

Automated Brain-Behavior Listening Assessment

DESCRIPTION

The automated brain-behavior assessment of listening is intended for use by non-specialists with minimal training to classify auditory fitness-to-duty in austere environments. Its successful development will significantly expand auditory system injury diagnosis capability beyond current auditory tests using pure tone audiometry.

PARTNERS/COLLABORATORS

University of California, Davis

AWARD NUMBER: W81XWH-20-1-0485

IMPACT: Changes in procedures/practice expands auditory system injury diagnosis capability beyond pure tone audiometry.

IMPACT: This development of a key technology toward the regeneration of neuronal cells in the inner ear could ultimately lead to new hearing restoration therapies.

3D Stem Cells Niche

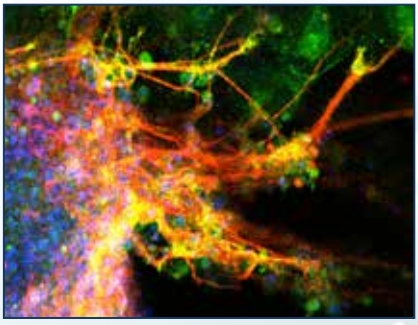
DESCRIPTION

The artificial three-dimensional stem cells niche was shown to enhance the survival and neuronal differentiation of transplanted otic neuronal progenitors. This is significant progress toward the goal of regenerating neuronal cells in the inner ear with a cell transplantation approach. This result was published in 2020 and also supported the filing of a provisional patent.

PARTNERS/COLLABORATORS

Northwestern University; Indiana University

AWARD NUMBER: W81XWH-18-1-0752



Neurite outgrowth from stem cell-derived otic neuronal progenitors.

Statins

DESCRIPTION

Recent research suggested that statins, a class of readily available drugs commonly used to treat high cholesterol, are protective against hearing threshold increases and cochlear structure damage in two animal models. Ongoing efforts aim to identify the most effective oral statin to protect against noise-induced hearing loss and cochlear damage and to investigate its effect, either alone or in combination with oral steroids, in both an animal model and in a pilot, first-in-kind clinical trial with human patients.

IMPACT: Results could significantly advance the capability to protect against hearing loss.

PARTNERS/COLLABORATORS

Northwestern University

AWARD NUMBER: W81XWH-20-1-0484

Human Inner Ear Model in a Dish

DESCRIPTION

Evaluating pharmaceutical treatments for inner ear hair cell regeneration is limited by the lack of cell culture systems outside of a living organism that mimic the inner ear. Funded by an FY17 Translational Research Award, researchers grew human inner ear organoids in a 3D format that mimics the structure and function of human inner ear tissues. The team successfully developed a protocol to use human stem cells capable of differentiating into one of many cell types to generate organoids containing sensory epithelia with hair cells. This protocol provides a platform for further research in the human inner ear, including a model system to discover therapeutic targets for hearing restoration.

IMPACT: This protocol opened vast opportunities for studying human inner-ear development, disease, and regeneration, and for testing potential therapeutics.

PARTNERS/COLLABORATORS

Indiana University-Indianapolis

AWARD NUMBER: W81XWH-18-1-0062

Hearing Research Funding Network (HRF-NET)

IMPACT: By building broad, open, and continuous communication, HRF-Net helps organizations coordinate activities, align initiatives, and create overall greater efficiencies in hearing health research and development.

DESCRIPTION

The HRRP hosted the inaugural meeting of the Hearing Research Funders Network in January 2023. The virtual meeting included more than 40 participants from 26 organizations with 14 presentations by representatives from various funding organizations, followed by an open-forum discussion of critical gaps in the hearing restoration research field. As a result of a successful meeting, HRRP is hosting quarterly virtual meetings of the Hearing Research Funders Network to continue to lead an effort in fostering collaboration toward advancements in hearing research.

PARTNERS/COLLABORATORS

American Academy of Audiology Foundation; American Cochlear Implant Alliance; American Hearing Research Foundation; American Neurotology Society; American Otological Society; American Speech-Language-Hearing Foundation; American Tinnitus Association; Association for Research in Otolaryngology; Cures Within Reach; Defense Advanced Research Projects Agency; Defense Health Agency; Department of Defense Hearing Center of Excellence; Department of Veterans Affairs; Fondation Pour l'Audition; Hearing Health Foundation; Hearing Loss Association of America; Hearing Restoration Research Program; Military Operational Medicine Research Program; National Institute on Deafness and Other Communication Disorders; Royal National Institute for Deaf People; U.S. Army Medical Materiel Development Activity

AWARD NUMBER: n/a

JOINT WARFIGHTER MEDICAL RESEARCH PROGRAM

Vision: Expedited delivery of highly impactful and effective military medical solutions

Mission: Support the logical continuation of DOD-funded research and development projects that augment and accelerate high-priority medical requirements to meet the needs of Service Members and other Military Health System beneficiaries

Years Program Appropriated: FY12-FY23

Total Appropriations: $595M

The Joint Warfighter Medical Research Program (JWMRP) is unique among CDMRP programs in that it is focused on supporting the logical continuation of DOD-funded medical research and development projects. Per Congressional language, JWMRP funds should not be used for new projects or basic research. Instead, these funds are intended to augment and accelerate projects that address high-priority medical requirements to meet the needs of Service Members and other Military Health System beneficiaries. The JWMRP also uniquely funds science and technology projects to mature those efforts and feed the pipeline toward advanced development as well as advanced development efforts across the services. This strategy helps to shuttle military medical solutions through the acquisition life cycle and to the Warfighter faster. The program obtains input into its priorities by coordinating with stakeholders from the Defense Health Agency, Army, Navy, and Air Force who review research and development gaps, funding shortfalls in the core programs, and unfinanced medical requirements. The JWMRP has historically supported a number of military medical research areas – the largest being military operational medicine, combat casualty care, and military infectious diseases.

SonicEye® Wearable Ultrasound Probe

IMPACT: Using the fine motor control unique to the fingertip, this device allows a novice or infrequent user to ergonomically perform ultrasound with one hand.

DESCRIPTION

The ergonomic design of traditional handheld ultrasound probes inhibits vascular access. Researchers advanced the development of the SonicEye, a fingertip wearable ultrasound probe system for battlefield use. The device connects to a tablet display or a wireless ultrawide-band smart phone display to show ultrasound images of the vascular system, organs, muscles, and tendons as the finger moves over them. An interface guides the user through a field examination and saves the images. The FDA granted 510(k) clearance to the complete portable system in 2020, and commercial opportunities are now being explored.

PARTNERS/COLLABORATORS

Sonivate Medical; Madigan Army Medical Center

AWARD NUMBER: W81XWH-17-C-0024

J-PRO Osteoarthritis Therapeutic

IMPACT: Among the military population, acute knee injuries comprise 5% of the reported injuries, and post-traumatic osteoarthritis is a primary source of disability. This injectable therapeutic can enhance the opportunity to return to duty and improve injured Service Members' quality of life.

DESCRIPTION

J-PRO is an injectable lyophilized extracellular matrix that is mixed with the patient's blood as a point-of-care therapeutic for post-traumatic osteoarthritis. This therapeutic restores articular cartilage after joint injury and prevents the development of osteoarthritis, thus maximizing joint function.

PARTNERS/COLLABORATORS

Massachusetts General Hospital; Boston Children's Hospital; Rhode Island Hospital

AWARD NUMBERS:

W81XWH-17-2-0016,
W81XWH-15-C-0052,
W81XWH-16-C-0043,
W81XWH-16-C-0172

PleuraPath™ Chest Tube System for Treatment of Severe Torso Trauma

IMPACT: This technology addresses the need for optimizing chest tubes for combat and simplified use in non-sterile areas and limits the short- and long-term consequences of severe hemorrhage.

DESCRIPTION

Thoracic trauma is a principal cause of combat death and a significant cause of mortality among civilians. Tube thoracostomy, which enables the evacuation of air and fluid from the pleural cavity, is the definitive treatment for the majority of severe chest injuries. Researchers developed the PleuraPath chest tube system, which removes nearly 20% more blood from the pleural cavity than a traditional chest tube. The improved system allows easy adjustment and/or replacement of chest tubes after the initial insertion procedure, instead of fully repeating the initial sterile procedure, making it amenable to battlefield use. It also has additional attachments for patient transport and performing advanced video-assisted thoracoscopic surgery procedures.

PARTNERS/COLLABORATORS

Critical Innovations, LLC

AWARD NUMBERS: W81XWH-19-C-0077, prior funding under W81XWH-17-C-0211 DHA Small Business Innovation Research (SBIR)

Targeted Normoxia Strategy to Define Oxygen Requirements for Combat Casualty Care

IMPACT: This strategy will impact supplemental oxygen use in combat to optimize patient outcomes, while conserving oxygen supplies in deployed combat settings.

DESCRIPTION

Oxygen therapy is critical in combat casualty care to treat/prevent morbidity associated with hypoxia. But overuse of routine supplemental oxygen can result in hyperoxia, which can be harmful. In a multicenter randomized implementation trial targeting normoxia (90-96% oxygen in the blood) as compared to conventional/generous oxygenation in adult trauma patients, researchers have shown that the targeted normoxia strategy reduced oxygen consumption (increased number of days without supplementary oxygen) without increasing hypoxemia. These results are leading to changes in DOD Joint Trauma System clinical practice guidelines.

PARTNERS/COLLABORATORS

University of Colorado Denver; DOD Joint Trauma System; Combat Casualty Care Research Program.

AWARD NUMBER: W81XWH-20-2-0001

SPRINT® Peripheral Nerve Stimulation (PNS) System

DESCRIPTION

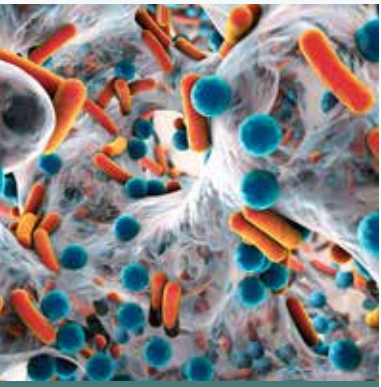
The PNS system is designed to improve functional outcomes by alleviating residual limb pain and phantom limb pain in major lower limb amputees. The FDA cleared this product in 2018 as a non-drug solution for managing post-amputation pain, which can lead to disability, reduced quality of life, frustration, and depression, factors that can impact function even more than the actual loss of a limb. The PNS system was later approved for chronic and acute back pain and extremity pain indications in 2021 and 2023.

PARTNERS/COLLABORATORS

SPR Therapeutics; Northwestern University; University of California San Diego; University of Texas Health Science Center at San Antonio; James A. Haley Veteran's Hospital; OtriMed Clinical Research Center; Duke University; Better Health Clinical Research; MedVadis Research (Boston PainCare)

AWARD NUMBERS: W81XWH-17-C-0019; additional funding from PRORP W81XWH-12-2-0132, W81XWH-18-1-0799, PRMRP W81XWH-18-1-0800

IMPACT: JWMRP accelerated the timeline for 510(k) clearance. This device addresses a significant health care need for non-narcotic pain relief.



AP-SA02, a Novel Bacteriophage Therapeutic for Targeted Treatment of Staphylococcus Aureus Bacteremia

IMPACT: This biologic alternative to antibiotics has the potential to save and improve lives and accelerate return-to-duty.

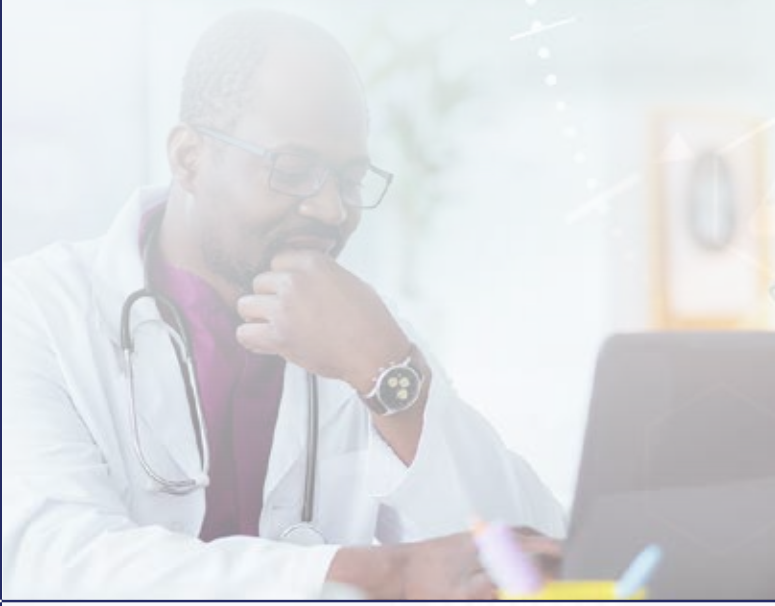
DESCRIPTION

Infections caused by multi-drug resistant bacteria are increasing worldwide. There are more complications and higher death rates, which has a direct impact on operational readiness. This presents a challenge for the treatment of combat extremity wound infections. AP-SA02, a two-phage therapeutic cocktail that targets Staphylococcus aureus and can penetrate biofilms, has advanced to a phase 2a trial as researchers look to further evaluate its efficacy. This includes an assessment of drug-resistant isolates, safety, tolerability, and efficacy/dosing of intravenous AP-SA02 as an adjunct to the best available antibiotic therapy.

PARTNERS/COLLABORATORS

Armata Pharmaceuticals; Naval Advanced Medical Development Program

AWARD NUMBER: W81XWH-20-9-0006



MeniscoFix™ for Total Meniscus Reconstruction

IMPACT: This medical device has the potential to accelerate return-to-duty, improve quality of life, and reduce long-term health costs.

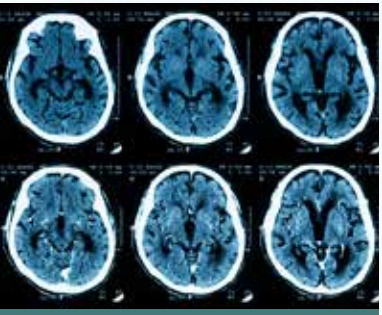
DESCRIPTION

Meniscal tears occur approximately ten times more frequently in the military than in the civilian population, which negatively affects readiness and resilience. Researchers developed MeniscoFix, a total meniscus replacement device that gradually resorbs and promotes neo-meniscus formation to restore mobility and prevent the onset of degenerative post-traumatic osteoarthritis. Pre-clinical safety and biocompatibility studies in a large animal model demonstrated ingrown tissue on the device including inflammatory cells, fibroblasts, and blood vessels. As inflammation subsides and polymer fibers lose strength, neo-meniscus tissue undergoes remodeling and maturation in response to biomechanical loading in the knee joint.

PARTNERS/COLLABORATORS

Rutgers State University; Armed Forces Institute of Regenerative Medicine

AWARD NUMBERS: W81XWH-20-1-0087; prior funding under Clinical and Rehabilitative Medicine Research Program W81XWH-14-2-0003



Intracranial Pressure Assessment and Screening System (IPASS)

IMPACT: This system provides the capability to triage casualties with closed-head brain injuries much closer to the time of the trauma, enabling rapid treatment to preclude further injury, thus improving patient care.

DESCRIPTION

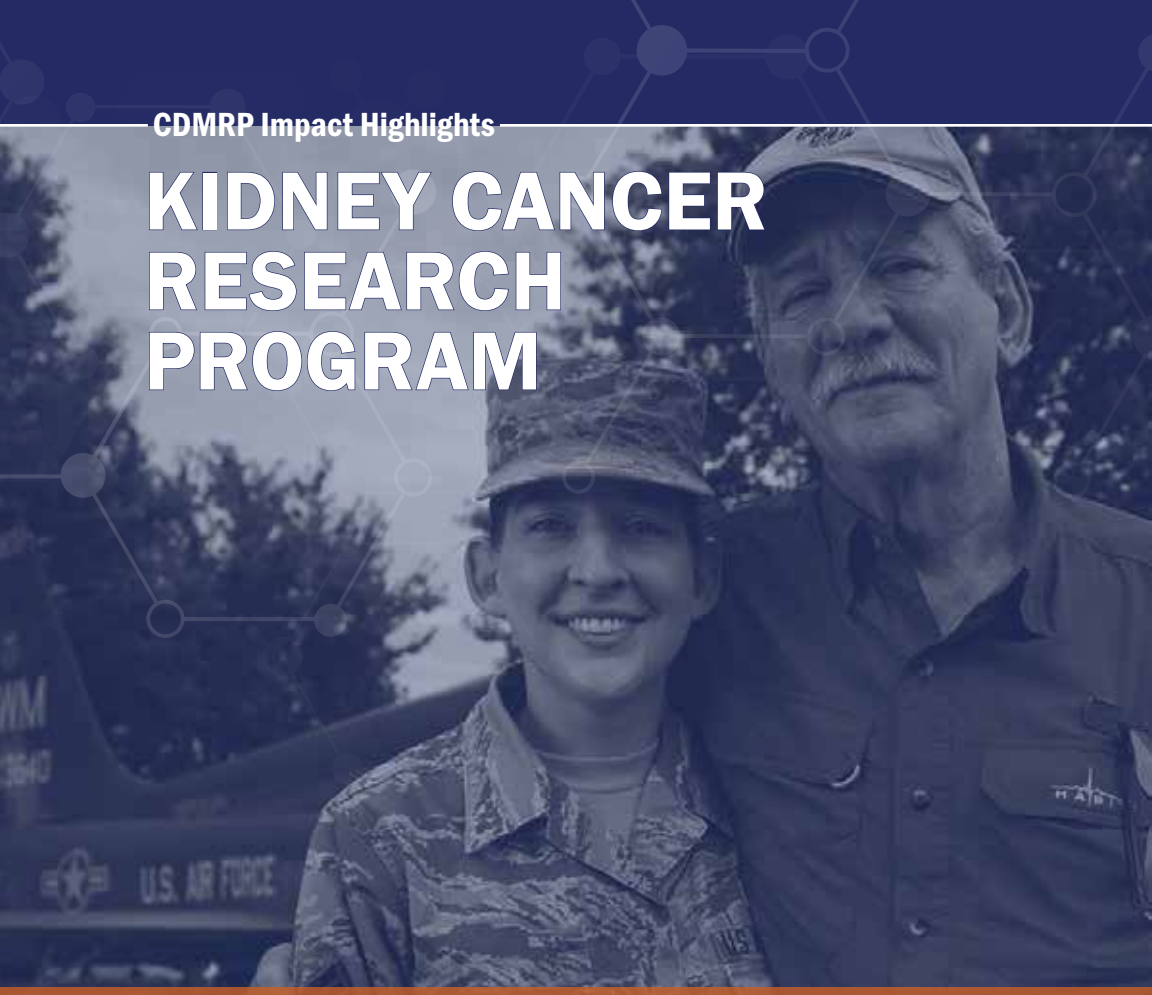
The IPASS is a compact, portable monitor for non-invasive measurement of intracranial pressure to assess impairments following TBI. This device eliminates the need for invasive neurosurgical procedures by using sensors placed on the forehead, earlobe, and/or fingertip and allows medics and clinicians to reliably monitor TBI patients across the spectrum of en-route care and facilities-based treatment.

PARTNERS/COLLABORATORS

Vivonics, Inc.; University of Miami; Johns Hopkins University School of Medicine; University of Pittsburgh; Baylor College of Medicine; Rhode Island Hospital; Tufts Medical Center; Beth Israel Deaconess Hospital

AWARD NUMBERS: W81XWH-17-C-0006; additional funding under W81XWH-13-0187, W81XWH-15-9-0001

KIDNEY CANCER RESEARCH PROGRAM



Vision: To eliminate kidney cancer through collaboration and discovery

Mission: To promote rigorous, innovative, high-impact research in kidney cancer for the benefit of Service Members, Veterans, and the American public

Years Program Appropriated: FY17-FY23

Total Appropriations: $235M

Started in FY17, the peer reviewed Kidney Cancer Research Program (KCRP) quickly became a leader in the drive to eliminate kidney cancer. The KCRP developed strategic goals to increase the understanding of kidney cancer biology and develop novel therapeutic strategies to treat kidney cancer. The program facilitates collaborative research to integrate bench research with bedside care to improve patient health outcomes.

Academy of Kidney Cancer Investigators (AKCI)

IMPACT: This virtual academy provides new opportunities for collaboration across kidney cancer disciplines and is expected to synergize with the KCRP's other signature effort, the KCRC, to accelerate translation of research for improved patient outcomes.

DESCRIPTION

The ACKI is an innovative, interactive virtual academy that connects an academy dean with a cadre of early-career researchers to develop a network committed to careers as kidney cancer experts and to accelerate advances in kidney cancer treatment. A major goal of the Academy is to provide a framework to further the innovative research being conducted by highly productive kidney cancer researchers in a collaborative research and career development environment.

Accomplishments include: 36 total first- or last-author publications, 20 podium presentations at national meetings, 45 peer-reviewed grants submitted with 13 funded, and 38 abstracts submitted to major meetings.

PARTNERS/COLLABORATORS

Vanderbilt University Medical Center; Dana-Farber Cancer Institute; Dartmouth College; Cleveland Clinic Foundation; Yale University; Harvard Medical School; Memorial Sloan Kettering Cancer Institute; Mayo Clinic (Jacksonville); University of Texas Southwestern Medical Center; University of Alabama at Birmingham

AWARD NUMBERS: W81XWH-20-2-0046, W81XWH-20-1-0882, W81XWH-20-1-0778, W81XWH-20-1-0804, W81XWH-21-1-0942, W81XWH-21-1-0678, W81XWH-21-1-0778, W81XWH-22-1-0764, W81XWH-22-1-0951, HT9425-23-1-0801, HT9425-23-1-0783

Kidney Cancer Research Consortium (KCRC)

IMPACT: To achieve improved kidney cancer patient outcomes, this award established a multi-site network of exceptional institutions and investigators who can rapidly execute kidney cancer trials that would otherwise be difficult to complete at any single center.

DESCRIPTION

The KCRP awarded a Consortium Development Award followed by a Clinical Consortium Award to establish and support a geographically dispersed KCRC composed of a coordinating center and six clinical trial sites. The KCRC will execute trials for patients with all types of renal cell carcinoma, including rarer forms like medullary, papillary, and chromophobe renal cell carcinomas. The ultimate goal is to discover more specific treatment approaches that are driven by an improved understanding of renal cell carcinoma biology and therapies targeted to the right patient subpopulations.

Clinical trials include: NCT048838, Disease Burden and Biology Using Tumor Cell Free DNA in Metastatic Kidney Cancer; NCT05501054, Phase 1b/2 Trial of Ipilimumab, Nivolumab, and Ciforadenant in First-Line Advanced Renal Cell Carcinoma; NCT05663710, Phase 1b/2 Study of 177Lu Girentuximab Plus Cabozantinib and Nivolumab in Treatment-Naive Patients With Advanced Clear Cell Renal Cell Carcinoma; and NCT06053658, Phase 2 Study of Combination Tivozanib and Nivolumab in Advanced Non-Clear Cell Renal Cell Carcinoma. Pending activation is award number HT9425-23-1-0926, Drug Development of ONC392, a Novel CTLA-4 Inhibitor in Advanced Renal Cancer.

PARTNERS/COLLABORATORS

M.D. Anderson Cancer Center; University of Texas, Southwestern Medical Center at Dallas; University of Pennsylvania; Beth Israel Deaconess Medical Center; Duke University; University of Michigan; Vanderbilt University Medical Center

AWARD NUMBERS: W81XWH-18-2-0052, W81XWH-20-2-0020, W81XWH-20-2-0021, W81XWH-20-2-0022, W81XWH-20-2-0023, W81XWH-21-2-0023, W81XWH-21-2-0024, W81XWH-21-2-0025, W81XWH-20-1-0910, W81XWH-22-1-0456

Prognostic Biomarker to Detect Recurrent Kidney Cancer

IMPACT: Identification of a possible new biomarker to accurately predict renal cell carcinoma recurrence following kidney removal may transform clinical care by allowing clinicians to identify patients who will benefit from additional therapy.

DESCRIPTION

The goal of this project is to develop and validate cell-free methylated DNA (DNA found freely circulating in the blood) as a prognostic biomarker to predict recurrent renal cell carcinoma following kidney removal. Samples are being analyzed from two randomized controlled clinical trials that compared the effectiveness of targeted therapy versus placebo in patients with advanced high-risk renal cell carcinoma treated with surgery. The advantages of cell-free methylated DNA as a biomarker are that it is a simple, non-invasive way to detect cancer cells and it allows identification of tumor tissue origin.

PARTNERS/COLLABORATORS

Dana-Farber Cancer Institute

AWARD NUMBER: W81XWH-19-1-0553

Preventing Therapeutic Resistance in Kidney Cancer

IMPACT: This project identified a possible new second-line therapy that could prevent tumor recurrence.

DESCRIPTION

One class of front-line therapy for patients with metastatic renal cell carcinoma targets tumor-associated new blood vessel growth in order to starve tumor cells of oxygen and nutrients carried by the bloodstream. Therapies that inhibit this blood vessel growth have shown promise to extend the lives of patients, although most eventually fail due to therapeutic resistance. Once treatment ends, the resistant tumor cells emerge from their dormant state, and tumor growth and metastasis resumes. This work describes how renal cell carcinoma tumors become resistant to therapies by inhibiting growth of new blood vessels and "starving" the tumor. This suggests that adding a second therapy that prohibits tumor cells from entering a dormant state may prevent tumor resistance and metastasis.

PARTNERS/COLLABORATORS

Health Research Inc., Roswell Park Division

AWARD NUMBER: W81XWH-14-1-0210 (PRCRP-funded award under the kidney cancer Topic Area)

Silk as a Scaffold to Model the Tumor Microenvironment

DESCRIPTION

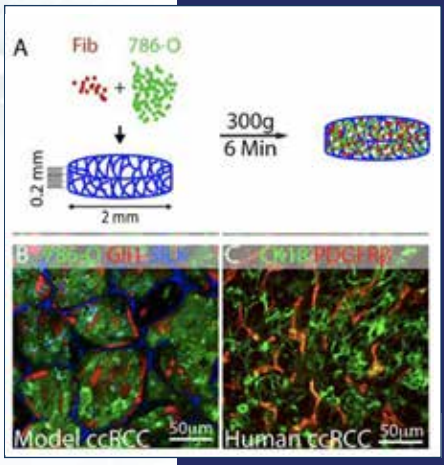
This KCRP-funded project establishes a synthetic tumor microenvironment to model clear cell renal cell carcinoma in an effort to better understand the role that tumor stromal cells play in disease progression. The team is developing an assay that mimics the extracellular matrix scaffolding "structure" to determine the complex interactions and influences that tumor-associated fibroblasts have on tumor aggressiveness. Use of the silk-based growth conditions that can mimic clear cell renal cell carcinoma in patients provides a robust system for detailed cellular and genetic analyses to better understand disease development, progression, and potential therapeutic targets.

PARTNERS/COLLABORATORS

The Rogosin Institute, Inc.

AWARD NUMBER: W81XWH-18-1-0620

IMPACT: Better understanding of disease progression via a new model allows for rapid and large-scale evaluation of novel therapeutics and the study of therapeutic resistance in clear cell renal cell carcinoma and potentially other cancers as well.



Validation of silk scaffolding for clear cell renal cell carcinoma cell coculture with fibroblasts. (A) Strategy for seeding cells into silk scaffolds: fluorescently labeled fibroblasts and tumor cells were mixed at 1:10 ratio, added to scaffolds, centrifuged into scaffolds, and cultured for 3 days before visualization. (B) Confocal micrograph of representative scaffolded tumor cells and fibroblasts from 6 replicates. The silk material is autofluorescent in the DAPI channel (blue). (C) Example of human clear cell renal cell carcinoma with tumor cells stained for cytokeratin 18 (green) and PDGFRβ-expressing stromal cells (red). Tumor cell clusters and stromal cell arrangement are similar between the scaffolded cells and the tumor.

C74–Tumor Cell Growth Inhibitor

IMPACT: This study could potentially provide a new tool to slow or prevent metastasis for the vast majority of clear cell renal cell carcinoma patients with more advanced disease.

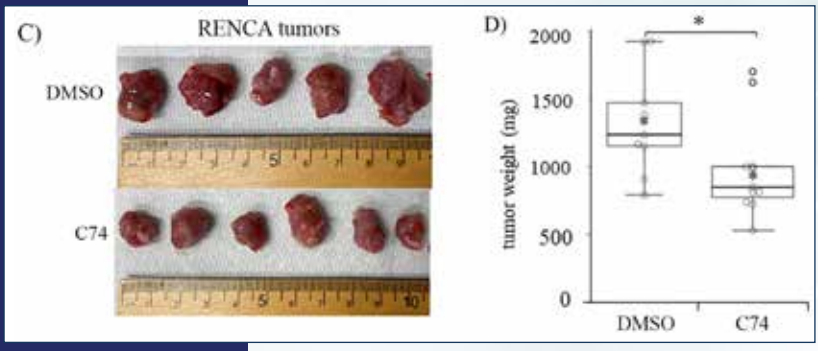
DESCRIPTION

Higher expression of the protein profilin-1 in clear cell renal cell carcinoma tumors is linked to advanced disease and poor patient outcomes. The research team conducted studies to understand the role of this protein in promoting tumor aggressiveness. This funding resulted in the development of a small molecule C74 that can bind to profilin-1 and interfere with pro-tumor activity. The study also showed the C74 molecule was able to limit tumor cell growth in a preclinical proof of concept study. Next steps include continued improvements in the formulation and delivery of the C74 molecule as well as derivative forms of this inhibitor.

PARTNERS/COLLABORATORS

University of Pittsburgh

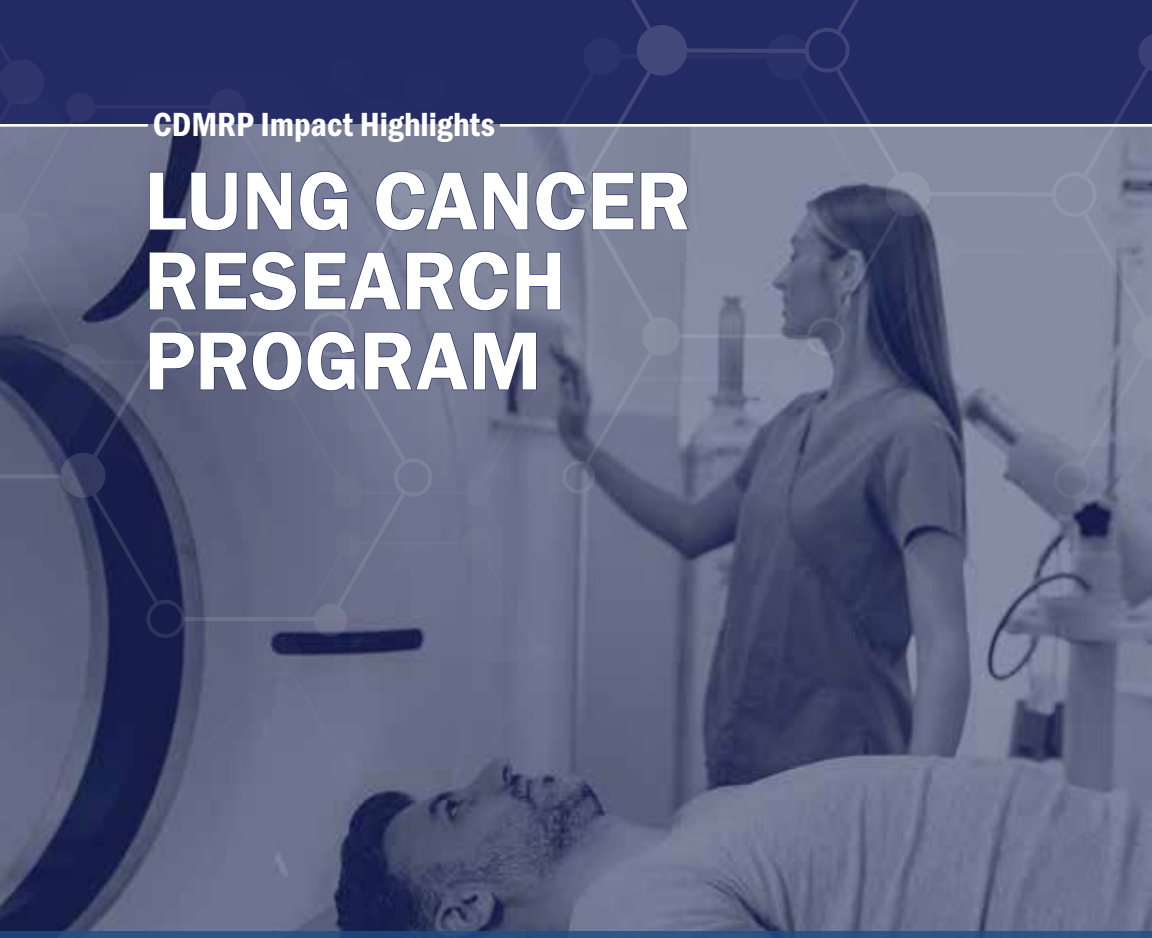
AWARD NUMBER: W81XWH-19-1-0768



C74 inhibits kidney tumor growth in vivo. Mice bearing subcutaneous RENCA tumors, a mouse model of clear cell renal cell carcinoma, were treated daily with either control (DMSO) or the profilin-1/Actin inhibitor C74. After 20 days, C74-treated tumors were found to be significantly smaller in size (C) and in weight (D), indicating a reduction in tumor aggressiveness.

Figure adapted from: Allen A, Gau D, et al. 2020. Actin-binding protein profilin1 promotes aggressiveness of clear-cell renal cell carcinoma cells. *Journal of Biological Chemistry* 295(46):15636-15649.

LUNG CANCER RESEARCH PROGRAM



Vision: To eradicate deaths and suffering from lung cancer to better the health and welfare of Service Members, Veterans, and the general public

Mission: Support and integrate research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, management, and treatment for the control and cure of lung cancer

Years Program Appropriated: FY09-FY23

Total Appropriations: $220.5M

The Lung Cancer Research Program's (LCRP's) mission is to eradicate deaths and suffering from lung cancer to better the health and welfare of Service Members, Veterans, and the general public by supporting and integrating research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer. The LCRP recognizes that there are a broad range of unanswered research questions in lung cancer; therefore, LCRP's strategic priorities seek to address an important gap in the funding of lung cancer research—specifically, the seeding of new and innovative ideas that, once proven, can proceed forward for further translational development and clinical trial testing under the auspices of other funding agencies, as well as the LCRP.

Detection of Early Lung Cancer Among Military Personnel (DECAMP) Clinical Consortium

IMPACT: The establishment of the DECAMP consortium provided the infrastructure and a unique cohort of military-relevant biospecimens to facilitate research on early detection of lung cancer through non-invasive means by the lung cancer research community.

DESCRIPTION

Initiated by the LCRP, the DECAMP consortium is a multidisciplinary and translational research program established to develop and validate biomarkers that could be used to improve the early detection of lung cancer among military personnel, military Family members, and Veterans believed to be at high risk. Consortium members include seven Veterans Administration hospitals, three Military Treatment Facilities, and two academic hospitals. DECAMP clinical research seeks to establish non-invasive clinical biomarkers to clarify the results of low-dose CT scans of patients where initial clinical findings are indeterminate for lung cancer, and to screen and identify individuals at highest risk for developing lung cancer. The DECAMP consortium secured subsequent funding through industry and other federal agency partnerships, which is ensuring the consortium continues beyond the original LCRP investment.

PARTNERS/COLLABORATORS

Boston University Medical Campus; VA Tennessee Valley Healthcare System; University of California Los Angeles; Brown University; M.D. Anderson Cancer Center; Boston University Medical Campus; Naval Medical Center San Diego; Walter Reed National Military Medical Center; Naval Medical Center Portsmouth; Brooke Army Medical Center*

AWARD NUMBER: W81XWH-11-2-0161

* Initial partner, currently no longer participating

Overcoming Apoptotic Defects in Therapy-Resistant Lung Cancers

DESCRIPTION

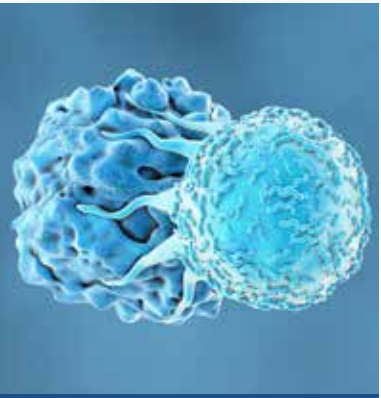
Lung cancers are frequently driven by specific oncogenes that offer unique opportunities to develop targeted therapies. Unfortunately, targeted therapies often have variable success rates owing to the heterogeneous nature of the tumors, and responsive tumors often develop resistance to therapy. LCRP-funded work evaluated the role that a pro-cell death (apoptosis) gene, BIM, plays as both a predictor of potential therapeutic success and as a therapy itself. Results demonstrated that defective apoptosis is a key mediator of resistance to tyrosine kinase inhibitor-targeted therapies. This work led to an NCI-supported clinical trial (NCT02520778) evaluating Navitoclax in combination with Osimertinib in metastatic EGFR-positive lung cancer patients.

PARTNERS/COLLABORATORS

Massachusetts General Hospital

AWARD NUMBERS: W81XWH-13-1-0226, W81XWH-13-1-0227

IMPACT: Researchers identified novel cell-signaling targets involved in cancer development, which led to testing of new therapeutics with the potential to improve care options for lung cancer patients.



Innovative Drug Combinations to Improve Immunotherapy for Lung Cancer Treatment

IMPACT: This work will pave the way for a new generation of combinatorial interventions aimed at concurrently targeting checkpoint inhibitory pathways and enhancing the recognition of tumor cells that cooperate to improve the activity of antitumor T cells. If successful, this will provide the opportunity for more patients with metastatic lung cancer to be long term survivors.

DESCRIPTION

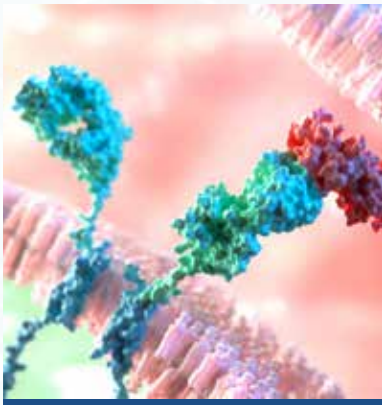
Today, nearly all patients with advanced non-small cell lung cancer are treated with immunotherapy and as many as 30% of people are long-term survivors. Despite this success, 70% of people still do not derive this long-term benefit. Immunotherapy that targets immune checkpoint pathways works well if immune cells (T cells) can recognize the tumor cells. But, in many patients, tumor cells can reduce the amount of a protein called MHC-1 on their surface that is necessary for T cells to recognize and kill the tumor cell. One way that tumor cells reduce MHC-1 expression is by secreting a protein called PCSK9, and treating tumor cells with an antibody that neutralizes PCSK9 prevents this from happening. The LCRP supports a clinical trial where patients are treated with anti-PSCK9 antibodies so tumor cells will no longer by ignored by T cells. This could further improve immunotherapy treatment outcomes.

PARTNERS/COLLABORATORS

Duke University

AWARD NUMBERS: W81XWH-21-1-0532, W81XWH-21-1-0533

GD2-Targeting Chimeric Antigen Receptor (CAR) T-Cell Therapy



DESCRIPTION

Lung cancer is the leading cause of cancer-related death in the U.S. Using immunotherapy with chemotherapy improves survival rates and cancer control. But two years after treatment, only 22% of patients remain alive and free from cancer growth. A common strategy used by cancer cells to evade the immune system is to stop making HLA, a protein that presents foreign elements from the cancer cells to T cells, thus preventing these immune cells from attacking and killing the cancer. CAR T-cell therapy, however, can recognize foreign material even when not presented by HLA. LCRP funding is supporting a phase 1 clinical trial using CAR T cells targeting GD2, a protein frequently expressed in lung cancers, in the treatment of extensive and late-stage lung cancers. The GD2 targeted CAR T cells express IL-15, which increases the ability of the CAR T cells to self-perpetuate and thus increase efficacy. These cells also express a "kill switch" that will allow the cells to be eliminated in case of side effects, thus increasing safety.

PARTNERS/COLLABORATORS

University of North Carolina at Chapel Hill

AWARD NUMBERS: W81XWH-22-1-1110, W81XWH-22-1-1111

IMPACT: Because CAR T-cell therapy is not dependent on antigen presentation by HLA (the most common mechanism of immunotherapy evasion by lung cancer tumors), it will offer the next-line immunotherapy for lung cancer. In addition, since CAR T cells are not restricted by HLA type, this therapy would be broadly available to patients of all races.

Novel Combination Therapy for Inoperable Lung Cancer

IMPACT: This combination therapy will potentially address inadequate treatment strategies for the nearly 20% of patients diagnosed with early stage non-small cell lung cancer who are not candidates for surgical or chemotherapeutic intervention.

DESCRIPTION

The LCRP funded a phase 1 clinical trial of TECENTRIQ® (atezolizumab) in combination with standard of care targeted radiation therapy in patients with early stage, inoperable, non-small cell lung cancer. Patients enrolled in this first-of-its-kind phase 1 study demonstrated no disease progression or dose-limiting toxicity while participating in this study. Additionally, several patients in the small cohort experienced a partial regression of their primary tumors. These exciting data led to the NCI-supported, ongoing phase 3 clinical trial (NCT04214262) to examine the benefit of adding atezolizumab to targeted radiation therapy for non-small cell lung cancer patients with inoperable stage I-IIA tumors.

PARTNERS/COLLABORATORS

University of California, Davis; Genentech

AWARD NUMBER: W81XWH-15-2-0063

Rigosertib: A Novel Non-Small Cell Lung Cancer Therapy

DESCRIPTION

The KRAS genetic mutation is a known driver of non-small cell lung cancer, but efforts to target the molecule therapeutically have proven challenging. The LCRP funded preclinical studies of novel small molecules that mimic and prevent an important binding function of RAS and can thus block signaling leading to progression of non-small cell lung cancer. Rigosertib is an orally available RAS mimetic that exhibits efficacy as a lung tumor growth inhibitor in mice. Additional work demonstrated that rigosertib may synergize with conventional immune checkpoint inhibitor therapies to reduce total lung tumor burden in mouse models. Based on these results, an Icahn School of Medicine at Mount Sinai-supported clinical trial (NCT04263090) launched to evaluate rigosertib in combination with immune checkpoint inhibition.

IMPACT: Successful results from preclinical studies supported clinical testing for rigosertib as a novel and potentially more effective therapeutic to improve treatment options for non-small cell lung cancer patients.

PARTNERS/COLLABORATORS

Icahn School of Medicine at Mount Sinai

AWARD NUMBER: W81XWH-17-1-0207

Lung Cancer Biospecimen Resource Network (LCBRN)

DESCRIPTION

The LCRP established the first national lung cancer biospecimen resource unattached to a clinical trial, the LCBRN, with the intent to further basic, translational, and clinical research in the understanding, diagnosis, and treatment of lung cancer. Over its active life, the LCBRN collected, annotated, stored, and distributed human lung cancer biospecimens and follow-up clinical data from 763 patients in a manner that embraced the highest ethical standards for human subjects research. The LCBRN participated in the Cancer Moonshot Program's APOLLO (Applied Proteogenomics OrganizationaL Learning and Outcomes) Consortium, a tri-agency effort between the DOD, VA, and NCI. All LCBRN samples are now managed through the NIH Cooperative Human Tissue Network (http://lungbio.sites.virginia.edu).

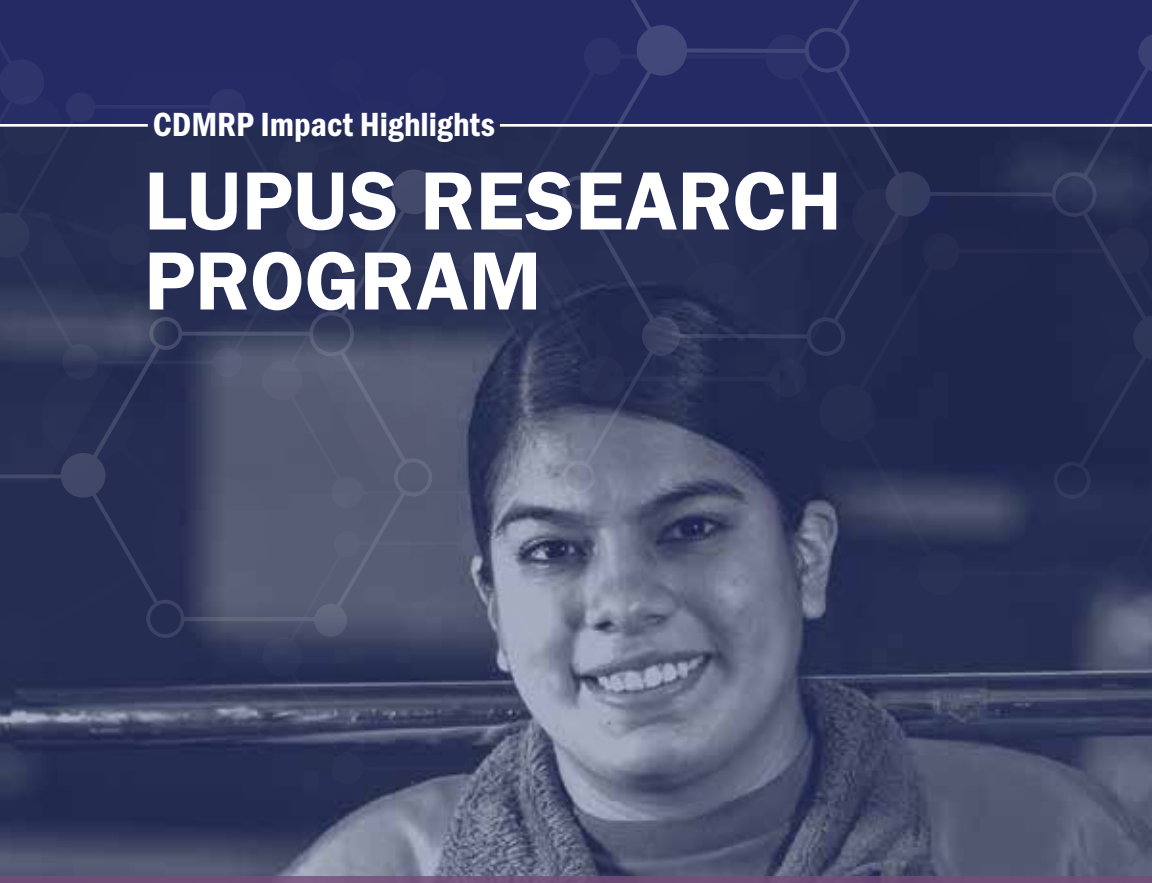
PARTNERS/COLLABORATORS

University of Virginia; Washington University in St. Louis; Medical University of South Carolina

AWARD NUMBER: W81XWH-10-1-0818

IMPACT: LCBRN-supplied tissue samples have been used to evaluate gene mutation and expression signatures associated with lung cancer recurrence and then to test these molecular changes as prognostic markers for use in clinical decision-making. The LCBRN is a valuable tool for discovery, development, and testing aimed at providing novel approaches to treatment and overall better care for lung cancer patients.

LUPUS RESEARCH PROGRAM



Vision: To cure lupus through partnership of scientists, clinicians, and consumers

Mission: Fund research to understand, prevent, and diagnose lupus and to improve treatments and quality of life of patients, including Service Members, Veterans, and beneficiaries

Years Program Appropriated: FY17-FY23

Total Appropriations: $55M

The LRP's mission is to fund research to understand, prevent, and diagnose lupus and to improve treatments and quality of life of patients, including Service Members, Veterans, and beneficiaries. Lupus is a heterogeneous autoimmune disease that is difficult to diagnose and treat. It can take months or years for an individual to be diagnosed, and treatment options are limited. Long-term use of current lupus treatments can result in serious side effects, including kidney problems, liver damage, and increased risk of infection. Priorities of the program include advancing the understanding of subsets of lupus patients to improve appropriate treatment of these patients, gaining insight into the disease mechanisms and heterogeneity, and improving patients' quality of life.

IMPACT: The use of cognitive and/or physical functioning reports enhances shared decision-making and helps achieve goal-oriented, patient-centered care for those living with lupus.

Utility of a Functioning Report for Lupus Patients and Their Providers

DESCRIPTION

Systemic lupus erythematosus is a chronic, heterogeneous autoimmune disease that causes inflammation in numerous tissues within the body. This research aims to improve recognition of the issue of functional impairment in systemic lupus erythematosus patients and facilitate discussion around it. The research team developed an app that 60 lupus patients used for assessments of physical and cognitive functioning. App-generated reports gave the results from self-reports and physician-guided exams using color and number scales. Reports included sections rating a patient's ease of performing everyday activities, their concern for falling, and their mobility, including walking speed, balance, and ease of leaving the house.

PARTNERS/COLLABORATORS

Emory University

AWARD NUMBER: W81XWH-18-1-0619

IMPACT: The results of this project have the potential to make a significant impact on the lives of individuals living with lupus by providing the first evidence to support targeting factor 5 hyperactivation as a novel treatment for systemic lupus erythematosus.

Targeting IRF5 Hyperactivation in Systemic Lupus Erythematosus as a Driver of Disease Risk and Pathogenesis

DESCRIPTION

Although the specific causes of systemic lupus erythematosus remain unclear, genetic risk factors and environmental stressors have been identified that are known to contribute to the disease. Previous research suggested a genetic association between lupus and certain genetic variants of interferon regulatory factor 5 (IRF5), a protein that controls inflammatory and immune responses. This project builds upon previous work to investigate whether IRF5 hyper-activation is a driver of lupus onset and severity and whether or not its inhibition will mediate protective effects in a spontaneous murine lupus model.

PARTNERS/COLLABORATORS

The Feinstein Institutes for Medical Research

AWARD NUMBER: W81XWH-18-1-0674

Improving the Rationale for Treatment Choices in a Heterogeneous Disease

DESCRIPTION

Lupus is different in each patient, so the treatments and responses will depend on understanding each patient. This project compares the immune patterns of responders versus non-responders to the lupus treatment methotrexate. Using clinical trial data to create a database, investigators were able to tease out differences in how various combinations of individual and overlapping treatments impact the patient's immune system. Understanding how these specific immune expressions correlate to treatments within a large cohort of lupus patients allows researchers to find commonalities and create subsets within the heterogeneous population.

PARTNERS/COLLABORATORS

Oklahoma Medical Research Foundation

AWARD NUMBER: W81XWH-18-1-0693

IMPACT: Positive results of this type of research may create new opportunities for care providers to optimize treatment regimens to the specific immune markers expressed in individual patients for improved therapeutic benefit. Additionally, integrating "precision medicine" in lupus clinical trials by understanding the phenotypic subtypes of individuals with lupus results in better clinical trials.

Therapeutic Targeting of Senescent Cells in Lupus

IMPACT: Rejuvenation of the reparative processes in tissues by eliminating senescent cells using senolytic drugs has already been achieved in vivo in animal models of aging. The results from this project support continued research and potential for using senolytic drugs to treat lupus.

DESCRIPTION

Senescent cells, or cells that have stopped dividing, are increased in systemic lupus erythematosus target tissue and contribute to organ dysfunction, disease activity, and poor long-term prognosis. Senolytic drugs can selectively eliminate senescent cells' rejuvenating tissues, improving organ function and promoting better disease management. The Principal Investigator documented that bone marrow cells from lupus patients are a mixture of senescent and non-senescent cells; and senolytic drugs, in particular FOXO4-DRI, are able to selectively induce cell death in the senescent cells. They have also documented a marker of senescent cells in kidneys of lupus-prone mice. These findings suggest that use of senolytic drugs in lupus may selectively eliminate senescent cells in kidneys and improve renal function.

PARTNERS/COLLABORATORS

University of Rochester

AWARD NUMBER: W81XWH-18-1-0704

MELANOMA RESEARCH PROGRAM

Vision: Prevent melanoma initiation and progression

Mission: Support development of earlier interventions to enhance mission readiness and diminish melanoma burden on Service Members, Veterans, their Families, and the American public

Years Program Appropriated: FY19-FY23

Total Appropriations: $140M

Active-duty Service Members are at risk of developing the deadliest form of skin cancer, melanoma, due to occupational sun exposure. Studies suggest exposure to high levels of solar radiation in young adulthood is associated with a higher risk of melanoma mortality. According to the DOD Office of the Deputy Assistant Secretary of Defense for Military Community and Family Policy, 45% of the active-duty force is 25 years or younger in age, and 92% are younger than 40 years of age. Furthermore, between 2005 and 2014 melanoma was the most commonly diagnosed cancer in active duty Service Members. In response, Congress appropriated funds in FY19 to establish an individual stand-alone program, the Melanoma Research Program (MRP).

The MRP challenges the research community to expand the concept of melanoma prevention beyond traditional measures like sunscreen and sun-avoidance. This shift in paradigm is particularly critical in rare subtypes of melanoma that are not thought to be caused by solar radiation, making traditional melanoma prevention measures not applicable. The MRP supports research that aims to inhibit melanoma earlier in the disease progression to prevent metastasis, reduce suffering, and increase survival.

IMPACT: The results of this study may lead to better diagnostic platforms for cutaneous (skin) melanoma and benefit the millions of Veterans who get care through the VA health care system.

Establishing a VA Teledermatopathology Consultant Network and Improving Artificial Intelligence Tools

DESCRIPTION

A multidisciplinary team led the effort to establish a VA consultation network and digital catalog of skin biopsy specimens to improve Veteran access to clinical care. Researchers are analyzing pathologist viewing behaviors of digital specimens to understand the association between viewing behaviors and accurate diagnoses. The results of this study are being used to improve training and education of pathologists and to develop computer-aided tools, like artificial intelligence tools, that will improve the accuracy of melanoma diagnoses. The ultimate goal of this research is to support the establishment of a national VA teledermatopathology system that reduces the burden on the limited number of VA-affiliated practitioners with expertise interpreting skin biopsies, and positively impacts the quality of Veteran melanoma diagnoses and care.

PARTNERS/COLLABORATORS

University of California at Los Angeles; University of Washington; Puget Sound VA Hospital

AWARD NUMBERS: W81XWH-20-1-0797, W81XWH-20-1-0798

Developing an Effective Therapy for Uveal Melanoma

IMPACT: Treatments for this rare variant of melanoma offer the potential to save lives.

DESCRIPTION

Uveal melanoma is a rare form of melanoma that develops in the pigmented portion of the eye. The characteristics of uveal melanoma are significantly different from the most common form of melanoma—cutaneous melanoma, an aggressive form of skin cancer. Recent successes in treating cutaneous melanoma have not translated to the same degree for uveal melanoma patients. A recent MRP-funded effort plans to address this unmet need for effective treatment through a two-pronged approach. The first prong will develop a multi-dose treatment regimen for a radiation therapy that targets a receptor present in most uveal melanoma tumors. A phase 2 clinical trial will assess whether the multi-dose regimen is superior to the single-dose regimen in reducing uveal melanoma growth and metastasis without increasing toxicity. The second prong will develop a much-needed imaging "tracer" that will be used in conjunction with the targeted radiation therapy. The imaging tracer will allow physicians to visualize how the targeted therapy distributes throughout the patient's body and measure the dose of the therapeutic that reaches the desired destinations (i.e., tumors and metastatic sites). Successful completion of the entire effort could lead to FDA-approval of a much-needed uveal melanoma therapeutic option.

PARTNERS/COLLABORATORS

H. Lee Moffitt Cancer Center and Research Institute; Modulation Therapeutics, Inc.

AWARD NUMBER: HT9425-23-1-0909

"I believe being part of a group with top medical clinicians and researchers evaluating proposals that might be the key to ending this and other melanoma and rare cancers is an opportunity unlike any other, and it is a chance to turn an unfortunate diagnosis into a cause for good. It's a chance to give a person I'll probably never meet, who receives similar news, a more hopeful future. It's a rare occasion when you can have a lasting impact on humanity, and I'm thankful I've been able to be a part of it."

Jon Davis, Air Force Veteran,
Uveal Melanoma Survivor, MRP Consumer Peer Reviewer

IMPACT: The ability to detect biomarkers of skin cancer recurrence in the sentinel lymph nodes may help identify early-stage melanoma patients who are most at risk for recurrence and therefore require more intensive initial treatment that will potentially improve outcomes.

Biomarkers of Cutaneous Melanoma Recurrence

DESCRIPTION

Approximately 90% of patients with stage I or stage II cutaneous melanoma can be cured with surgical removal of the tumor, but those who recur have poor long-term outcomes. Many patients at the time of surgery undergo lymph node dissection or sentinel lymph node biopsy, a procedure to assess whether the primary tumor has spread to the lymphatic system. The goal of this project is to extract information from this procedure to identify patients at high risk for tumor recurrence, hence a poorer prognosis. B cell status in the sentinel lymph node may predict prognosis and long-term outcomes. This study will potentially innovate how we identify and define biomarkers predictive of recurrence.

PARTNERS/COLLABORATORS

Duke University

AWARD NUMBER: W81XWH-20-1-0808

MILITARY BURN RESEARCH PROGRAM

Vision: Advancing combat burn trauma care for the Warfighter

Mission: Identify and close gaps in combat burn trauma care through military-focused research

Years Program Appropriated: FY11-FY23

Total Appropriations: $110M

The Military Burn Research Program (MBRP) envisions a medical community that is ready to support the burn-injured Warfighter through the delivery of the best burn trauma care. The ability of health practitioners to provide top-notch care to military Service Members facilitates the goal of improving health and performance outcomes among those who sustain burn injuries while serving the nation. The MBRP seeks to identify and address current and ongoing gaps in burn trauma care through funding of military-focused clinical and translational research. The MBRP funds innovative and impactful research through all phases of the health care continuum, with an emphasis on complex polytrauma burn casualties.

Amicidin-α Surgical Gel and Amicidin-β Solution

IMPACT: Amicidin-α and Amicidin-β represent a novel class of antimicrobials with the potential to prevent and treat life-threatening wound infections in both military and civilian clinical settings.

DESCRIPTION

Susceptibility to infection after burn, traumatic injuries, or surgery remains a problem for patients, threatening to negatively impact health outcomes and potentially lead to drug-resistant bacterial infections. Generated by the A-BLOCKS™ (antimicrobial block copolymers) technology platform, Amicidin-α surgical gel and Amicidin-β solution are innovative, synthetic biomaterials developed for direct application to tissues exposed by surgery or trauma. They are designed with the key qualities of broad microbicidal activity, ease of application, and safety. The MBRP supported early product development efforts for Amicidin-α and Amicidin-β and successfully advanced both products toward clinical use, with additional funding obtained through the Peer Reviewed Medical Research Program and the National Institute of Allergy and Infectious Diseases Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator.

PARTNERS/COLLABORATORS

Amicrobe, Inc.; University of Cincinnati

AWARD NUMBER: W81XWH-15-2-0065

Phases of Illness Paradigm (POIP) Checklist

IMPACT: The POIP checklist may help clinicians better assess patient condition, thus providing more appropriate and timely treatment, potentially improving patient outcomes.

DESCRIPTION

Clinical care of patients within the burn intensive care unit is complex and challenging, particularly in the face of new technologies, new knowledge, and the diversity of perspectives on clinical best practices. Checklists may help to ensure clinicians adhere to local protocols, best practices, clinical practice guidelines, and specific care bundles. The MBRP funded the refinement, validation, and implementation of the POIP Checklist. This checklist-centric health care model promises to enable health care teams to better focus care priorities and to more reliably provide key elements of patient care. This pilot project validated the POIP by measuring changes in clinician understanding of the patient's condition and plan of care, such as their perceptions of communication, teamwork, quality of life, and cognitive workload. Use of the POIP checklist decreased certain aspects of cognitive workload for nurses and physicians and improved the consistency of clinician perception of the patient's condition.

PARTNERS/COLLABORATORS

The Geneva Foundation; U.S. Army Institute of Surgical Research

AWARD NUMBER: W81XWH-13-2-0011

Acute Burn ResUscitation Prospective Multicenter Observational Trial (ABRUPT)

IMPACT: Military injuries frequently involve burns, which are also a major problem in the civilian community. Determining the optimal way to replace fluid when treating burn injuries will improve outcomes for all patients with burns.

DESCRIPTION

Military personnel who sustain severe burn injuries in the line of duty face prolonged convalescence and may never return to duty. One way to reduce mortality and improve outcomes is to provide optimized fluid resuscitation in the crucial hours immediately after burn injury. The ABRUPT examined the effect of albumin during the first 48 hours after burn injury and whether it results in fewer edema-related adverse effects and complications. The results of this study suggest that adding albumin has the potential to reduce fluids required for patients with massive burns and informed the design of a follow-on clinical trial funded by the Combat Casualty Care Research Program that compares crystalloid use versus albumin use for acute burn resuscitation.

PARTNERS/COLLABORATORS

American Burn Association; University of California, Davis

AWARD NUMBER: W81XWH-16-2-0048

Oral Fluid Resuscitation for Burn Injuries

DESCRIPTION

While large, severe burns are survivable, patients often experience adverse effects such as systemic inflammatory response syndrome and multiple organ dysfunction due to the loss of plasma (the liquid portion of the blood) in the bloodstream. These complications significantly increase the risk of death or worsened outcomes and require large–but carefully delivered–volumes of fluid to replace what has been lost. There is a need to develop a minimally invasive, comprehensive burn resuscitation strategy. This study demonstrated that fluids delivered directly into the stomach may be a viable option for resuscitation of burn patients when intravascular access cannot be obtained or supplies are limited, as in austere environments with limited resources. The results of this study helped researchers get funding for a clinical trial to examine the use of oral rehydration solutions to reduce the need for intravascular fluids.

PARTNERS/COLLABORATORS

The Geneva Foundation; U.S. Army Institute of Surgical Research

AWARD NUMBER: W81XWH-16-2-0041

IMPACT: This hydration method may offer a viable option for burn resuscitation in a prolonged field care situation, in the aftermath of natural disasters, or anywhere resources may be limited. This study facilitated the development of a clinical protocol for the use of oral fluid as an adjunctive treatment in the care of burn patients.

Revised Goniometry for Measuring Burn Scar Contracture

IMPACT: Revised goniometry provides a more accurate projection of recovery time as well as degree of recovery after burn injury. This capability helps define a patient's response to treatment and influence the development or modification of a patient's plan of care related to functional recovery.

DESCRIPTION

Permanent shortening of muscle, tendon, and skin as a result of burn scarring all too frequently plagues burn survivors in terms of range of motion limitations and ability to perform activities of daily living. Goniometry is the most commonly and widely used assessment method to measure patient range of motion and subsequent severity of burn scar contracture in burn populations. While standard goniometry is described as a reliable method of functional measurement, the validity has not been established, especially as related to functional patient outcomes. This study critically assessed standard goniometry as compared to a new paradigm of revised goniometry. The study findings suggest that the standard underestimates the clinical impairment for individuals whose motion is limited by scars and that revised goniometry is a more appropriate measure of motion limitation for patients with burn scars. The researchers developed a freely distributed mobile application and also won the Best American Burn Association Clinical Research Award in 2019.

PARTNERS/COLLABORATORS

The Geneva Foundation; U.S. Army Institute of Surgical Research

AWARD NUMBER: W81XWH-14-2-0148

Omega-3 Fish Skin for Burn Wound Coverage and Advanced Healing

DESCRIPTION

In situations where access to care is delayed, or limited due to exhausted or insufficient resources, coverage products demonstrate anti-infective and/or wound healing properties. A novel capability that can be kept on the shelf without refrigeration in a rural medical clinic or in a first responder's bag for the Warfighter would be ideal when resources are limited. This study advanced the novel Kerecis® fish skin technology for use as an alternative to human cadaver skin, current standard of care, to provide temporary burn wound coverage in the treatment of deep-thickness and full-thickness burns. Under the MBRP award, the Kerecis fish skin graft demonstrated temporary burn wound coverage in a relevant animal model with full-thickness burns (third-degree burns) following debridement. Ninety-day outcomes showed healed skin and improved skin appearance with the fish skin graft versus traditional treatments. The completed preclinical studies and resultant data supported a Kerecis FDA Investigational New Drug Application to conduct a pilot clinical study to evaluate and establish the clinical relevance of the Kerecis-modified fish skin product for third-degree burns.

PARTNERS/COLLABORATORS

Kerecis Limited; U.S. Army Institute of Surgical Research

AWARD NUMBER: W81XWH-16-2-0045

IMPACT: This study demonstrates the safety and efficacy of an alternative treatment for severe burn wounds in resource limited environments. Kerecis® fish skin has simple storage requirements and minimal preparation before application; the product has a 3-year shelf life at room temperature and can be prepared by hydrating the material for 30 to 60 seconds in saline.

Enzymatic Debridement for Prolonged Field Care of Military Burn Wounds

IMPACT: I-Debride allows for non-surgical debridement of burn wounds closer to the point-of-injury without the need for surgical intervention. The product is shelf-stable at temperature extremes and can be applied by medical or non-medical first responders.

DESCRIPTION

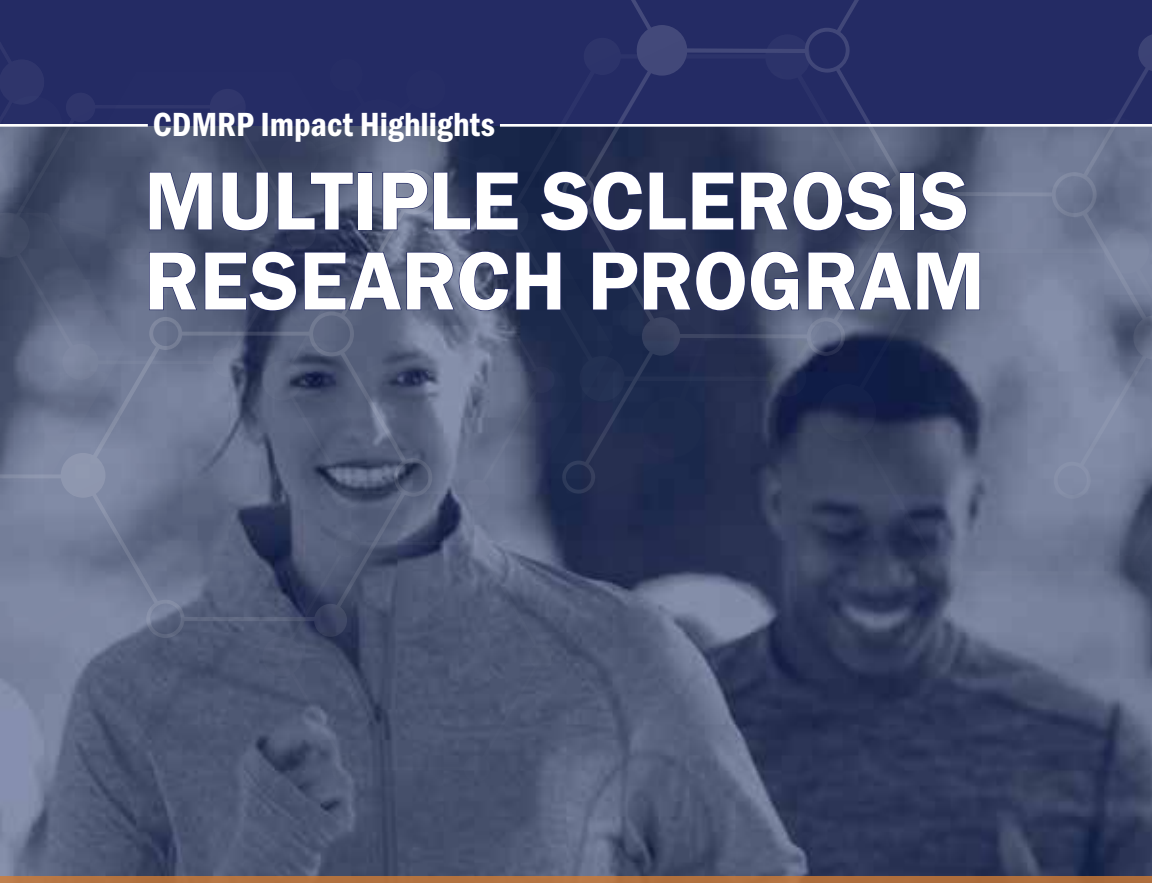
Debridement is a process that involves the manual removal of infected or dead tissue, often through surgery, which allows the skin to better heal, repair, and prevent life-threatening systemic infection. Service Members who suffer burn injuries may have delayed access to a hospital and require immediate burn care and treatment in the field by nonsurgical medical personnel. Non-surgical debridement methods use certain enzymes to break down infected or dead tissue and can be effectively used by non-medical personnel in a prolonged field care environment. A single FDA-approved nonsurgical debridement product currently exists, but it has several drawbacks limiting its field-use potential, including specific storage temperature requirements. To address this need, the MBRP funded the idea development of I-Debride™, a novel, nonsurgical burn wound debridement product that is suitable for use during prolonged time in the field. It is intended for use at the point-of-injury by first responders, such as combat medics, with the potential for use by civilian paramedics and burn units. I-Debride is based on BioSciences' ImmobiZyme™ technology, which combines a mixture of enzymes with support matrix materials and a crosslinker to improve the enzyme performance. Results from this work may offer the potential for application to non-burn wounds such as diabetic wounds and pressure ulcers.

PARTNERS/COLLABORATORS

Guild Associates, Inc.

AWARD NUMBER: W81XWH-20-1-0329

MULTIPLE SCLEROSIS RESEARCH PROGRAM



Vision: To prevent, cure, reverse, or slow the progression, and lessen the personal and societal impact of multiple sclerosis

Mission: To support pioneering concepts and high-impact research relevant to the prevention, etiology, pathogenesis, assessment, treatment, and ultimate cure of multiple sclerosis for the benefit of Service Members, Veterans, and the American public

Years Program Appropriated: FY09-FY23

Total Appropriations: $133.1M

Multiple Sclerosis (MS) is a chronic immune-mediated disease that causes damage to the central nervous system and affects nearly 1 million individuals in the U.S. It has a higher prevalence in U.S. Armed Forces personnel than in the general population. MS is characterized by the demyelination of axons due to the immune system incorrectly attacking healthy tissues in the central nervous system. Symptoms of MS vary widely in type and severity and may include pain, fatigue, depression, anxiety, loss of bladder control, impaired mobility, and cognitive, motor, visual, or sexual dysfunction. Currently, there is no cure for MS. Since its inception, the Multiple Sclerosis Research Program (MSRP) has supported innovative and impactful research that addresses fundamental issues and gaps in MS.

Online Toolkit for Self-Management of MS Symptoms

IMPACT: *My MS Toolkit* is freely available to the public online. It provides a supportive tool for individuals with MS, as a complement to their medical support team, to self-manage fatigue, pain, and depressed mood.

DESCRIPTION

This project developed and validated *My MS Toolkit*, a web-based self-management intervention for people with MS (www.mymstoolkit.com). Individuals with MS frequently have multiple co-occurring symptoms, and self-management interventions have been shown to be effective and have the potential to improve behavioral health via remote delivery. This toolkit provides evidence-based education, guidance, and skills-building exercises for people with MS and their support community. Pilot study participants completed pre-treatment outcome measures followed by 12 weeks of intervention and post-treatment outcome measures. As a result, 30% of participants showed clinically significant improvements, while 60% of participants reported feeling "moderately better" and noticed a "slight change" in their physical and emotional symptoms.

PARTNERS/COLLABORATORS

University of Michigan

AWARD NUMBER: W81XWH-17-1-0367

Serum Biomarker for Multiple Sclerosis

DESCRIPTION

Using an existing longitudinal cohort study with relapsing and progressive forms of MS, biomarkers were evaluated for disease staging, disease outcomes, and treatment response. Focusing on serum neurofilament light chain, a protein that signals neural-axonal damage, revealed it as a marker of clinical relapse. This protein, sNfL, received FDA Breakthrough Device Designation as a biomarker for people with relapsing and remitting MS.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital, Inc./Quanterix

AWARD NUMBER: W81XWH-18-1-0648

IMPACT: The new test is much more convenient than neuroimaging and could be used to monitor the risk of relapse, achieve better treatment outcomes, and ultimately prevent long-term disability.

Physical Telerehabilitation Program to Improve Quality of Life for MS Patients

DESCRIPTION

Physical rehabilitation is effective in improving mobility and the overall quality of life for patients with MS. A major barrier for MS patients with limited mobility is their ability to travel to and participate in rehabilitation programs. The physical telerehabilitation program allows MS patients to participate in the program from the comfort of their own homes. This pilot trial demonstrated a high acceptance rate by the patients. The program led to significant improvements in disease-specific quality of life aspects, including fatigue, balance, muscle resistance, and patients' perceptions of the physical and psychological impact of MS.

PARTNERS/COLLABORATORS

Columbia University Medical Center

AWARD NUMBER: W81XWH-16-1-0704

IMPACT: This telehealth program makes rehabilitation more accessible to patients with MS and limited mobility and potentially improves their quality of life.

Bioengineered Particles to Promote Regulatory T Cells and Temper Immune Response in Multiple Sclerosis

IMPACT: These bioengineered microparticles could serve as a new therapeutic to modulate the immune response in MS and reduce or reverse MS symptoms.

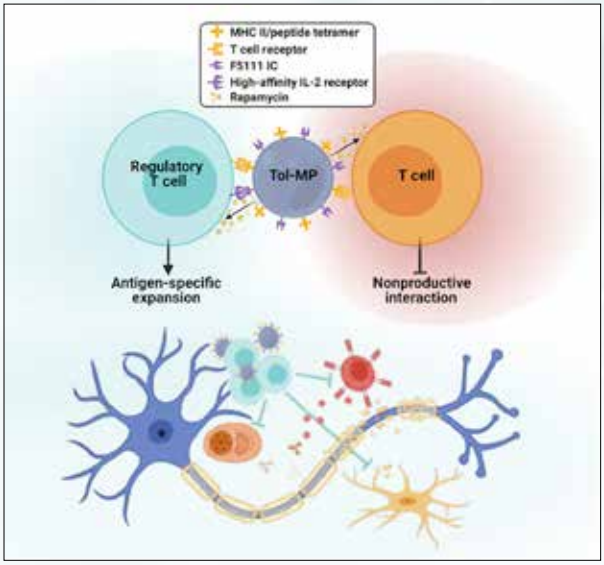
DESCRIPTION

Researchers developed biodegradable microparticles that stimulate the expansion of myelin-specific regulatory T cells, called Tregs. Tregs are a type of immune cells that are responsible for suppressing other cells of the immune system to prevent autoimmune disease and maintain self-tolerance. When microparticles were administered in a mouse model of MS prior to disease induction, they delayed the disease onset and reduced disease severity. When microparticles were administered after disease induction, they almost completely reversed MS-like symptoms.

PARTNERS/COLLABORATORS

Johns Hopkins University

AWARD NUMBER: W81XWH-21-1-0892



Remotely Supervised Transcranial Direct Current Stimulation (RS-tDCS) for Patients with Progressive Multiple Sclerosis

IMPACT: The RS-tDCS has the advantage of improved accessibility, reduced cost, and scalability to treat MS-related impairment.

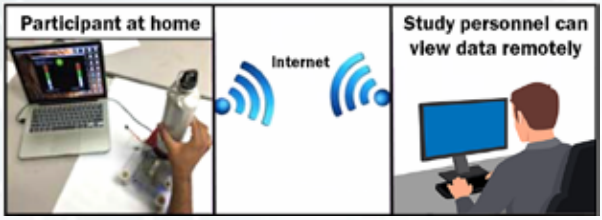
DESCRIPTION

Transcranial direct current stimulation is a safe and non-invasive method to stimulate the firing of neurons and can boost motor learning and sensory perception. This method has been used to treat depression, Alzeheimer's disease, and other neurological diseases. Researchers aimed to extend this treatment method to patients with progressive multiple sclerosis at their homes using a telemedicine platform. Supervised manual dexterity training sessions were offered to train the patients to learn the new treatment modality and outcome measurement tools. The RS-tDCS demonstrated a high adherence rate and strong benefit from transcranial direct current stimulation treatment. This new delivery system scaled up the treatment tool available to progressive MS patients at their homes who have limited access to health care facilities.

PARTNERS/COLLABORATORS

New York University School of Medicine

AWARD NUMBER: W81XWH-17-1-0320



Tina Rosenthal, MSRP Consumer Peer Reviewer

"The MS community is vast: patients, clinicians, caregivers, foundations, volunteers, physical therapists, MSRP, etc. Before a cure is found we need to push forward with research for innovative treatments and continue supporting programs that disrupt isolation and despair. Efforts to change the course of the disease are somewhat effective, but as with all patients with a chronic disease, I hope there will be more and better interventions for MS sooner rather than later. CDMRP is helping to drive this innovation."

Staff Sgt. James West, U.S. Army, Retired,
MBRP Programmatic Panel Member and Consumer

"Burns are one of the most devastating injuries. Disfigurement, chronic pain, and the constant medical procedures can lead to depression, then suicidal ideation which Service Members/ Veterans are more likely to act on. Knowing that we can not only save lives, but also provide a better quality of life after injury is why I will continue to serve the burn community."

NEUROFIBROMATOSIS RESEARCH PROGRAM

Vision: Decrease the clinical impact of neurofibromatosis

Mission: Promote research directed toward the understanding, diagnosis, and treatment of NF1, NF2, and schwannomatosis to enhance the quality of life for persons with these disorders that impact Service Members, Veterans, and the general public

Years Program Appropriated: FY96-FY23

Total Appropriations: $427.9M

The Neurofibromatosis Research Program (NFRP) seeks to support innovative, high-impact research that will foster new directions for and address neglected issues in neurofibromatosis (NF) research. It will also sponsor multidisciplinary and multi-institutional collaborations that will bring new perspectives to the field, promote translational and clinical studies to move promising ideas from bench to bedside, and develop a balanced portfolio of meritorious research. To address the near- and long-term gaps and needs of the NF community of researchers, clinicians, and consumers, the NFRP has established four goals: (1) fostering basic and exploratory research to increase understanding of the underlying causes of NF1, NF2, and schwannomatosis, which is vital to identifying potential therapeutics; (2) facilitating rapid testing of potential therapeutics by supporting the transition of findings in basic research through preclinical studies and clinical testing of promising interventions; (3) increasing research capacity by supporting development of vital research resources which enable investigators; and (4) encouraging research in areas of critical interest to NF patients.

MEK Inhibitors: From Bench to Bedside

IMPACT: This first NF therapeutic offers the hope that the collaboration between funders and the dedication of patients and scientists will lead to treatments.

DESCRIPTION

Neurofibromatosis is a rare disease. The time it takes from bench to bedside in identifying potential therapeutics to delivery in patients is measured in decades. The NFRP has been instrumental in moving the field of NF research from understanding the basic biology of the disorder to identifying potential therapeutics and testing in clinical trials. Multiple studies from the NFRP on MEK inhibitors and their potential as a therapeutic provided the foundations of preclinical studies and subsequent clinical trials. In 2020, a MEK inhibitor, Koselugo (selumetinib) produced by AstraZeneca and Merck became the first FDA-approved drug for treatment of NF. This major milestone in NF research was possible because of many collaborative efforts among multiple private and federal funding groups.

PARTNERS/COLLABORATORS

Neurofibromatosis Therapeutic Acceleration Program; National Institutes of Health (NIH); Children's Tumor Foundation

AWARD NUMBERS: W81XWH-17-1-0695, W81XWH-17-2-0037, plus 9 historical NFRP awards

Novel Light Therapy for Optic Glioma

DESCRIPTION

This award supported the investigation of light exposure as a potential therapeutic tool for NF1-related optic gliomas. Six-week-old transgenic NF1 mice reared in the dark until 12 weeks of age, then exposed to a normal light cycle for 4 weeks, showed no signs of optic tumor formation. This study identified a window of opportunity for NF1-related optic glioma initiation and uncovered the potential for interventions such as modulating light exposure using glasses as a means to reduce or eliminate optic glioma development. In addition, these findings provided a foundation to investigate potential drug targets that could inhibit neuronal activity of retinal ganglion cells. As a result, a second award was funded to interrogate the molecular mechanisms of retinal ganglion cell neuronal activity and investigate the possibility of drug intervention for the prevention of optic glioma. This important body of work resulted in a high impact publication in the journal *Nature* in 2022.

IMPACT: This study identified the potential for using light exclusion as a therapy to reduce or eliminate the development of optic gliomas from birth.

PARTNERS/COLLABORATORS

The Leland Stanford Junior University

AWARD NUMBERS: W81XWH-15-1-0131, W81XWH-19-1-0260

Neurofibromatosis Clinical Trials Consortium (NFCTC)

IMPACT: The NFCTC leveraged the power of collaboration to bring together the expertise required to strategically plan, prioritize, and execute multi-institutional clinical trials, which would otherwise not be possible.

DESCRIPTION

The NFCTC was established to develop and perform phase 1 and 2 clinical trials for the management and treatment of NF complications in children and adults. Over the years, the NFCTC has brought together preeminent institutions and investigators and expanded to 25 sites. To date, the NFCTC has led or collaborated on 16 clinical trials with five additional trials in development, all focused on several manifestations of NF.

For more information, visit https://cdmrp.health.mil/nfrp/consortium/nfrpctc.

PARTNERS/COLLABORATORS

University of Alabama at Birmingham; Boston/Harvard Center for NF and Allied Disorders; Children's Hospital at Westmead, University of Sydney; Children's Hospital of Los Angeles; Children's National Medical Center; Children's Hospital of Philadelphia/University of Pennsylvania; Cincinnati Children's Hospital Medical Center; Indiana University; Mayo Clinic; National Cancer Institute; New York University Medical Center; University of Chicago; University of Texas Southwestern; University of Utah; Washington University; Ann & Robert H. Lurie Children's Hospital of Chicago; Children's Healthcare of Atlanta/Emory University; Johns Hopkins Hospital; Massachusetts General Hospital; Dana Farber Cancer Institute; Memorial Sloan Kettering Cancer Center; Royal Children's Hospital/Murdoch Children's Research Institute; Texas Scottish Rite Hospital; University of California, Los Angeles; University of Minnesota

AWARD NUMBERS: W81XWH-12-1-0155, W81XWH-17-2-0037, W81XWH-22-3-0001, plus 11 historical NFRP awards. Additional funds provided by the University of Alabama at Birmingham, National Cancer Institute, Children's Tumor Foundation, Array Biopharma, Pfizer, Exelixis, Genentech, Novartis, Medtronic, and private donors.

Targeted Research into NF Specific Area of Emphasis: Pain

DESCRIPTION

The NFRP has worked to bring awareness and focus research funding on pain, a major clinical manifestation of neurofibromatosis. NF patients have reported pain as one of the symptoms that most affects their quality of life. Primary treatment is usually surgery to resect painful tumors, but it often does not help patients' pain and may make it worse. Pain medication has not been shown to be highly effective for relieving NF pain, either. NFRP-funded research is helping examine the relationship between the known genetic drivers of NF and pain receptors, signaling, and processing. It has been shown that the presence and intensity of pain does not always correlate with the number, location, and size of NF tumors. NFRP-funded studies are investigating why some types of NF tumors are more likely to become painful than others and are working to reveal the mechanisms behind pain specifically caused by neurofibromatosis.

PARTNERS/COLLABORATORS

House Research Institute; Oregon Health and Science University; University of California, Los Angeles; Yale University; and other key collaborators

AWARD NUMBERS: W81XWH-10-1-0070, W81XWH-15-1-0592, W81XWH-18-1-0776, W81XWH-19-1-0618, and others

IMPACT: Primary treatments for neurofibromatosis-related pain, like surgery and pain medicine, have not been shown to be highly effective. Research into how NF pain develops and persists is revealing possible novel therapeutic targets that could greatly improve NF patients' quality of life.

Early-Phase Study to Evaluate MEK and MDM2 Inhibition in Patients with Neurofibromatosis Type 1 and Premalignant and Malignant Peripheral Nerve Sheath Tumors

IMPACT: This study will evaluate a novel therapeutic strategy for malignant peripheral nerve sheath tumors treatment through combination oral medications and potentially benefit patients for whom surgery is not a feasible option.

DESCRIPTION

Malignant peripheral nerve sheath tumor is an aggressive soft tissue cancer more commonly seen in persons with NF1. These tumors arise from plexiform neurofibroma, benign nerve sheath tumors and some atypical neurofibromas called atypical neurofibromatosis neoplasm with uncertain biologic potential. Investigators examined signaling targets for pre-cancerous and cancerous NF1 to identify novel therapies. Animal studies using drugs to inhibit signaling targets MEK and MDM2 showed shrinkage in tumor size. A combination treatment of Selumetinib, an FDA-approved drug for inoperable plexiform neurofibroma NF1, and the inhibitor drug APG-115 are being evaluated in patients with cancers that failed other treatments. APG-115 has been tested alone and with other drugs, but not with Selumetinib. The research team will conduct a phase 1 trial to evaluate the Selumetinib and APG-115 combination and will assess optimal tolerable dosing. A phase 2 study will evaluate if this therapy shrinks or stabilizes tumors. These early trials aim to evaluate how this drug combination inhibits growth and to capture tumor response to treatment.

PARTNERS/COLLABORATORS

Children's National Medical Center; DOD Neurofibromatosis Clinical Trial Consortium

AWARD NUMBER: W81XWH-22-1-1120

NFRP Research Resources

DESCRIPTION

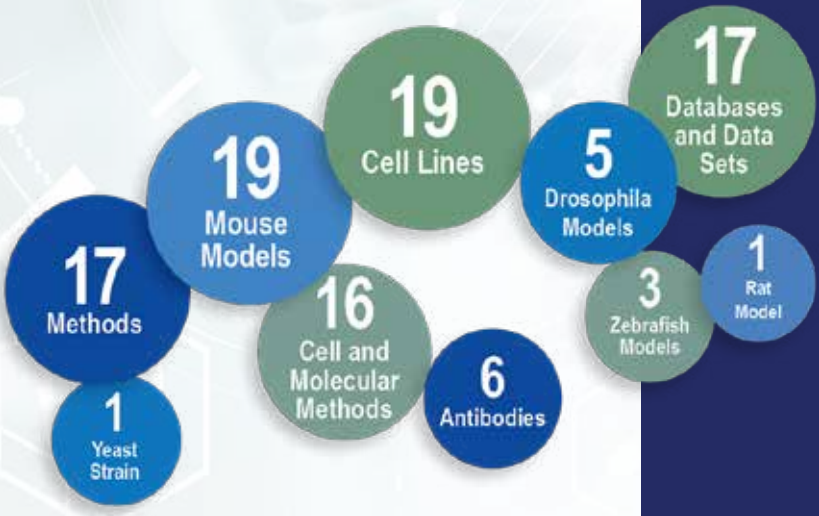
From the start, NFRP has been critical to the progress made to advance NF research. The NFRP support of innovative studies have yielded vital research resources that were previously unavailable to neurofibromatosis investigators. To date, over 119 resources have been developed and shared with the NF community. The collection of resources is publicized on the CDMRP website to encourage collaboration and provide access to the tools necessary for researchers conducting NF research. This collection includes five drosophila models, 31 mouse models, one rat model, seven antibodies, 19 cell and molecular methods, 18 cell lines, three zebrafish models, one yeast strain, and 15 databases and data sets.

PARTNERS/COLLABORATORS

Various

AWARD NUMBERS: 84 NFRP awards totaling $76.7M in funding

IMPACT: The NFRP-developed resources are widely shared with the research community to facilitate research and collaborations to further scientific advances and knowledge that will ultimately lead to better care for NF patients.



https://cdmrp.health.mil/nfrp/resources/nfrpresources

Tracy Wirtanen, NFRP Consumer Peer Reviewer

"Having a child with NF has changed my and my family's entire lives; we live with a lot of uncertainty. However, we decided to be part of the solution by creating the Littlest Tumor Foundation, which advocates for research in NF, but also by serving on the peer review panel for the NFRP. Being a part of such a well-run program that is a crucial part of moving us toward a treatment for NF has made me even more passionate about the NFRP and is a highlight in my life."

Susannah Engdahl, Ph.D., OPORP Programmatic Panel Member

"Supporting the stories [of advocates] with data emphasizes the value of O&P [orthotics and prosthetics] care to policymakers who might be unfamiliar with our community's needs. Because I have first-hand experience as a prosthesis user, a researcher, and an advocate, I've tried to apply all three perspectives in discussions about OPORP investment strategies and funding decisions."

ORTHOTICS AND PROSTHETICS OUTCOMES RESEARCH PROGRAM

Vision: To attain the highest possible quality of life for individuals with limb loss and limb impairment

Mission: Advance orthotic and prosthetic research to optimize evidence-based care and clinical outcomes for Service Members, Veterans, and persons with limb loss and limb impairment

Years Program Appropriated: FY14–FY23

Total Appropriations: $125M

Loss of limb or limb functionality is one of the most debilitating injuries suffered by U.S. military personnel, Veterans, and civilians. Recent advancements in commercially available orthotics and prosthetics have dramatically improved device capability; however, there remains an urgent need for outcomes data to inform patients, clinicians, caregivers, and policymakers. The Orthotics and Prosthetics Outcomes Research Program (OPORP) supports research on outcomes-based best practices through analysis of prosthetic and/or orthotic device options that are currently available to advance device prescription, treatment, rehabilitation, and prevention of secondary health effects.

New Clinical Balance Test for Lower Limb Prosthesis Users

IMPACT: Through early and more accurate assessment of balance, clinicians are able to minimize fall risk and subsequent re-injury, which helps Service Members return to active duty and Veterans or civilians reintegrate into their communities where they can safely engage in physical activities that could improve their quality of life.

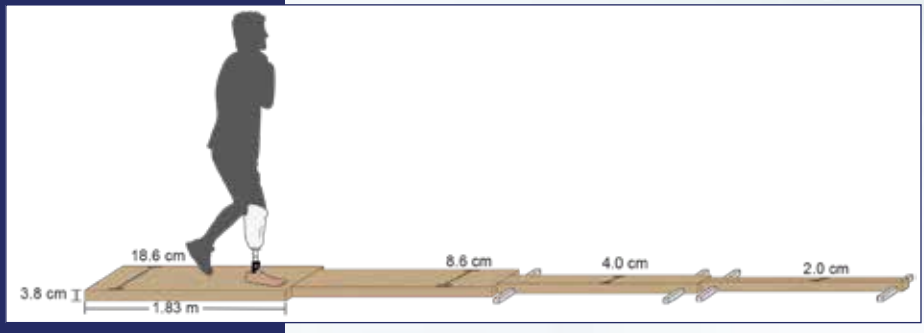
DESCRIPTION

Researchers developed a new clinical balance test for lower limb prosthesis users, the Narrowing-Beam Walking Test, which discriminates fallers and non-fallers with greater accuracy than existing tests in lower limb prosthesis users. The new balance test and four contemporary performance-based balance tests were administered to 60 lower-limb prosthesis users and the new test proved to be a better predictor of future falls at 6 months. The test and its new parameters/best practices are now being used in a number of clinical, industry, and academic centers as well as VA clinics, and are helping to ensure that balance impairments are diagnosed early and that individuals receive timely treatment before they experience falls and incur secondary injuries.

PARTNERS/COLLABORATORS

University of Illinois at Chicago; University of Washington

AWARD NUMBER: W81XWH-17-1-0547



Narrowing-Beam Walking Test. Participants walk along four progressively narrower beam segments with their arms crossed over their chest. If participants move their arms or step off the beam the trial is ended and the distance walked to that point is recorded. Height of each segment is 3.8 cm.

Personalized Mobility Interventions Using Smart Sensor Resources for Lower Limb Prostheses Users

DESCRIPTION

Identifying sensitive, quantitative measures that predict real-world mobility and social interactions enables clinicians to provide optimal, cost-effective care in the context of the individual's personal goals – including a return to active duty and deployment. This research project uses smartphone sensors paired with sensors on the prosthesis to continuously gather multimodal information on real-world mobility. Data includes how many steps are taken with the prosthesis; whether the individual walks outside of their home; if they can negotiate stairs, curbs, or ramps; where they go and how they get there – outside of the clinic. Combining data on actual prosthesis use in the home and community with standard in-clinic outcome measures and participant-reported measures provides a comprehensive picture of prosthesis use.

PARTNERS/COLLABORATORS

Shirley Ryan AbilityLab; Walter Reed National Military Medical Center; Minneapolis VAMC; University of Notre Dame

AWARD NUMBER: W81XWH-18-2-0057

IMPACT: Data on real-world use of prosthetic devices greatly informs prescription and clinical practice to improve quality of life, reduce secondary injuries, maintain physical and psychological health, and reduce health care costs.

Needs, Preferences, and Functional Abilities of Veterans and Service Members with Upper Limb Amputation

IMPACT: Findings demonstrated the value of active prostheses in improving quality of life and highlighted the clinical imperative to encourage prosthesis use by addressing factors such as early prosthetic training to improve satisfaction with devices and reduce abandonment.

DESCRIPTION

Abandonment of a prosthesis is a significant problem for upper limb amputees, and it comes at a significant cost to the DOD and VA alike. This project provided comprehensive cross-sectional and longitudinal data on function, needs, preferences, and satisfaction of Veterans and Service Members with major upper limb amputation and found that amputees who do not use a prosthesis report more difficulty in activities, greater overall disability, and lower physical function compared to amputees who use any type of active prosthesis. Additionally, those who do not use a prosthesis are more likely to need help with activities of daily living compared to those who use a body-powered prosthesis.

PARTNERS/COLLABORATORS

Ocean State Research Institute/Providence VAMC; University of Massachusetts Medical School; University of South Florida; Center for the Intrepid; FDA; Tampa VA Research & Education Foundation/Tampa VAMC; North Florida Foundation for Research and Education/Gainesville VA; McGuire Research Institute/Richmond VAMC; Seattle Institute for Biomedical and Clinical Research/VA Puget Sound Healthcare System

AWARD NUMBER: W81XWH-16-2-0065

OVARIAN CANCER RESEARCH PROGRAM

Vision: To eliminate ovarian cancer

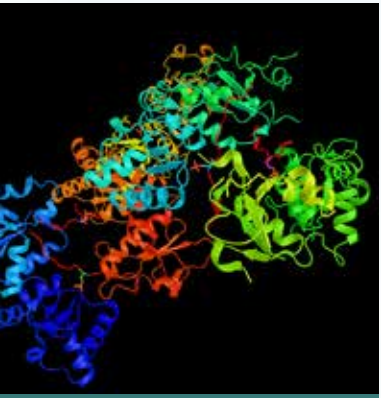
Mission: To support patient-centered research to prevent, detect, treat, and cure ovarian cancer to enhance the health and well-being of Service Members, Veterans, retirees, their Family members, and all women impacted by this disease

Years Program Appropriated: FY97-FY23

Total Appropriations: $496.5M

Ovarian cancer is the fifth leading cause of cancer-related death in women and the deadliest gynecologic cancer. The Ovarian Cancer Research Program (OCRP) was established in 1997 to define and address the critical research gaps facing the ovarian cancer community. The Strategic Plan of the OCRP identifies the high-impact research goals, which are most important to its stakeholders, while providing a framework that is adaptable to changes in the medical research environment to address those goals.

As the second-leading funder of ovarian cancer research in the U.S., the OCRP has transformed the landscape of ovarian cancer for the benefit of patients everywhere by funding high-impact, cutting-edge research, which developed a number of diagnostics, therapeutics, and preventive measures. Besides the scientific advancement, OCRP is also instrumental in developing a unique strategy to identify and foster talented young investigators who are committed to studying this disease.



BRCAness Profile Identifies Tumors More Sensitive to Chemotherapy

IMPACT: This research improves our understanding of responsiveness to chemotherapy in ovarian cancer and expands the cohort of patients who may benefit from chemotherapy.

DESCRIPTION

A BRCAness 60-gene expression profile which tracks the mechanisms that cause defective homologous recombination was evaluated for its ability to identify tumors with a BRCAness phenotype and predict chemotherapy sensitivity. The BRCAness profile was determined to correlate with platinum sensitivity and survival in patients with sporadic disease. This profile also revealed that the HSP90 inhibitor, 17-AAG, enhances sensitivity of non-BRCA1/2 (Breast Cancer susceptibility genes 1 and 2) mutated ovarian cancer cells to poly (ADP-ribose) polymerase (PARP) inhibitors. Patients with homologous recombinant proficient ovarian cancer do not respond well to PARP inhibitor and platinum chemotherapy. The BRCAness profile identifies BRCA-like tumors deficient in homologous recombination and more sensitive to platinum and PARP inhibitors.

PARTNERS/COLLABORATORS

Dana-Farber Cancer Institute

AWARD NUMBER: W81XWH-10-1-0585

OTTA-SPOT Gene Expression Signature as a Prognostic for Overall Survival

DESCRIPTION

Twenty different studies provided tumor samples from 4,071 women diagnosed with ovarian cancer to develop a prognostic signature for ovarian cancer overall survival. The expression levels of 276 genes were associated with overall survival, and the best performing prognostic signature, the Ovarian Tumor Tissue Analysis consortium - Stratified Prognosis of Ovarian Tumours (OTTA-SPOT), included 101 genes enriched in pathways with treatment implications. The OTTA-SPOT signature was shown to perform substantially better than age and stage alone for prognosis of both two- and five-year overall survival in women with high-grade serous ovarian cancer.

PARTNERS/COLLABORATORS

University of Melbourne; Cedars-Sinai Medical Center; and 120 collaborators, including the Australian Ovarian Cancer Study and numerous national and international institutions

AWARD NUMBERS: W81XWH-12-1-0104, W81XWH-17-1-0144

IMPACT: There are no well-established gene expression signatures associated with prognosis for ovarian cancer patients. The OTTA-SPOT provides a robust prognostic signature for high-grade serous ovarian cancer that can be used to stratify patients and identify those in need of alternative treatments. It may also indicate targets for therapeutic approaches.

A Diagnostic to Identify Ovarian Cancer Patients Likely to Respond to PARP Inhibitor Treatment

IMPACT: PARP inhibitors, including rucaparib, have differential activity in ovarian cancer patients depending on their BRCA mutations and loss of heterozygosity. CDxBRCA is an FDA-approved companion diagnostic that can identify ovarian cancer patients likely to respond to PARP inhibitor treatment.

DESCRIPTION

Researchers confirmed the accuracy of the companion diagnostic, CDxBRCA, in detecting the presence of mutations in the BRCA1 and BRCA2 genes and genomic loss of heterozygosity in tumor tissue samples from patients with ovarian cancer. This was done by the sequencing analysis of samples from the Assessment of Rucaparib in Ovarian Cancer: phase 2 (ARIEL2) clinical trial.

PARTNERS/COLLABORATORS

University of Washington; Foundation Medicine

AWARD NUMBER: W81XWH-13-1-0484

Predicting Treatment Response to Rucaparib in Ovarian Cancer

DESCRIPTION

BRCA gene mutations and homologous recombination deficiencies were examined as clinical predictors of a patient's response to PARP inhibitor treatment. Samples from the Assessment of Rucaparib in Ovarian Cancer: phase 2 clinical trial, which tested cancer patients' responsiveness to treatment with the PARP inhibitor rucaparib, were sequenced and the results helped establish the relationship between homologous recombination status of the tumors and outcome of PARP inhibitor treatment. These results revealed that ovarian cancer patients with BRCA1 or BRCA2 mutations and loss of heterozygosity were most likely to respond to rucaparib treatment.

PARTNERS/COLLABORATORS

University of Washington; Mayo Clinic; Clovis Oncology

AWARD NUMBERS: W81XWH-13-1-0484, W81XWH-13-1-0485

IMPACT: These results predict which women are most likely to benefit from treatment with a PARP inhibitor (rucaparib) and supported the FDA-accelerated approval for oral therapy rucaparib. This therapy is currently used to treat Service Members.

IMPACT: This new screening technology has been patented and has the potential to solve the problem of resistance to chemotherapy in high-grade serous ovarian cancer.

Identification of a Mechanism of Recurrence of High-Grade Serous Ovarian Cancer

DESCRIPTION

High-grade serous ovarian cancer shows a remarkable response to surgery and chemotherapy. However, recurrent disease is frequent and often accompanied by a resistance to the same chemotherapeutics that were previously effective. Ovarian cancer recurrence is driven by a small population of chemotherapy-resistant cancer stem-like cells. CDMRP-funded researchers developed a rapid, high throughput screening technology of cancer stem cell libraries, and used paclitaxel-carboplatin to identify the surviving, chemotherapy resistant cancer stem-like cells in high-grade serous ovarian cancer.

PARTNERS/COLLABORATORS

University of Houston; Brigham and Women's Hospital; University of South Florida Health, Tampa General Hospital Cancer Center

AWARD NUMBER: W81XWH-20-1-0755

IMPACT: This study provides potential means to identify women with ovarian cancer who do not have BRCA1 or BRCA2 mutations but who also have a good chance of responding to PARP inhibitors, offering more effective personalized treatment strategies.

Clinical Predictors for PARP Inhibitor Therapy

DESCRIPTION

PARP inhibitors are effective treatment options for ovarian cancer patients with mutations in BRCA1 or BRCA2; however, there is no optimal test that predicts which patients with BRCA-wildtype (no BRCA gene mutations) ovarian cancer will respond to PARP inhibitor therapy. A new clinical test is being developed using whole genome sequencing to look for gene mutation and alteration patterns beyond BRCA 1 and BRCA 2 that lead to specific DNA repair process deficiencies and may be more predictive of PARP inhibitor response.

PARTNERS/COLLABORATORS

University of Washington; Clovis Oncology; University of Cambridge

AWARD NUMBER: W81XWH-17-1-0070

Mobile Application for Genetic Information on Cancer (mAGIC)

DESCRIPTION

Based on data from a focus group of women diagnosed with ovarian cancer who received varying levels of genetic counseling, the mAGIC intervention was developed to motivate ovarian cancer survivors and their families to undergo genetic counseling. The effectiveness of the intervention was tested with a randomized controlled trial of 104 women with a diagnosis of ovarian cancer who had not previously received genetic counseling. Participants in the intervention group reported high satisfaction with the mAGIC application and would recommend the intervention to others. Guidelines published by the National Comprehensive Cancer Network and the Society of Gynecologic Oncology recommend ovarian cancer survivors receive further genetic risk evaluation by a genetic counselor; however, these women under-use genetic services.

IMPACT: This mobile application provides a means to encourage genetic counseling and preventive health care for ovarian cancer survivors.

PARTNERS/COLLABORATORS

University of Minnesota, Twin Cities

AWARD NUMBER: W81XWH-14-1-0102

Olaparib and AT13387 for Recurrent Ovarian Cancer

IMPACT: This research presents a potential novel therapeutic strategy to treat patients with cyclinE1-amplified ovarian cancer tumors who have poor outcomes due to the ineffectiveness of standard treatment.

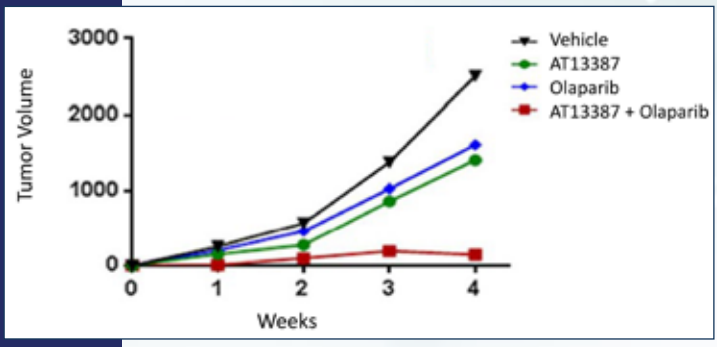
DESCRIPTION

Heat shock protein 90 (HSP90) is a novel therapeutic target for cyclinE1-amplified ovarian cancer, which is the most deadly ovarian cancer due to a lack of responsiveness to standard chemotherapy. In a mouse model of patient-derived cyclinE1-amplified ovarian cancer tumors, the HSP90-inhibitor AT13387, synergized with PARP inhibitors and inhibited tumor growth better than either treatment alone. Results from this Ovarian Cancer Academy Collaborative Award, which required academy early career investigators to collaborate with a non-academy co-principal investigator, developed into a phase 1 clinical trial of the PARP inhibitor, olaparib, in combination with AT13387 for the treatment of recurrent ovarian cancer.

PARTNERS/COLLABORATORS

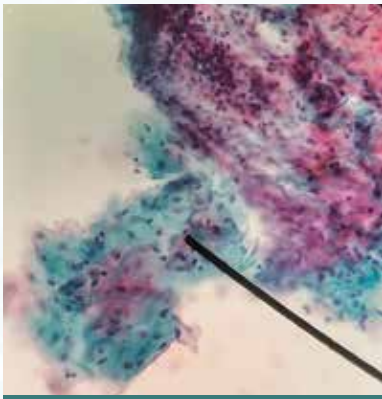
Dana-Farber Cancer Institute; The Wistar Institute; National Cancer Institute

AWARD NUMBERS: W81XWH-15-1-0564, W81XWH-15-1-0565, W81XWH-15-1-0566



In a patient-derived cyclinE1-amplified ovarian cancer mouse model, the combination of AT13387 and olaparib induced inhibition of tumor growth, as opposed to vehicle control, olaparib alone, and AT13387 alone.

Biomarkers from Pap Tests for Detection of Ovarian Cancer



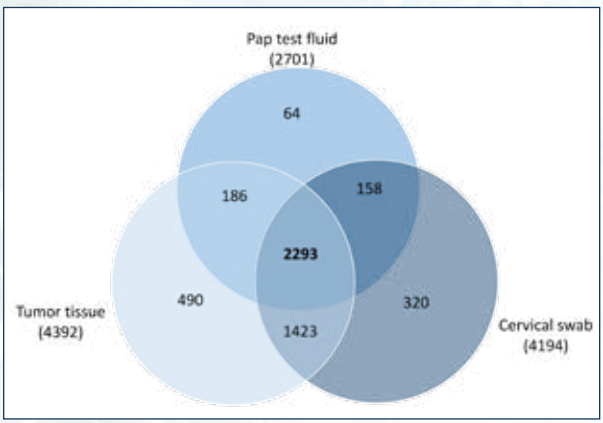
DESCRIPTION

Early detection of ovarian cancer increases survival, but screening tools for use in the general population are lacking. Investigators examined Pap tests for the presence of proteins, or biomarkers, shed by ovarian cancer cells. When comparing Pap test samples and cervical swabs of ovarian cancer patients with their tumor tissue, researchers identified more than 2,000 proteins expressed in the Pap test and cervical swab samples that were also present in the tumor tissue, including several known ovarian cancer biomarkers, such as CA125. These results suggest that Pap test fixatives and cervical swabs may be a rich source of tumor-specific biomarkers for ovarian cancer detection.

PARTNERS/COLLABORATORS

University of Minnesota

AWARD NUMBER: W81XWH-16-1-0070



Researchers identified 2,293 expressed tumor tissue proteins in both Pap tests and cervical swab samples, including known ovarian cancer biomarkers.

IMPACT: Identified biomarkers for ovarian cancer detection may be developed into an easy, non-invasive screening test for ovarian cancer that can be incorporated as part of a routine Pap test, so that women can be tested simultaneously for cervical and ovarian cancer.

IMPACT: Clinical trial results may validate a non-invasive screening tool to evaluate PARP-1 expression and identify patients who will benefit from PARP inhibitor and DNA damaging agent therapy, which has the potential to greatly improve treatment for women with ovarian cancer.

A Novel Radiolabeled Tracer to Predict Chemotherapy Response

DESCRIPTION

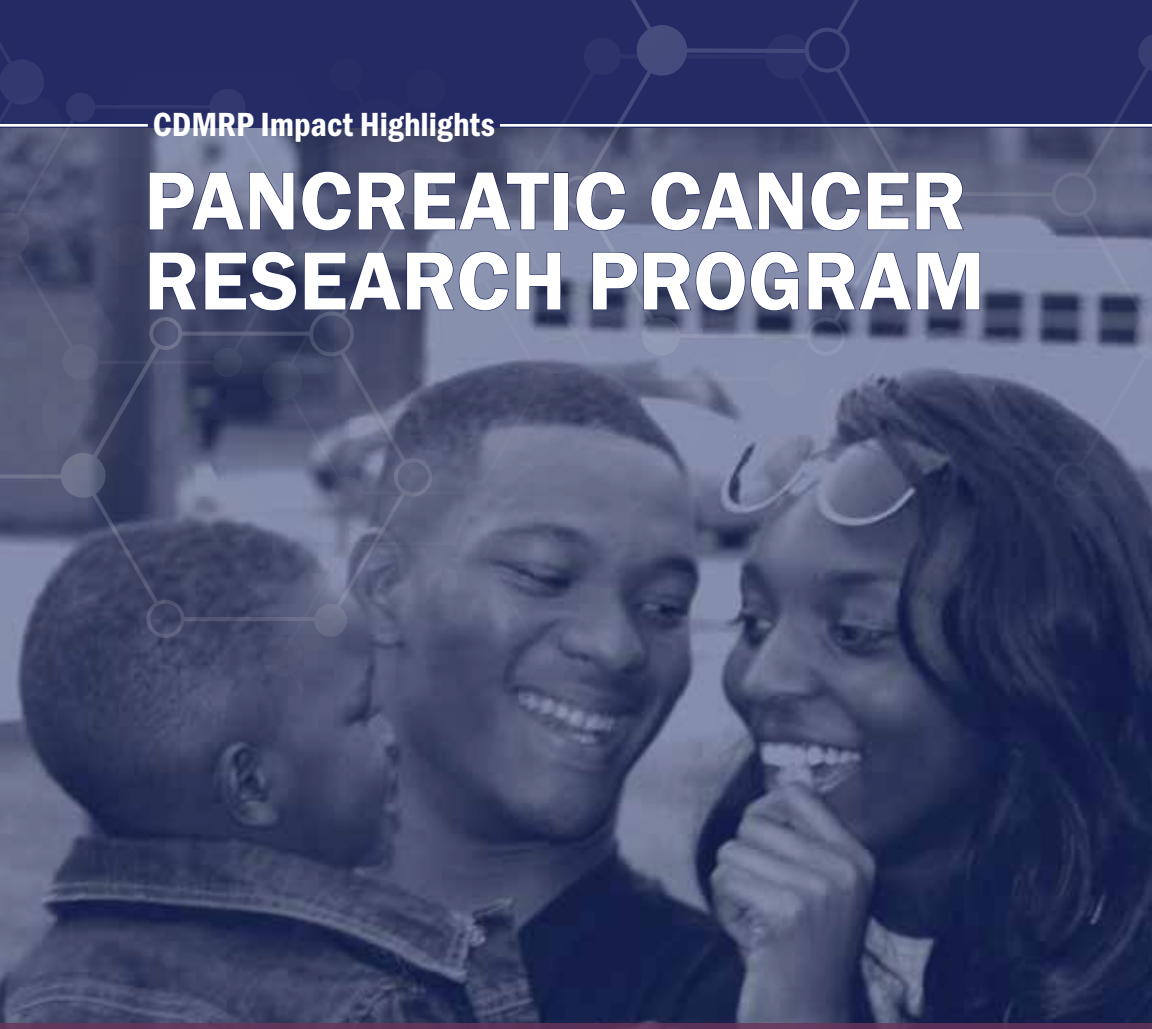
The challenge with PARP inhibitor therapy is that not all ovarian cancers will respond, and there is currently no good indicator as to which will. Researchers evaluated a novel radiolabeled tracer, [^{18}F]FluorThanatrace ([^{18}F]FTT), which identifies PARP-1 protein expression in patient tumors, in a predictive assay for tumor response to DNA-damaging agent chemotherapy with the added benefit of PARP inhibitor agents. The [^{18}F]FTT tracer is currently being assessed in a phase 1 clinical trial to validate it as a predictor of response to PARP inhibitor therapy in ovarian cancer by imaging patients with [^{18}F]FTT before and after initiating PARP inhibitor therapy. Results from this trial will help provide the data needed for larger multicenter clinical trials, with the goal of fully evaluating the importance of PARP-1 expression as a biomarker for cancer therapy and the use of the [^{18}F]FTT tracer for measuring PARP-1 expression and PARP inhibitor sensitivity.

PARTNERS/COLLABORATORS

University of Pennsylvania

AWARD NUMBER: W81XWH-17-1-0092

PANCREATIC CANCER RESEARCH PROGRAM



Vision: Reduce the burden of pancreatic cancer among Service Members, Veterans, their Families, and the American public

Mission: Promote rigorous, innovative, high-impact research that leads to earlier pancreatic cancer diagnosis, new therapeutic tools, and improved outcomes

Years Program Appropriated: FY20-FY23

Total Appropriations: $51M

Based on the mission of the Pancreatic Cancer Research Program (PCARP), a four-prong strategic direction was developed to fulfill the program's goal. These include: (1) fill gaps and advance knowledge that will drive new and innovative clinical trials for pancreatic cancer, (2) expand pancreatic cancer expertise by bridging diverse scientific fields, (3) facilitate a multidisciplinary approach to advancing scientific knowledge of pancreatic cancer, and (4) recruit and retain young investigators dedicated to pancreatic cancer research.

IMPACT: Using artificial intelligence methods on real-world clinical records enables development of a pancreatic cancer risk prediction model that will shift focus to early detection and enable better treatment of early-stage cancer.

Pancreatic Cancer Risk Prediction Model Using Artificial Intelligence

DESCRIPTION

The identification of high-risk pancreatic cancer patients is an urgent need in clinical practice. This team will utilize artificial intelligence methods to develop a model for predicting pancreatic cancer risk in the Veteran population using nationwide data from the Veterans Affairs health care system. The model will be validated externally in a civilian cohort system. Given the low predictive value of current screening methods, this model could provide an alternative and cost-efficient tool for pancreatic cancer risk assessment and assist with early detection of this disease.

PARTNERS/COLLABORATORS

Harvard University; Boston VA Research Institute, Inc.

AWARD NUMBERS: HT9425-23-1-0463, HT9425-23-1-0464

IMPACT: The STRONG intervention will provide patient self-management for tracking nutrition and improve quality of life through effective, comprehensive monitoring against malnutrition among patients who receive surgery as a part of their treatment.

Support through Remote Observation and Nutrition Guidance (STRONG)

DESCRIPTION

The research team developed the STRONG intervention for pancreatic cancer patients undergoing pancreatectomy (partial or full removal of the pancreas). The current project tests the STRONG intervention against the current standard of care for malnutrition monitoring post-pancreatectomy. Study participants will receive malnutrition screening and an individualized dietary plan. Telehealth visits and a smartphone application that connects to a wearable sensor allows patients to track and share dietary intake with a dietician in real-time.

PARTNERS/COLLABORATORS

H. Lee Moffitt Cancer Center and Research Institute

AWARD NUMBER: HT9425-23-1-0514

PARKINSON'S RESEARCH PROGRAM

Vision: Improve the health and lives of people with Parkinson's disease through innovative, clinically meaningful treatments

Mission: To support high impact Parkinson's research that alters disease progression, improves disease symptoms, and develops treatments that benefit Service Members, Veterans, and all others living with Parkinson's disease

Years Program Appropriated: FY22-FY23

Total Appropriations: $32M

Parkinson's disease is a degenerative movement disorder of the central nervous system resulting from a loss of neurons in the brain. These neurons produce dopamine, a neurotransmitter important for motor control; however, as Parkinson's progresses, the death of dopaminergic neurons results in reduced dopamine levels and impairment of motor control.

In FY22, Congress transitioned the Neurotoxin Exposure Treatment Parkinson's Research Program to the Parkinson's Research Program (PRP), broadening the focus to develop the most impactful research that will advance the understanding of the disease with the ultimate goal of ending it. The PRP Strategic Plan identifies research goals with the potential to address major knowledge gaps and underfunded areas of research. The PRP believes that investing in these goals will advance the field of Parkinson's research and benefit Service Members, Veterans, and the general public.

Pesticide Exposure and Parkinson's Disease Risk

IMPACT: This work is providing quantifiable evidence for the impact of pesticides on Parkinson's disease.

DESCRIPTION

A combination of genetic and environmental factors may lead to Parkinson's disease, with genetic factors currently explaining only 10% to 15% of all diagnoses.[1] There is a need for research on specific environmental factors, particularly the interaction between genes and the environment that contribute to Parkinson's. The research team analyzed data from the Pesticide-Wide Association Study and found agricultural pesticide-application for 33 pesticides occurred in close proximity to Parkinson's patients, including those carrying common Parkinson's disease-associated mutations in alpha-synuclein protein and Gaucher protein.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital and Harvard Medical School; University of California, Los Angeles; Harvard Stem Cell institute

AWARD NUMBERS: W81XWH-19-1-0695, W81XWH-19-1-0696, W81XWH-19-1-0697

[1] Causes. 2022 Parkinson's Foundation, https://www.parkinson.org/understanding-parkinsons/causes.

Parkinson's Disease Risk Assessment Tool

DESCRIPTION

The Parkinson's Associated Risk Syndrome Study used the loss of smell combined with brain imaging to determine an individual's Parkinson's risk. Results showed this approach was successful in identifying persons who ultimately developed Parkinson's prior to the appearance of symptoms. This tool holds promise for earlier diagnosis, understanding of the disease, and earlier treatment.

PARTNERS/COLLABORATORS

Institute for Neurodegenerative Disorders

AWARD NUMBER: W81XWH-06-1-0678

IMPACT: This tool identifies individuals at risk for Parkinson's based on smell capacity and neuroimaging, enabling earlier intervention.

Neuroprotective Effects of Carnosine

DESCRIPTION

The investigative team sought to determine the neuroprotective potential and mechanisms of carnosine, a protein building block, for prevention and treatment of Parkinson's disease. Following intranasal administration of carnosine in a rodent model, fewer Parkinson's-associated alpha-synuclein positive cell bodies compared to control animals was found in the region of the brain that undergoes degeneration in human Parkinson's patients. Another extremely significant finding was that a higher dose of carnosine essentially eliminated the progression of gait deficits seen with age in the mice.

PARTNERS/COLLABORATORS

University of Cincinnati

AWARD NUMBER: W81XWH-17-1-0699

IMPACT: Carnosine may be a potential treatment for Parkinson's disease-related neurodegeneration.

Israel Robledo, PRP Programmatic Panel Consumer Reviewer

"As a consumer member for several years, I've had the opportunity to witness first-hand how the PRP is able to reach out and focus on areas of research need and/or interest that aren't covered by other funding sources, which gives me hope for a breakthrough and help for today in knowing that some of the best researchers/scientists/physicians are able to seek PRP funding."

Sarah Hornback, PRARP Programmatic Panel Consumer Reviewer

"I am honored to be a part of the PRARP. As the wife of a Veteran with Alzheimer's disease, I appreciate the need for innovative approaches to study traumatic brain injury in relation to dementia. The impact of studying the relationship between military risk factors and the devastation of brain degeneration as well as possible disease modifiers, caregiver support, and progress toward treatment/prevention will be life changing. Our veterans and their families will greatly benefit from this vital process."

PEER REVIEWED ALZHEIMER'S RESEARCH PROGRAM

Vision: To address and mitigate long-term implications of traumatic brain injury and military service as they pertain to Alzheimer's disease and Alzheimer's disease-related dementias

Mission: Support research to (1) understand the association between TBI and other military Service-related risk factors and Alzheimer's disease/Alzheimer's disease-related dementias, and (2) improve quality of life and reduce the burden on affected individuals and caregivers for the military, Veterans, and the public

Years Program Appropriated: FY11-FY23

Total Appropriations: $183M

Military personnel face an increased risk for developing Alzheimer's disease or a related dementia as they age. Dementia risk factors such as traumatic brain injury, cardiovascular disease, sleep disruption, and post-traumatic stress disorder have an increased impact on Service Members when compared to the general public. The Peer Reviewed Alzheimer's Research Program (PRARP) prioritizes efforts aimed at improving diagnosis and prognosis, culturally competent innovation to accelerate research and interventions in dementia risk reduction and prevention, and improving the lives of people living with dementia or caring for loved ones with dementia.

Telehealth-Based Mind-Body Interventions to Improve Cognition and Quality of Life in Individuals with Mild Cognitive Impairment and Their Caregivers

IMPACT: This program represents an accessible, home-based strategy to reduce caregiver burden and improve daily functioning and quality of life. Patients and their families are active participants in this research.

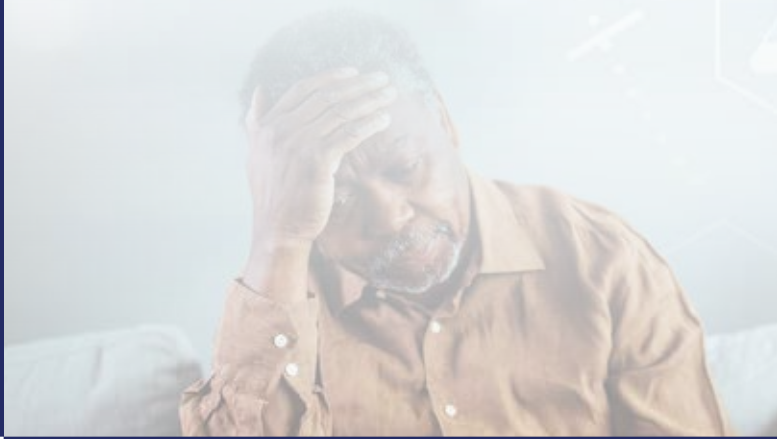
DESCRIPTION

A telehealth mind-body intervention to improve the quality of life for older adults living with cognitive decline and their care-partners uses a group exercise program designed to enhance procedural learning, functional movement, goal orientation, mindfulness, breathing, positive emotions, and social interaction. In the initial PRARP-funded trial, participants showed increased neural functional connectivity during brain imaging as well as improved cognition, interoceptive self-regulation, well-being, and reduced feelings of social isolation. This program is delivered in collaboration with a community organization, Together Senior Health and the partnership has resulted in increased access to diverse populations, and a scalable framework for use in at home as well as in assisted-living facilities, retirement homes, and clinics.

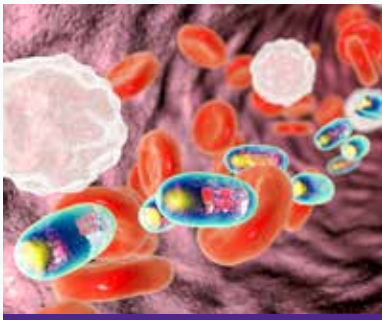
PARTNERS/COLLABORATORS

Northern California Institute for Research and Education; San Francisco VA Medical Center; Together Senior Health

AWARD NUMBERS: W81XWH-17-1-0490, W81XWH-21-1-0147



Ultrasensitive Blood Tests for Investigating Pathogenesis of Post-TBI Neurological Conditions



DESCRIPTION

This project enabled the development of commercially available laboratory tests that identify minute levels of proteins implicated in TBI and/or Alzheimer's disease/other dementias. Ultrasensitive tests are now able to use minimally invasive blood sampling to detect disease-associated proteins, microvasculature damage, and neuroimmune responses underlying cognitive decline following a TBI.

PARTNERS/COLLABORATORS

Meso Scale Diagnostics, LLC

AWARD NUMBER: W81XWH-17-1-0648

IMPACT: This study will provide an accessible, simple, and sensitive blood test for protein biomarkers indicative of Alzheimer's disease/other dementia. This is a key first step in improving early diagnosis and treatment and meets a crucial need, particularly for Veterans living with TBI.

Modular Design-Accelerated Development of Minimally Invasive Dried Plasma and Saliva Tests for Detecting TBI Sequelae for Alzheimer's Disease Dementia

IMPACT: This minimally invasive test efficiently tests blood and saliva to allow more consistent, affordable, and easy diagnosis and disease management for populations at high-risk for post-TBI Alzheimer's disease.

DESCRIPTION

This first-of-its-kind project aims to develop an easily accessible, minimally invasive sampling method using dried plasma spots from finger-prick blood collection or saliva to detect multiple protein or microRNA biomarkers. This design allows investigators to test different assays in parallel across many time points following a TBI and to observe the relationship between cognitive status and age group. Although the technology is undergoing final validation steps, this sampling system's easy accessibility and cost effectiveness make it a potential game-changer for early diagnosis and monitoring of Alzheimer's disease in military, Veteran, and civilian populations.

PARTNERS/COLLABORATORS

Gryphon Bio, Inc.

AWARD NUMBER: HT9425-23-1-0392

PEER REVIEWED CANCER RESEARCH PROGRAM

Vision: To advance mission readiness of U.S. military members affected by cancer and to improve quality of life by decreasing the burden of cancer on Service Members, their families, Veterans, and the American public

Mission: To successfully promote high-impact research for cancer prevention, detection, treatment, quality of life, and survivorship

Years Program Appropriated: FY09-FY21

Total Appropriations: $654.8M

The Peer Reviewed Cancer Research Program (PRCRP) supports innovative and impactful research in cancers and other specialty areas specifically authorized by Congress. A total of 34 Topic Areas have been eligible for PRCRP funding over the years. Congress directed that PRCRP-funded research should be relevant to Service Members and their Families. It is a central initiative of the PRCRP that applications address how the proposed research is related to military health, mission readiness, and the cancer health needs of both deployed and non-deployed military personnel, their dependents, Veterans, and other military beneficiaries (i.e., family members and retirees). Some cancers, such as mesothelioma, stomach, and blood cancers, are risk factors for active-duty Service Members due to exposures related to military service and deployment. Other cancers may affect the military because a diagnosis may impact mission readiness. In this way, the PRCRP focuses on strategic capabilities of the military and fills knowledge gaps in cancer prevention, detection/diagnosis, treatment, and survivorship.

IMPACT: XPOVIO is an easy-to-use oral therapeutic and a major milestone in blood cancer treatment.

XPOVIO® (Selinexor)

DESCRIPTION

This study revealed that over-expressing the protein exportin blocks tumor suppressors out of the nucleus to protect their active role in DNA repair. Researchers identified exportin as a therapeutic target, and the work culminated in drug combination studies of the exportin inhibitor now known as selinexor. The FDA granted selinexor accelerated approval for relapsed/refractory multiple myeloma in 2019 and full FDA approval in 2020 for diffuse large B-cell lymphoma. The VA acknowledged that exposures to herbicides, such as Agent Orange, may lead to the development of multiple myeloma and other blood cancers in Veterans. PRCRP funded the groundwork for this breakthrough advancement in blood cancer treatment. As of August 2023, there are 72 active clinical trials using selinexor as an intervention, and an ongoing clinical trial of patients with advanced or recurrent endometrial cancer shows that the therapeutic may prolong progression-free survival.

PARTNERS/COLLABORATORS

The Ohio State University

AWARD NUMBER: W81XWH-14-1-0190

Carcinogenic Risk Factors in Testicular Cancer

DESCRIPTION

Exposure to chemical carcinogens poses a great risk to Service Members. To investigate the relationship between per- and poly-fluoroalkyl substances (PFAS) exposure and testicular cancer in U.S. Air Force Servicemen, researchers used serum samples from 500 men diagnosed with testicular cancer and 500 men without testicular cancer, supplied by the DOD Serum Repository. The team analyzed serum levels of 12 PFAS to determine whether Servicemen who developed testicular cancer had higher concentrations of PFAS than those who did not. Their findings suggested a potential link between PFAS exposure and testicular cancer risk. This study has received follow-up funding from CDMRP's Toxic Exposure Research Program (TERP) to investigate potential links between PFAS and other service-related factors.

IMPACT: This project will shed light on the extent of PFAS exposure among Air Force Servicemen and help researchers better understand the health impacts of PFAS exposure.

PARTNERS/COLLABORATORS

National Cancer Institute; Uniformed Services University of the Health Sciences

AWARD NUMBERS: W81XWH-19-1-0444; follow-up funding TERP HT9425-23-1-0968

Denosumab to Augment Immunotherapy in Melanoma

IMPACT: Denosumab potentially provides a novel and more powerful combined therapeutic approach to the treatment of melanoma.

DESCRIPTION

Researchers investigated whether blocking central tolerance enhances immune checkpoint blockade effects in treating melanoma. A key mediator of central tolerance is the autoimmune regulator, Aire. Antibodies against receptor activator of nuclear factor kappa-B ligand (RANKL) block Aire expression and increase activation of T cells that could potentially target melanoma. Denosumab is an FDA-approved antibody therapeutic that targets RANKL. Denosumab has a synergistic effect with checkpoint inhibitors anti-CTLA4 and anti-PD1 and significantly decreased tumor growth and prolonged survival. The results of this project informed the development of a phase 2 clinical trial for stage III/IV melanoma patients, cutaneous and mucosal, in which denosumab will be used in combination with anti-PD1 immunotherapy.

PARTNERS/COLLABORATORS

University of North Carolina at Chapel Hill

AWARD NUMBER: W81XWH-15-1-0411

Protection Against the Damaging Effects of Radiation

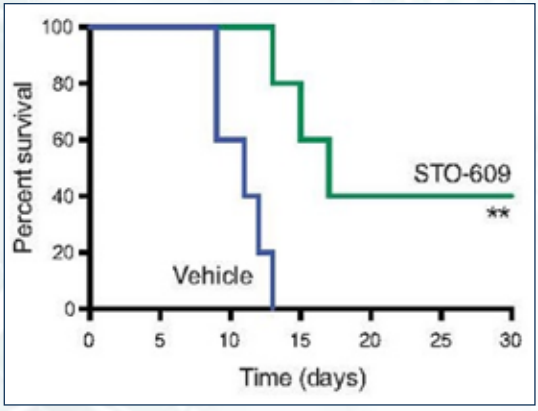
DESCRIPTION

Ionizing radiation induces injuries that may be long-term, including damage to the blood cell proliferation cascade — hematopoiesis — within the bone marrow. Studies show that the deletion of Ca^{2+}/calmodulin (CaM)-dependent protein kinase 2 (CaMKK2) promotes hematopoetic recovery following radiation injury. Administration of a small molecule CAMKK2 inhibitor, STO-609, enhances the recovery of hematopoiesis and improves survival in mice. Not only do the studies show the utility of STO-609 in radiation survival, they also demonstrate the importance of CAMKK2 in cellular processes.

PARTNERS/COLLABORATORS

Duke University

AWARD NUMBER: W18XWH-15-1-0443



IMPACT: Exposure to ionizing radiation, which includes high-energy types of radiation like X-rays and gamma radiation, increases the risk of developing blood cancers like leukemia and multiple myeloma. Active-duty Service Members may be exposed to radiation sources during military activities, and thus be at risk for developing different types of cancers, especially blood cancers.

Peptide Nanofiber Precursors Improved Delivery of Chemotherapy to Diffuse Intrinsic Pontine Glioma

IMPACT: This new therapeutic delivery system has the potential to increase drug localization to the tumor site and improve patient outcomes.

DESCRIPTION

Diffuse intrinsic pontine glioma, also known as diffuse midline glioma, is a form of pediatric brain cancer with very high resistance to currently available treatments. This research aims to develop a new treatment plan using methods to bypass the blood-brain barrier for better access to tumor cells. The team used a previously developed drug delivery system platform, called peptide nanofiber precursors, to directly deposit drugs at the tumor sites. This research analyzed peptide nanofiber precursor delivery of a drug called emtansine in animal brain cells and found increased inhibition of tumor progression and enhanced localization of the drug in brain cells post-administration.

PARTNERS/COLLABORATORS

Weill Medical College of Cornell University

AWARD NUMBER: W81XWH-17-1-0518

CIBERSORTx — Genomic Signatures for Integrative Models of Clinical Heterogeneity in Patients with Follicular Lymphoma

DESCRIPTION

Currently available cancer treatments do not account for the diversity and complexity of tumors across patients and cancer types. Researchers aimed to understand patient likelihood of response to specific cancer treatments based on gene expression and genomic biomarkers. This PRCRP-funded work led to the development of a novel computational tool, CIBERSORTx. The tool characterizes gene expression data collected from tissue samples to examine distinct genetic differences potentially linked to treatment response.

PARTNERS/COLLABORATORS

Stanford University (The Leland Stanford Junior University)

AWARD NUMBER: W81XWH-17-1-0518

IMPACT: CIBERSORTx generates data that can aid in providing personalized precision medicine to patients based on unique genetic features and could revolutionize cancer treatment.

Novel CAR-T Therapy Targeting BAFF-R Against B-Cell Lymphomas

DESCRIPTION

Non-Hodgkin's lymphoma affects cells of the immune system, especially B cells. This research developed a novel CAR T-cell therapy targeting lymphoma by recognizing B cell activating factor receptor (BAFF-R). Researchers conducted optimization experiments to develop a therapeutic approach that promoted cytotoxicity during treatment and outperformed current therapy during in vitro experimentation. This work led to FDA approval of the new BAFF-R CAR T cell therapy and supported a phase 1 clinical trial through other funding sources.

PARTNERS/COLLABORATORS

Beckman Research Institute of City of Hope

AWARD NUMBER: W81XWH-18-1-0205

IMPACT: This FDA-approved CAR T-cell therapy outperforms currently available non-Hodgkin's lymphoma treatment in cell studies.

Listeria-Based Cancer Vaccine for Colorectal Cancer

IMPACT: A safe, effective colorectal cancer vaccine demonstrating translatability to humans has the potential to prevent disease relapse.

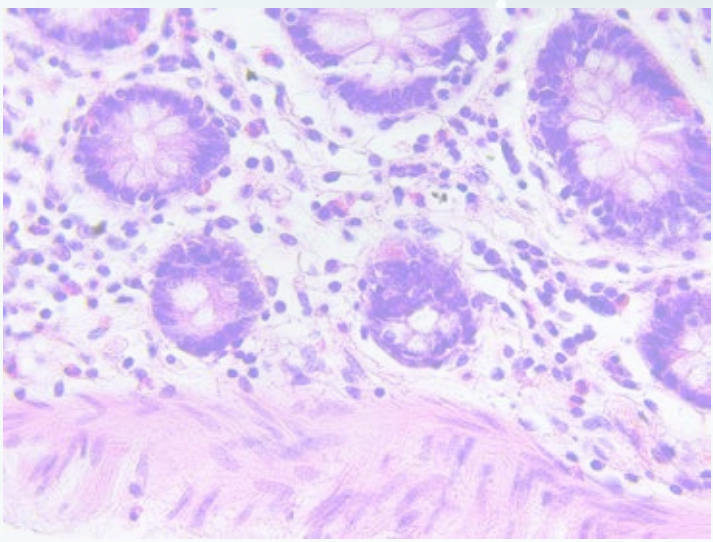
DESCRIPTION

This research involves studying a vaccine approach to the delivery of colorectal cancer immunotherapy. In the first of two awards funded by the PRCRP, modified Listeria monocytogenes carried colorectal cancer tumor-associated antigen, GUCY2C, to immune cells to induce a response and target tumor cells. Researchers tested this vaccine treatment in an animal model, where it safely restored immune cell function after multiple exposures. A phase 1 clinical trial funded by the PRCRP focuses on investigating the use of this vaccine in patients with minimal residual disease, defined by the presence of circulating tumor DNA, who may be more prone to relapse after treatment. This research continues to examine the safety and efficacy of the treatment and the clearance of circulating tumor DNA from the body.

PARTNERS/COLLABORATORS

Thomas Jefferson University

AWARD NUMBERS: W81XWH-17-1-0299, W81XWH-22-1-0207, W81XWH-22-1-0208



PEER REVIEWED MEDICAL RESEARCH PROGRAM

Vision: Improve the health, care, and well-being of all military Service Members, Veterans, and their Families

Mission: Encourage, identify, select, and manage medical research projects of clear scientific merit that lead to impactful advances in health care of Service Members, Veterans, and their Families

Years Program Appropriated: FY99-FY06, FY08-FY23

Total Appropriations: $3.82B

The Peer Reviewed Medical Research Program (PRMRP) supports innovative and impactful research across congressionally directed Topic Areas that address a wide range of disciplines, including cardiovascular health, autoimmune diseases and immunology, infectious diseases, rare diseases, internal medicine, neurological and psychological health, orthopaedic and regenerative medicine, and respiratory and environmental health. Over 210 Topic Areas have been authorized for funding over the years. Congressional language has directed that the PRMRP support scientifically meritorious research that is relevant to military health. To accomplish its vision, the Program focuses on advancing knowledge in disease etiology, improving prevention, detection/diagnosis, treatment, and quality of life for those affected by the relevant disease or condition. The PRMRP also emphasizes development and validation of clinical practice or public health guidelines.

i-STAT™ TBI Plasma Test and Alinity i TBI Lab Test

IMPACT: The Abbott i-STAT TBI Plasma test provides a rapid and cost-effective test that can be used to evaluate Service Members and civilians who may have experienced a mild TBI.

DESCRIPTION

The i-STAT TBI Plasma test, previously the Banyan Brain Trauma Indicator®, is manufactured and distributed by Abbott Laboratories for use on the i-STAT Alinity instrument. Using a plasma sample collected within 12 hours of a suspected head injury, the i-STAT TBI Plasma test measures the levels of biomarkers to complement other clinical parameters to determine the need for a CT scan of the head in three to four hours. The rapid test can decrease the number of CT scans performed on patients seeking emergency room care, saving patient health care costs and exposure to radiation. The technology could be used by the military in 2025 to determine if a head injury acquired in the operational environment requires an evacuation for a CT scan.

PARTNERS/COLLABORATORS

Banyan Biomarkers, Inc.; University of Florida; Walter Reed Army Institute of Research

AWARD NUMBERS: DAMD17-03-1-0066, W81XWH-07-2-0075; additional funding from TBIPHRP W81XWH-07-2-0075 and Combat Casualty Care Research Program W81XWH-10-C-0251

BIO 300 (Genistein)

IMPACT: BIO 300 has the potential to reduce inflammation from acute COVID-19-related infections and to protect Service Members from imminent radiological danger.

DESCRIPTION

PRMRP and JWMRP supported studies that developed and tested novel oral suspension and solid powder formulations of genistein, a naturally occurring compound known for its anti-inflammatory properties. Genistein, or BIO 300, has the potential to prevent negative health effects, like pulmonary fibrosis, resulting from radiation exposure. The team received further funding to test for the ability to reduce inflammation and prevent the development of pulmonary fibrosis for those living with COVID-19-associated acute respiratory distress syndrome. Most recently, in 2022, Humanetics Corporation received a $5.1 million award from PRMRP toward completing research required to qualify for authorization from the FDA to use BIO 300 in case of an emergency for the military. Additionally, this award is funding the development of an injectable formulation of BIO 300 for military use in case of radiological exposure as a more convenient version than the oral formulation of BIO 300.

PARTNERS/COLLABORATORS

Humanetics Corporation

AWARD NUMBERS: W81XWH-22-1-0516, W81XWH-21-1-0010, W81XWH-17-1-0584; additional funding from JWMRP W81XWH-19-2-0060

Everolimus in Pediatric Heart Transplantation

IMPACT: Everolimus may potentially improve the long-term safety and survival of children after heart transplant. It may also have medical applications for treating military injuries that require a vascular composite allograft, such as hand or face transplantation, and for understanding wound healing problems.

DESCRIPTION

Median survival after pediatric heart transplantation is only 15 years due to the occurrence of late complications after heart transplant, most of which stem from the medications used to suppress the immune system to prevent organ rejection. PRMRP funded a phase 3 clinical trial (TEAMMATE; http://med.stanford.edu/teammate.html) to determine whether a novel treatment, Everolimus and low-dose tacrolimus, for children who have undergone recent heart transplant can reduce or prevent several key complications of transplant, including rejection, coronary artery disease, and kidney disease, when compared to usual care. TEAMMATE investigators successfully established the first-ever collaborative clinical research network specific to pediatric heart transplantation. Enrollment is now complete, with a total of 211 pediatric heart transplant recipients, and follow-up is underway. Pending results of the trial, this may lead to FDA approval of the first immunosuppression regimen specific to pediatric heart transplantation.

PARTNERS/COLLABORATORS

Boston Children's Hospital; Stanford University; and 23 additional clinical sites across the U.S.

AWARD NUMBER: W81XWH-17-1-0532

Pancreatic Cooling Using a Gastric Balloon for Treatment of Acute Pancreatitis

IMPACT: A gastric cooling balloon may be used as a therapeutic modality to treat acute pancreatitis, as well as obesity.

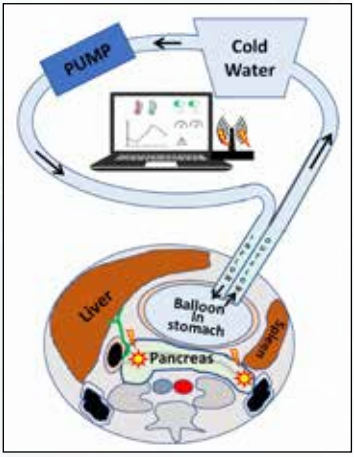
DESCRIPTION

Pancreatitis affects more than 300,000 Americans every year. Cooling the pancreas by 6-12 degrees Celsius is relatively quick to achieve, and slows multiple harmful mechanisms operating alongside pancreatitis. Cooling protects the pancreas in a way that would have required multiple drugs—most of which currently do not exist. PRMRP-funded studies demonstrated that a balloon placed transgastrically, or across the internal abdominal space, can provide such cooling. Transgastric cooling may also be effective for treating obesity. Obesity, a widespread public health concern, is a risk factor for severe pancreatitis, which often requires intensive care or may result in death. For obesity, a gentler cooling of the stomach to drain body heat results in a loss of calories. This accelerates metabolism by breaking down fat to produce heat and energy. Transgastric heat exchange thus results in highly efficient weight loss, equivalent to that achieved by more invasive therapies like bariatric surgery.

PARTNERS/COLLABORATORS

Mayo Clinic in Arizona

AWARD NUMBERS: W81XWH-20-1-0400, W81XWH-12-1-0327



Schematic showing the setup of transgastric pancreatic cooling of the pancreas

Trauma Survivors Network and NextSteps Interactive Self-Management Program for Patients with Serious Injury

IMPACT: The Trauma Survivors Network created a peer network across the U.S. and Australia for trauma survivors to access for support during recovery.

DESCRIPTION

The Trauma Survivors Network was developed through the PRMRP award and adopted by the American Trauma Society. The goal of the network is to provide peer support programs for trauma survivors to improve post-trauma outcomes and stabilize recovery. This program has connected trauma survivors from 170 hospitals across the U.S. and Australia. The NextSteps interactive self-management program is free to join, and offered as part of the network. The program involves group classes: some classes are held in six-week sessions with two 20-30 minute meetings a week, while other centers offer the class once a week for 90 minutes. The lessons cover a variety of recovery-related subjects like goal-setting, problem-solving, managing emotional reactions, how trauma impacts friends and family, and communicating with friends and professionals. Participants also take part in a weekly online chat with other survivors, guided by a trained leader. As of May 2023, the online NextSteps has had 3,262 total participants, including health care providers, peers, and survivors. Classes are ongoing.

PARTNERS/COLLABORATORS

Johns Hopkins University; Walter Reed Army Medical Center; Carolinas Medical Center; The University of Maryland Shock Trauma Center; Bowman Gray Trauma Center; Harborview Trauma Center; Vanderbilt University Trauma Center

AWARD NUMBER: W81XWH-06-1-0343

MeMed BV® Test and the MeMed Key® Platform for Differentiating Bacterial versus Viral Infections

IMPACT: MeMed BV, a test cleared for use in hospital emergency rooms, helps physicians rapidly diagnose if an infection is bacterial or viral and if there is a need for antibiotics.

DESCRIPTION

Bacterial and viral infections are clinically indistinguishable. MeMed BV is a pioneering test that measures three immune system proteins: TRAIL, IP-10, and CRP. These measurements help MeMed BV to diagnose if an infection is bacterial or viral, which helps physicians decide whether or not to treat with antibiotics. MeMed BV performance achieved validation through multi-national, double-blind clinical studies and real-world settings on over 20,000 subjects in the U.S. and Europe. The MeMed Key, the device which runs the MeMed BV test, measures less than one cubic foot and weighs 22 pounds, which could allow for use in military and resource-limited point-of-care settings. MeMed Key is a cutting edge, point-of-need, compact immunoassay platform that makes it possible to conduct highly sensitive, rapid, multiplexed protein measurements that previously could only be done on large, central lab equipment. In September 2021, the FDA granted 510(k) clearance to use the MeMed BV test on children and adults. As of January 2023, Beckman Coulter obtained the rights to develop and co-promote the proprietary MeMed BV test on its Access Family of Immunoassay Analyzers. The test was initially for blood serum, but in July 2023, the FDA granted 510(k) clearance for a new version of the MeMed BV test on whole blood samples that eliminates the time needed for clotting and isolating blood components.

PARTNERS/COLLABORATORS

MeMed Diagnostics Ltd.; Naval Health Research Center

AWARD NUMBER: W81XWH-17-1-0694

Noninvasive Sensor Systems for Patient Vitals Monitoring

IMPACT: Noninvasive technology incorporated in medical monitors and sensors provides advanced patient monitoring, evidence-based defibrillation, and decision support to improve clinical outcomes in hospitals and the military.

DESCRIPTION

This award supported the development of medical monitors to noninvasively and continuously monitor muscle oxygen, muscle pH, and blood hematocrit—three key parameters to diagnose and treat shock. The monitoring technology was originally intended to help medics identify when they had provided adequate resuscitation from shock. In 2013, the Mobile CareGuide™ received FDA 510(k) clearance as the first-ever noninvasive sensor of muscle oxygen saturation and pH. Now, the technology is incorporated in the Sotera Digital Health ViSi Mobile System, which continuously monitors patients' blood pressure, SpO2, heart rate, pulse rate, respiration rate, skin temperature, ECG, posture, arrhythmias, and can also detect falls. The CareGuide technology developed under the PRMRP award is also incorporated in the currently commercialized Zoll Propaq® MD series and X series® monitors and defibrillators. The Propaq MD is a compact, lightweight, military airworthy device that provides advanced monitoring, evidenced-based defibrillation, and decision support to improve clinical outcomes.

PARTNERS/COLLABORATORS

University of Massachusetts; U.S. Army Institute of Surgical Research; Luxtec Corp.

AWARD NUMBER: DAMD17-03-1-0005

Minimally and Noninvasive Technologies for Diagnosis of Mitochondrial Disease and Dysfunction

DESCRIPTION

Improperly functioning mitochondria are present in many diseases, so having a tool that is capable of monitoring mitochondrial function would be beneficial and widely applicable, even for use in field hospitals. This research aims to develop a minimally invasive or noninvasive method to assess mitochondrial function that could be used for diagnosis of any type of mitochondrial dysfunction. The current method is an invasive muscle biopsy that measures mitochondrial aerobic capacity and often involves exercise that is not possible for patients with mitochondrial dysfunction. This research aims to develop four technologies to provide quantitative readouts of mitochondrial function: an implantable nanosensor to monitor muscle tissue oxygen, a breathalyzer, a pupil-measuring device to determine brain oxygen levels, and methods to measure muscle oxygen consumption during passive exercise on a platform bed that will not promote calorie burn or increase muscle mass. This team science award supports one team for each of the four technologies. As of this publication, the team has started to enroll for two clinical trials to assess the diagnostic efficacy of (1) pupillometry and cerebral oxygenation measurement via functional near infrared spectroscopy, and (2) periodic acceleration-based passive exercise.

IMPACT: Minimally-invasive diagnostic tools for mitochondrial disease will reduce the need for invasive muscle biopsies and can provide monitoring of mitochondrial function.

PARTNERS/COLLABORATORS

Children's Hospital of Philadelphia; University of Pennsylvania, Singh Center for Nanotechnology; Mount Sinai Medical Center

AWARD NUMBER: W81XWH-22-1-0590

Selective Cytopheresis Device (SCD) Therapy

IMPACT: If proven effective, SCD therapy could reduce mortality and improve clinical outcomes of critically-ill COVID-19 patients and Service Members who have experienced ALI/ARDS.

DESCRIPTION

Acute respiratory distress syndrome (ARDS) is a life-threatening inflammation of the lungs brought on by factors released after injury or during infection. The Selective Cytopheretic Device is an immune modulating device shown to be effective in reducing inflammation and multi-organ dysfunction, conditions associated with acute lung injury (ALI) and ARDS. A combat-relevant animal model for ALI was developed, and efficacy of SCD therapy to treat ALI/ARDS was assessed. The SCD demonstrated significant therapeutic benefits in the ALI/ARDS porcine model, which provided evidence to advance this technology into clinical trials. The FDA granted Emergency Use Authorization of SCD therapy for COVID-19 patients with acute kidney injury and ARDS, and a multicenter clinical trial is underway.

PARTNERS/COLLABORATORS

Innovative BioTherapies, Inc.

AWARD NUMBER: W81XWH-16-1-0463

SX600, a Sustained-Release, Non-Opioid Injectable Steroid Drug to Treat Lumbosacral Radiculopathy (Sciatica)

DESCRIPTION

More than one in three Americans experience back pain each year. Although epidural steroid injections are a common treatment for lower back pain, current steroid injections carry safety risks. SX600 encapsulates the well-known steroid, dexamethasone acetate, in small, biodegradable microspheres that, when injected, allow for the medicine to be slowly released. SX600 microspheres are smaller than red blood cells, have a hydrophilic non-aggregating surface, and risks are minimal. SX600 has been evaluated in preclinical epidural testing in two species with successful outcomes. Those successes enabled an ongoing phase 1/2 clinical study. Epidural injection of biodegradable microspheres may provide localized, sustained release of dexamethasone acetate for more than 60 days, and provide 60 to 90 days of pain relief for patients. Further testing aims to refine the safety profile for dosing, as well as to optimize the manufacturing process.

IMPACT: This project advances a non-opioid, slow-release, long-lasting, steroid injection for sciatica pain.

PARTNERS/COLLABORATORS

SpineThera, Inc.; Northern Biomedical Research; StageBio

AWARD NUMBER: W81XWH-21-1-0425

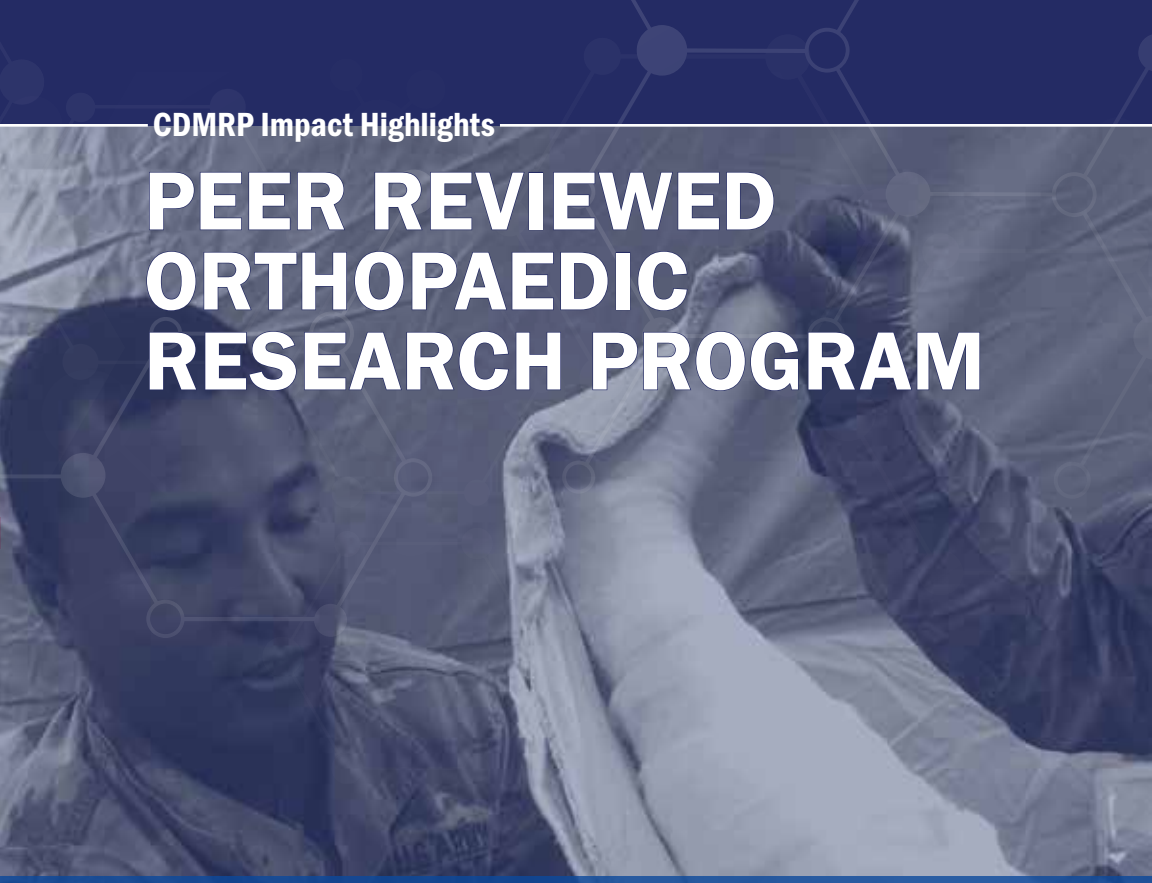
Karen B. Schmaling, Ph.D., PRMRP Peer Reviewer

"Relevant is a hallmark of the research supported by the PRMRP. The PRMRP integrates scientific, consumer, and military expertise to identify timely and innovative research. Clinical, translational, and basic research is reviewed that has promise to advance diagnosis and treatment of a range of conditions and to enhance the lives of Service Members, their families, and civilians."

Barbara Kelley
HRRP Programmatic Panel Member

"Hearing loss is a global health concern, with the number of people with hearing loss expected to double by 2050 according to the World Health Organization. Any degree of hearing loss disrupts daily communication and affects people's ability to work, enjoy life, and stay active and not isolated. People use technology, strategies and medication, but there's a continued unmet need to treat hearing loss. While curative therapies are not yet available, the Hearing Restoration Research Program is working toward solutions that could restore or improve hearing, bringing a future of hope to those living with hearing loss."

PEER REVIEWED ORTHOPAEDIC RESEARCH PROGRAM



Vision: Provide all military Service Members with orthopaedic injuries the opportunity for optimal recovery and restoration of function

Mission: Address the most significant gaps in care for the leading burden of injury and for facilitating return-to-duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat and Service-related activities

Years Program Appropriated: FY09–FY23

Total Appropriations: $518.5M

A large majority of the injuries sustained by military personnel in U.S. combat efforts involve soft tissue wounds and skeletal fractures, pointing to an urgent need for orthopaedic research that will result in superior medical care and treatment options for injured Service Members. Orthopaedic injuries sustained during combat- and Service-related activities tend to occur in harsh environments where access to optimal acute care can be limited. They are also distinct from those seen in the civilian setting, frequently involving multiple limb trauma, open fractures, major tissue loss, and a high degree of wound contamination. The Peer Reviewed Orthopaedic Research Program (PRORP) provides funding for high-impact, clinically relevant research projects that address the most significant gaps in orthopaedic injury care to facilitate return to duty and return to work.

Repairing Large Gaps in Injured Peripheral Nerves

IMPACT: Restoring function to a limb that has sustained a large-gap peripheral nerve injury could significantly improve an injured Service Member's quality of life by preventing paralysis, increasing independence, and decreasing neuropathic pain.

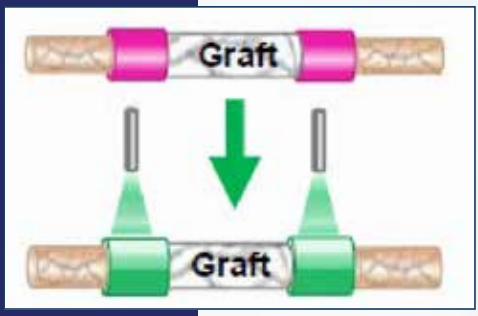
DESCRIPTION

Repair of large gaps in the peripheral nerve after blast injury is a significant challenge in restoring function to injured limbs. Researchers created a light-activated material that can be used to wrap the injured peripheral nerve. When light is applied to the wrap, it creates a seal and also releases compounds that help the injured nerve regenerate and prevent inflammation.

PARTNERS/COLLABORATORS

Massachusetts General Hospital; Walter Reed National Military Medical Center

AWARD NUMBERS: W81XWH-12-1-0511, W81XWH-12-1-0512, W81XWH-12-1-0513; follow-on funding from JWMRP W81XWH-17-1-0059



Schematic of photosealing approach. The nerve is wrapped with the graft device. When the pink dye is illuminated with green light, the graft is sealed and releases compounds to help the nerve regenerate. (Modified from image in Final Report, W81XWH-17-1-0059)

SPRINT Peripheral Nerve Stimulation (PNS) System

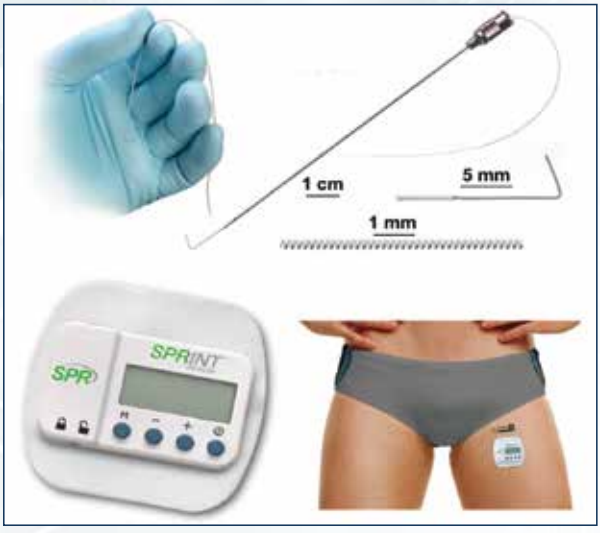
DESCRIPTION

The SPRINT PNS System consists of a microlead that is placed under the skin by a physician during an outpatient procedure without surgery, incisions, tissue destruction, or anesthesia. The microlead, connected to a wearable stimulator, can be left in place up to 60 days and delivers small pulses of electrical stimulation. The stimulation therapy is intended to produce a comfortable sensation where the pain is felt and decrease or eliminate the perception of pain. Additional studies of the therapeutic effects of the SPRINT PNS are being explored for low back pain relief and after knee replacement surgery.

PARTNERS/COLLABORATORS

SPR Therapeutics; Naval Medical Center San Diego; VA Palo Alto Health Care System; and several other clinical sites

AWARD NUMBERS: W81XWH-12-2-0132; follow-on funding from JWMRP W81XWH-17-C-0019, PRORP W81XWH-18-1-0799, PRMRP W81XWH-18-1-0800



IMPACT: The SPRINT PNS has shown to provide relief from residual and phantom limb pain in patients with amputations and decrease opioid usage due to sustained pain relief even after device removal.

Four-Drug Cocktail to Relieve Post-Traumatic Acute Pain

IMPACT: The combination nerve block will reduce or eliminate the complexity involved with inserting nerve block catheters in injured soldiers while preserving active range-of-motion and minimizing pain during evacuation.

DESCRIPTION

Study data provides evidence that single-injection combinations of four drugs (bupivacaine-bupivacaineclonidine-buprenorphine-dexamethasone and midazolam-bupivacaineclonidine-buprenorphine-dexamethasone) are safe, chemically compatible with each other, and have the apparent potential to provide long-term pain relief. Additional benefits will include the development of a continuous nerve block drug combination that (1) preserves active range-of-motion while acute pain is controlled without using conventional narcotic drugs and (2) allows for pain-free evacuation and transport of injured Warfighters.

PARTNERS/COLLABORATORS

University of Pittsburgh; Walter Reed Army Medical Center

AWARD NUMBERS: W81XWH-10-2-0097; follow-on funding from DMRDP W81XWH-15-1-0294

New Approaches to Prevent Cartilage Degeneration and Treat Post-Traumatic Osteoarthritis

IMPACT: Results from this research could accelerate the development of novel therapies to improve the skeletal health of the military population.

DESCRIPTION

Understanding how osteoarthritis develops is critical in advancing treatments for both Service Members and the general public who are suffering from chronic joint disease. Researchers hope to one day identify new agents that can rescue osteocyte (bone cell) remodeling and testing their ability to protect cartilage from conditions that drive post-traumatic osteoarthritis or osteonecrosis. This work identified the pathway by which heavy loads, such as those experienced by fully-outfitted Warfighters, compromise bone quality, which in turn promotes cartilage degeneration. It also found that this pathway is impaired in, contributes to, and can be targeted for prevention of the progression of post-traumatic osteoarthritis. The knowledge gained from this research will be applied to develop novel therapies that prevent or mitigate post-traumatic osteoarthritis and osteonecrosis.

PARTNERS/COLLABORATORS

University of California, San Francisco; San Francisco VAMC

AWARD NUMBERS: W81XWH-14-1-0497; follow-on funding from DMRDP W81XWH-18-1-0155

Local Vancomycin Powder Administration at a Surgical Fracture Site

IMPACT: Preventing infections in open fractures will reduce the risk of long- term infection-related complications and the need for additional treatments and prolonged recovery time, which impact mission readiness and delay return to duty.

DESCRIPTION

During military combat operations, Service Members have a high risk of fractures with open wounds, which can easily become contaminated. Surgical repair of traumatic bone fracture sites using plates, screws, and other metal hardware is associated with a high rate of infection and subsequently poor outcomes. Use of vancomycin powder at the surgical site prior to closing the wound significantly decreases deep surgical site infections. Building on this, researchers are investigating whether using vancomycin powder in the emergency department before surgical repair will reduce wound infections. Vancomycin powder is an FDA-approved topical antibiotic that is available as a low-cost generic drug, requires no refrigeration, and could easily be carried in a medic's bag and potentially be used for battlefield treatment.

PARTNERS/COLLABORATORS

University of Maryland, Baltimore; Johns Hopkins University; METRC consortium clinical sites; University of Texas, Health Science Center at San Antonio; U.S. Army Institute of Surgical Research

AWARD NUMBERS: W81XWH-10-2-0134, W81XWH-18-2-0074

Keratin HaloGel Drug Delivery System

DESCRIPTION

Keratin hydrogels are effective biocompatible carriers of a variety of drugs and have anti-inflammatory effects. This work demonstrated that an application of a Halo-infused keratin hydrogel in immobilized knees prevents post-traumatic contracture resulting from inflammation and TGF-β-induced excessive synthesis and deposition of type 1 and 3 collagens. This mechanism of drug delivery is now applied for treating infections, wound healing, and functional tissue regeneration.

PARTNERS/COLLABORATORS

KeraNetics LLC; Wake Forest University Health Sciences; Synecor Labs

AWARD NUMBERS: W81XWH-13-1-0466; follow-on funding via multiple SBIR awards

IMPACT: Success of the Keratin hydrogel drug delivery system resulted in its application in various fields, such as prevention of scar contracture after burn injuries, prevention of post-traumatic joint contracture, functional tissue regeneration, and bone graft.

Prevention of Neuropathic Pain in Limb Amputations Using Targeted Muscle Reinnervation

IMPACT: This study was instrumental in changing the standard of care for both upper and lower limb amputations and has also impacted the treatment of neuroma pain.

DESCRIPTION

Targeted muscle reinnervation is a surgical nerve-transfer procedure, originally developed to provide more intuitive control for upper limb prosthetics users. With this procedure, the residual nerve stumps are coapted to cut motor nerves that innervate new target muscles. Investigators hypothesize that targeted muscle reinnervation works because it provides a physiologically appropriate environment for regenerating axons, encouraging organized nerve regeneration into target muscles and preventing the chaotic and misdirected nerve growth that leads to neuroma formation. By preventing development of phantom and residual limb pain, this approach has the potential to improve patient-reported outcomes and decrease opioid medication use. In addition to publishing their results, the research team shared their skills and knowledge with over 100 surgeons during several in-person, interactive surgical learning sessions. The website www.tmrnerve.com is an excellent resource for patients who are looking for more information or a provider who can perform targeted muscle reinnervation surgery.

PARTNERS/COLLABORATORS

Northwestern University; Rehabilitation Institute of Chicago; The Ohio State University; Walter Reed National Military Center; Henry M. Jackson Foundation

AWARD NUMBER: W81XWH-13-2-0100

Adenosine, Lidocaine, and Magnesium Drug Therapy

DESCRIPTION

The anterior cruciate ligament (ACL) supports the knee joint and is the most injured ligament in the knee. Following injury and surgical intervention, which is required to repair the ligament, the joint experiences increased inflammation and fibrosis which can lead to post-traumatic osteoarthritis. This condition can impact surgical outcomes affecting return-to-duty rates and long-term quality of life. Researchers examined the effects of a combination therapy of adenosine, lidocaine, and magnesium in a military-relevant rat model of ACL rupture, on inflammation, fibrosis, and tissue repair. Overall, this therapy decreased the inflammatory and immune response in both male and female rats. However, sex-specific differences in the inflammatory response molecules and immune system components were noted that may lead to differences in healing. Several potential targets of inflammation and the immune system were identified to leverage these sex-specific differences in inflammatory and immune responses to improve surgical outcomes through personalized therapy post-injury.

PARTNERS/COLLABORATORS

Royal Australasian College of Surgeons; James Cook University; Orthopaedic Research Institute of Queensland

AWARD NUMBER: W81XWH-20-1-0931

IMPACT: Identification of sex-specific differences in the post-surgery knee environment and in response to adenosine, lidocaine, and magnesium combination therapy has the potential to change the standard of care after ACL surgical repair. Using a personalized approach for post-surgery therapy may improve surgical outcomes and return-to-duty rates for Service Members.

TARPIN System

DESCRIPTION

The prosthetic socket is a custom-built interface between a residual limb and the prosthesis. The residual limb is known to fluctuate in volume, often reducing the connection at the prosthetic socket interface and creating discomfort while performing daily living activities. Lower-limb amputees often use prosthetic socks or elevated vacuum systems to counteract this effect; however, both commonplace interventions provide dissatisfactory and inconsistent relief to users. The TARPIN (To Auto-release & Relock a PIN) system is an operationally seamless device that utilizes a motor-driven tether to permit efficient and easy socket release, partial doffing during sitting, and subsequent relock prior to standing. The study team further tested a microprocessor-adjustable socket that in conjunction with the TARPIN, maintains optimal prosthetic fit using sensory data from the user's changing limb volume captured from within the socket.

IMPACT: A novel hardware system for a prosthetic liner will allow individuals with lower limb amputation to discreetly relieve residual limb pressure caused by their prosthetic socket. The accommodation of residual limb volume fluctuation allows users to experience less discomfort throughout the day from extended prosthesis use, and increases the individual's ability to perform activities while using their prosthesis successfully and comfortably.

PARTNERS/COLLABORATORS

University of Washington

AWARD NUMBERS: W81XWH-18-1-0595, W81XWH-19-2-0049

Dynamic Air Exchange Prosthesis

DESCRIPTION

Advances in prosthetics technology have allowed more Service Members, Veterans, and civilians living with lower limb amputations the opportunity to return to work and maintain active lifestyles. However, those who engage in vigorous activities or work in hot, humid environments may still experience uncomfortable skin temperatures and the accumulation of perspiration inside their prostheses, which negatively impacts residual skin health and increases fall risk. The novel Dynamic Air Exchange prosthetic system creates an air flow inside the prosthesis, providing a way to decrease perspiration while maintaining a secure suspension for lower limb amputees who work in demanding environments.

PARTNERS/COLLABORATORS

Veterans Affairs Puget Sound Health Care System; Arusha Control, Inc.

AWARD NUMBERS: W81XWH-14-1-0188, W81XWH-18-1-0559

IMPACT: This significant advance may provide Service Members with lower limb amputations an option to return to duty in demanding environments (deployability) and may impact prosthetic prescription for all lower limb amputees.

Prototype Dynamic Air Exchange Prosthesis system worn by a research participant while standing. Additional sensors were added to monitor humidity, perspiration, liner slippage, and other important factors during the research project.

Petty Officer 2nd Class Tyler Burdick, U.S. Navy, Retired , PRORP Consumer Peer Reviewer

"Helping others, just as others helped me, is incredibly rewarding... I believe that input from the consumer advocate plays an invaluable role in the process of researching and developing new treatments and technologies that ultimately benefit us."

Molly A. Brewer, D.V.M., M.D., M.S., OCRP Programmatic Panel Member

"The DOD OCRP is one of the largest ovarian cancer research funders... We are funding new research to better understand ovarian cancer, to improve treatment, to reduce side effects and most importantly to train the next generation of ovarian cancer researchers."

PROSTATE CANCER RESEARCH PROGRAM

Vision: Conquer prostate cancer

Mission: Fund research that will eliminate death and suffering from prostate cancer and enhance the well-being of Service Members, Veterans, and all the men and their Families who are experiencing the impact of the disease

Years Program Appropriated: FY97-FY23

Total Appropriations: $2.26B

Prostate cancer is the most commonly diagnosed non-skin cancer in men and is the second most common cause of male death from cancer. In 2023, approximately 288,300 men in the U.S. were expected to be diagnosed with prostate cancer, with an estimated 34,700 deaths from the disease. Prostate cancer is a real threat to U.S. Service Members, as 80% of the active-duty population are men. While the Prostate Cancer Research Program (PCRP) has been successful in supporting advancements that have changed clinical practice, the program remains focused on addressing the knowledge, research, and clinical gaps that continue to make prostate cancer a global health issue. For the PCRP to accomplish its goal, all applicants are required to address overarching challenges that focus on developing treatments that improve outcomes for men with lethal prostate cancer, reducing lethal prostate cancer in African Americans, Veterans, and other high-risk populations, defining the biology of lethal prostate cancer to reduce death, and improving quality of life for prostate cancer survivors.

XGEVA® (Denosumab)

DESCRIPTION

XGEVA is an antibody that slows the progression of prostate cancer bone metastases. It blocks the bone resorption protein RANKL, thus slowing bone loss during cancer treatment and preventing fractures or skeletal-related events for cancer patients.

The drug indication has been expanded to include multiple myeloma patients.

PARTNERS/COLLABORATORS

University of Michigan

AWARD NUMBER: DAMD17-03-1-0092

IMPACT: Approved by the FDA in 2010, XGEVA is the number one oncologist-prescribed agent in the U.S. for the prevention of skeletal-related events in patients with bone metastases, including those for prostate cancer.

NuSAP1 Biomarker

DESCRIPTION

NuSAP1 is a gene that promotes invasion and metastasis of prostate cancer and is overexpressed in recurrent prostate cancer tumors. The PCRP funded the early work characterizing NuSAP1 overexpression and validating its potential as a prognostic marker. NuSAP1 has been incorporated into the Prolaris® and Decipher® commercial gene expression assays that have been validated in several clinical contexts and are used in the clinic to determine prognosis in men with early-stage prostate cancer.

PARTNERS/COLLABORATORS

Leland Stanford Junior University

AWARD NUMBER: W81XWH-11-1-0447

IMPACT: Assays incorporating NuSAP1 are widely available and their use can help newly diagnosed patients with localized prostate cancer assess their likelihood of disease progression and therefore, make better informed treatment decisions.

ZYTIGA® (Abiraterone Acetate)

DESCRIPTION:
ZYTIGA is an oral anti-androgen used to treat prostate cancer by blocking testosterone activity. Mechanistically, ZYTIGA blocks the enzyme CYP17A1, which is responsible for the production of circulating androgens in the body. When used in combination with the corticosteroid prednisone, ZYTIGA is effective at stopping the growth of prostate cancer cells that have metastasized to other parts of the body. Approved by the FDA in 2011 in combination with prednisone, ZYTIGA was the first approved hormone therapy to demonstrate a survival benefit for men with late-stage metastatic castration-resistant prostate cancer who have received prior docetaxel (chemotherapy).

PARTNERS/COLLABORATORS
Memorial Sloan Kettering Cancer Center; The Prostate Cancer Clinical Trials Consortium: includes University of Michigan; M.D. Anderson Cancer Center; The University of Wisconsin; The University of Chicago; Duke University Medical Center; Dana Farber Cancer Institute; Oregon Health and Science University; Johns Hopkins Kimmel Cancer Center; Rutgers University; Wayne State University; University of California, San Francisco; University of Washington

AWARD NUMBER: W81XWH-09-1-0147 (Clinical Consortium Award)

IMPACT: ZYTIGA provides a treatment option for men with late-stage prostate cancer who have received prior treatment and were left with very few therapeutic options to stop their prostate cancer from progressing further, changing clinical practice.

XTANDI® (Enzalutamide)

DESCRIPTION

XTANDI is an oral androgen receptor inhibitor for the treatment of prostate cancer. It is able to block testosterone activity at multiple steps of the androgen receptor signaling pathway, which are required for the growth of prostate cancer cells. Initially FDA-approved in 2012 for men with metastatic castration-resistant prostate cancer, XTANDI has been associated with better overall survival and significantly lower resource use and health care costs than ZYTIGA.

PARTNERS/COLLABORATORS

Memorial Sloan Kettering Cancer Center; The Prostate Cancer Clinical Trials Consortium

AWARD NUMBER: W81XWH-09-1-0147 (Clinical Consortium Award)

IMPACT: The FDA expanded the indication of XTANDI in 2018 for men with non-metastatic castration-resistant prostate cancer and in 2019 for men with metastatic castration sensitive prostate cancer.

ERLEADA® (Apalutamide)

DESCRIPTION

ERLEADA is an oral anti-androgen used for the treatment of prostate cancer that selectively blocks the function of the androgen receptor. ERLEADA is structurally and functionally similar to XTANDI but has been shown to have higher anti-androgen activity. In 2018, ERLEADA became the first medication to be FDA-approved for non-metastatic castration-resistant prostate cancer.

PARTNERS/COLLABORATORS

Memorial Sloan Kettering Cancer Center; The Prostate Cancer Clinical Trials Consortium

AWARD NUMBER: W81XWH-15-2-0018 (Clinical Consortium Award)

IMPACT: Approval of new treatment options for this group of patients was critical, as men with non-metastatic castration-resistant prostate cancer and a rapidly rising prostate-specific antigen level are at high risk for developing metastatic disease, which is lethal if unsuccessfully treated.

Oncotype DX AR-V7 Nucleus Detect Test

DESCRIPTION

This liquid biopsy assay measures levels of a variant of the androgen receptor, AR-V7, in the nucleus of prostate cancer cells in the blood and can help predict whether or not a patient will respond to certain prostate cancer treatments. Detection of AR-V7 predicts which patients with metastatic castration-resistant prostate cancer may not respond to androgen-receptor signaling inhibitors and should consider taxane therapy instead, helping patients avoid costly treatments that may not provide any benefit.

PARTNERS/COLLABORATORS

Sloan Kettering Institute for Cancer Research; University of Michigan; Johns Hopkins University; University of Washington; Dana-Farber Cancer Institute; Fred Hutchinson Cancer Research Center

AWARD NUMBER: W81XWH-13-2-0070

IMPACT: This assay is commercially available through Genomic Health/Epic Sciences and is used clinically as a non-invasive tool to better guide treatment decision-making.

IMPACT: The AdnaTest ProstateCancer assay provides a minimally invasive way to help determine the most effective treatment options and is also used as a diagnostic.

AdnaTest ProstateCancer

DESCRIPTION

AdnaTest ProstateCancer is a clinically validated, minimally invasive assay that enriches tumor cells from whole blood samples and detects the androgen receptor variant AR-V7, a biomarker for castration-resistant prostate cancer. The AdnaTest ProstateCancer assay is commercially available through Qiagen for research use to investigate drug resistance, and it was clinically validated by the Prostate Cancer Clinical Trials Consortium in the PROPHECY trial to be clinically relevant for identifying patients who are likely to not respond well to treatment with androgen signaling inhibitors, such as abiraterone and enzalutamide. Exclusive licensing from Johns Hopkins University allows for the assay to also be used for diagnostic purposes.

PARTNERS/COLLABORATORS

Johns Hopkins University; University of Washington; Institute of Cancer Research Royal Cancer Hospital

AWARD NUMBERS: W81XWH-15-2-0050, W81XWH-15-2-0051, W81XWH-15-2-0052

IMPACT: Today, this approach is used as the standard for precision radiation treatment of prostate and other cancers. Over 80% of radiation machines sold in 2014 were equipped with it.

Elekta Synergy CT System

DESCRIPTION

The Elekta Synergy CT System is a high-precision cone-beam CT imaging system that produces real-time 3D images of the prostate. These images allow for a highly accurate delivery of low-dose radiation to the tumor site while minimizing damage to nearby healthy tissues. Before the system received FDA clearance in 2003, radiation therapy was often less curative due to the uncertain position of the prostate during treatment. This anatomical uncertainty therefore required larger treatment areas, which exposed normal tissues to harmful radiation. The Elekta Synergy CT System provides precision-targeted radiation at curative doses without harming the structures supporting the prostate.

PARTNERS/COLLABORATORS

William Beaumont Hospital Research Institute

AWARD NUMBER: DAMD17-98-1-8497

Quantitative Total Extensible Imaging Software (QTxI)

DESCRIPTION

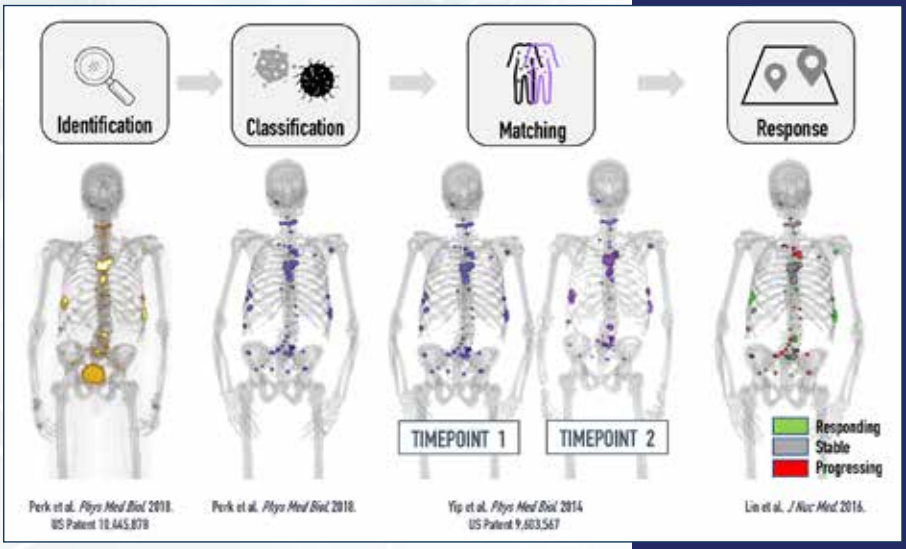
QTxI is an image-processing software that identifies and highlights areas of potential concern from standard positron emission tomography/CT scans using a patented machine-learning process. QTxI corrects for patient positioning and maps the identified areas of interest to track and quantify changes during the course of treatment at both the individual tumor and whole patient levels. The QTxI tool provides spatial information on tumors over time to improve clinical management for patients with metastatic disease. Originally developed to track the treatment response and metastatic disease progression in prostate cancer patients, the tool received FDA clearance in 2018 and is now approved to provide detailed confirmation about individual tumor response for all cancers.

IMPACT: Oncologists use QTxI to make precise and informed changes in real time to the patient's care plan, and its use has also been expanded for metastatic bone disease in breast cancer.

PARTNERS/COLLABORATORS

University of Wisconsin

AWARD NUMBER: W81XWH-14-2-0155



Virgil Simons, M.P.A., PCRP Programmatic Panel Member and Consumer

"Clinical cancer research and therapeutic health care are in the midst of an evolutionary process driven by expansion of the concepts of big data, artificial intelligence, and technological integration. Many research organizations are unclear as to direction or constrained by traditional research foci. The PCRP has no such boundaries because, each year, it will reinvent itself to meet the needs of the patient and professional communities in funding research. While broad in scope, the PCRP is precise in patient-centered delivery. Vision is the driving force for the PCRP."

Lori Stephen, RCRP Programmatic Panel Member

"Every person in the room during the programmatic review meetings approached each discussion with confidence in their area of expertise, as well as humility and an open mind, and always with high regard for the ultimate impact on the patient and caregiver community. I have enormous gratitude for the work being done in the scientific community, and I now have the unique perspective of witnessing the commitment those folks have to benefiting those who rely on their scientific efforts the most."

RARE CANCERS RESEARCH PROGRAM

Vision: To greatly improve outcomes for people with rare cancers through discovery and community building, and expansion of knowledge across the cancer landscape

Mission: Elevate rare cancers research to enable clinically impactful discoveries for the benefit of Service Members, their Families, Veterans, and the American public

Years Program Appropriated: FY20-FY23

Total Appropriations: $60M

Based on the metrics provided by the American Cancer Society, rare cancers are defined as those with an incidence of fewer than 6 cases per 100,000 individuals per year.[1] Data from the Veteran Affairs Health Care System indicate that ~16% of all VA cancer patients are diagnosed with a rare form of cancer.[2] Lack of information, therapeutics, and research are major obstacles to patient care for rare cancers. Major obstructions in patient care of rare cancers are lack of information, therapeutics, and research.

Congress established the Rare Cancer Research Program (RCRP) in FY20. RCRP supports novel research ideas for rare cancers to foster the development of platforms for resource sharing across multiple rare cancer types. The Resource and Community Development Award mechanism supports the development of clinical or preclinical research resources that would advance the field of rare cancers research and improve outcomes for individuals with rare cancers. Another mechanism, the Idea Development Award, promotes new ideas that are still in the early stages of development and could lead to critical discoveries or major advancements toward eradicating deaths and suffering from rare cancers.

[1] DeSantis CE, Kramer, JL, Jemal, A. 2017. The Burden of Rare Cancers in the United States, CA: A Cancer Journal for Clinicians 67:261–272. | [2] news.va.gov/101361/vas-progress-on-treating-cancer-since-2016

IMPACT: Knowledge gathered from open sharing of data and resources improves researchers' understanding of specific forms of rare ovarian cancers and treatment options for patients.

Network for Rare Tumors of the Ovary

DESCRIPTION

The Network for Rare Tumors of the Ovary facilitates collaboration among international researchers, clinicians, charities, patient advocacy organizations, and experts in data dissemination to advance research and improve treatment options. The network collects and shares research and disease data and biological samples through a web portal accessible to researchers and patients worldwide. Data and sample collection started with existing datasets and biobanks, and new data and samples are added over time. The team launched two websites and registries for two rare sub-types of ovarian cancers.

PARTNERS/COLLABORATORS

McGill University Health Centre Research Institute, Canada; The Bellvitge Institute for Biomedical Research, Spain; Institute of Health Carlos III, Spain; The Eve Appeal, UK; Small Cell Ovarian Cancer Foundation, U.S; Katie Oppo Research Fund, U.S.

AWARD NUMBER: W81XWH-21-1-0954

IMPACT: Results suggest RNA methyltransferase is a potential clinical target for developing novel therapeutics.

A Novel Therapeutic Approach in Neuroblastoma

DESCRIPTION

Neuroblastoma is a type of cancer that typically affects children under the age of five and has low survival rates. The protein RNA methyltransferase plays a critical role in neuroblastoma tumor progression, and researchers sought to better understand the protein's role in the proliferation of neuroblastoma cells. Inhibiting RNA methyltransferase led to reduced tumor growth and enhanced survival rates in pre-clinical mouse models.

PARTNERS/COLLABORATORS

University of New South Wales

AWARD NUMBER: W81XWH-21-1-0799

RECONSTRUCTIVE TRANSPLANT RESEARCH PROGRAM

Vision: Reconstructive transplant: an accessible and realistic choice

Mission: Advance science and standardized clinical practice of vascularized composite allotransplantation to improve access, safety, and quality of life for catastrophically injured Service Members, Veterans, and American civilians

Years Program Appropriated: FY12; FY14-FY23

Total Appropriations: $141M

The Reconstructive Transplant Research Program (RTRP) supports research to advance vascularized composite allotransplantation procedures, i.e., face and hand transplants, to improve access, safety, and quality of life for catastrophically injured Service Members, Veterans, and civilians. Vascularized composite allotransplantation refers to the transplantation of multiple tissues such as muscle, bone, nerve, skin, and blood vessels as a functional unit from a deceased donor to a recipient with a severe injury. The ultimate goal is to return injured Service Members to duty and restore their quality of life.

Actigraphy to Quantify Functional Hand Use in Hand Transplant and Replant Recipients and Amputees

IMPACT: Results from this study provided the first quantitative data defining the benefits of hand transplantation compared to prosthetics.

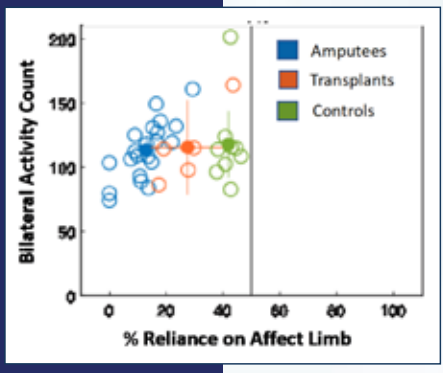
DESCRIPTION

The decision to pursue hand transplant requires thoughtful conversations between the potential recipient and the clinical team to discuss the risks and benefits. However, the benefits of hand transplantation compared to prosthetics in daily hand use patterns were unknown. Researchers used actigraphy to quantify limb activity levels by leveraging Fitbit-like technology worn on a participant's forearm and upper arm. Collected data enabled investigators to evaluate hand use patterns during regular daily activities in people with hand transplants, replants, and peripheral nerve repair. These data were compared with those from both healthy controls and people who had prostheses. This study was the first to objectively demonstrate that hand transplant recipients had similar patterns of movement to healthy controls and exhibited greater use of their affected arm than prosthetic users.

PARTNERS/COLLABORATORS

University of Missouri; Washington University in St. Louis; University of Louisville

AWARD NUMBER: W81XWH-15-2-0037



Upper limb activity in unilateral prosthesis users, healthy controls, and hand replants/transplants. During everyday life, hand transplant recipients use their transplanted hands more than amputees use their prostheses, but less than able-bodied controls use their intact limbs. Open circles represent individuals' average data across three days.

Engineered Microparticles to Promote Transplant Tolerance

IMPACT: Two sets of engineered microparticles were developed to promote transplant tolerance through the modulation of regulatory T cells.

DESCRIPTION

Recruitment-microparticles were designed to attract a subset of lymphocytes called regulatory T cells (Tregs), which suppress the effects of other T cells that would ordinarily attack cells recognized as foreign, like from a donor graft. Tregs are a rare population of lymphocytes (~2%-3%), however, and they may not be present in sufficient quantities to prevent graft rejection. Face and hand transplantation currently requires recipients to take immunosuppression medication with known negative side effects to minimize the risk of graft rejection. Promoting tolerance of the transplanted face or hand will minimize or eliminate the need for such harsh drug regimens. To address this problem, Treg-inducing microparticles were designed to induce production of more Tregs by converting the more populous naïve CD4+ T cells into Tregs. This combination approach resulted in significantly longer graft survival in an animal model.

PARTNERS/COLLABORATORS

University of Pittsburgh; Wake Forest University

AWARD NUMBER: W81XWH-15-1-0244

Treg-inducing microparticles prevents rejection and promotes long-term limb allograft survival in recipients. Treg-inducing microparticle–treated hindlimb allograft (post-operative day > 300) showing no signs of rejection and an actively rejecting untreated control graft (post-operative day = 38).

Biomarkers to Predict Rejection in Vascularized Composite Allotransplantation Grafts

IMPACT: A biomarker such as MMP3 that can be routinely monitored non-invasively via blood samples could allow for earlier detection and treatment of rejection episodes.

DESCRIPTION

More than 80% of vascularized composite allotransplantation recipients experience an episode of acute rejection within the first year of their transplant. Rejection can often be observed visually on the skin, but it would be ideal to identify rejection before changes are visible to the eye. Skin biopsies and the Banff classification system are currently the standard for detection of graft rejection, but the biopsy itself can cause additional morbidity for the patient, including scarring, bleeding, and infection. Matrix metalloproteinase 3 (MMP3) has been identified as a biomarker in blood samples that can discriminate severe and non-severe episodes of vascularized composite allotransplantation graft rejection from samples with no rejection in face transplant recipients.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital

AWARD NUMBER: W81XWH-16-1-0647

Utilizing Vascularized Bone to Improve Outcomes of Face Transplantation

DESCRIPTION

Complex face transplant procedures were personalized using a systematic approach for 3D modeling and virtual planning. Personalized cut guides were fabricated for both graft procurement and the recipient transplant procedure. This combination of virtual planning and personalized tools reduced surgical time by up to 60% and improved accuracy of allograft transplantation. Efforts from this project resulted in the first successful combination transplant of face and both hands for a 21-year-old man, which amazingly took just 23 hours to complete.

PARTNERS/COLLABORATORS

New York University School of Medicine

AWARD NUMBER: W81XWH-15-2-0036

IMPACT: The world's first successful combined face and two-hand transplant represents a critical milestone for what is possible with vascularized composite allotransplantation.

Photos with permission/copyrights retained by Eduardo D. Rodriguez MD DDS.

"There's always light at the end of the tunnel. Never give up and never let your appearance slow you down. Always look at the good things... I feel like it's a big step in science. I'm pretty proud to be a part of it."

Joe DiMeo, first successful combination face and double hand transplant

Harnessing Single-Cell Technologies to Understand and Diagnose Rejection in Clinical Face and Upper Extremity Transplantations

IMPACT: This research offers the opportunity to treat graft rejection episodes with more precision.

DESCRIPTION

Face or limb transplantation is a transformative reconstructive option for traumatic injury, but it is not without risk. Graft rejection can occur even with immunosuppression. Researchers received an FY17 RTRP award to study the biological processes underlying rejection in face transplant recipients. Researchers studied skin biopsies from seven face transplant recipients taken at times of non-rejection (grade 0) through severe rejection (grade 3). The team discovered that in grade 2, upregulation of tissue injury genes was balanced by an equal and opposite upregulation of immunoregulatory and anti-inflammatory genes. As a result, there was inflammation in the skin but no tissue injury. In grade 3, the balance shifted toward tissue injury. Perhaps most notably, it was found that grade 1 (mild) rejection does not represent a pathologic state and therefore does not need treatment with increased dosing of immunosuppression. Researchers also compared the genes upregulated during rejection in vascularized composite allotransplantation with those in solid organ (e.g., kidney, heart) rejection. They identified genes unique to vascularized composite allotransplantation, including 10 immunoregulatory genes. Understanding these immunoregulatory pathways could lead to developing novel therapies and minimizing the need for immunosuppression.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital

AWARD NUMBER: W81XWH-18-1-0798

SPINAL CORD INJURY RESEARCH PROGRAM

Vision: Advance the treatment and management of spinal cord injury and ameliorate its consequences relevant to injured Service Members

Mission: To fund research and encourage multidisciplinary collaborations for the development and translation of more effective strategies to improve the health and well-being of Service Members, Veterans, and other individuals with spinal cord injury

Years Program Appropriated: FY09-FY23

Total Appropriations: $437.9M

The Spinal Cord Injury Research Program (SCIRP) was established to support medical research into traumatic spinal cord injury and treatments, with the goal of enhancing the long-term care of wounded Soldiers. Congress specifically highlighted the complexity of neurotraumatic wounds as well as promising treatment regimens including regenerating/repairing damaged spinal cords and improving rehabilitation therapies. To meet this directive, the SCIRP focuses on funding within strategic priority areas that meet the needs of the spinal cord injury consumer community and address critical gaps in research, patient care, and quality of life.

Exoskeletal-Assisted Walking to Improve Mobility

IMPACT: The major takeaway from this study was that exoskeleton technology made walking possible in over 80% of individuals with chronic non-ambulatory spinal cord injury.

DESCRIPTION

This project is a multi-site clinical trial exploring the benefits of exoskeletal-assisted walking in 50 non-ambulatory participants. The results from this study provide guidelines for estimating the potential of individuals with spinal cord injury to achieve proficient and safe walking skills and include the proposed time commitment necessary to obtain meaningful functional gains. These guidelines are targeted to medical professionals, caregivers, and people living with a spinal cord injury regarding utilization of two commercially available exoskeleton devices in both institutional and personal use settings. The research team also investigated secondary health benefits to exoskeletal-assisted walking and observed significant improvements in bowel measures, cardiovascular function, and body composition in chronically injured participants.

PARTNERS/COLLABORATORS

Bronx Veterans Medical Research Foundation; University of Maryland; Kessler Foundation

AWARD NUMBER: W81XWH-14-2-0170

U.S. Marine Corps Veteran William Lehman walks in the Ekso exoskeletal-assisted walking device under the supervision of study staff.

Improved Bladder and Bowel Function via an Implantable Stimulator

DESCRIPTION

Electrical stimulation via an implantable, pacemaker-like, stimulator is being tested to aid in bladder and bowel continence and voiding in spinal cord injury patients. This technology has been available for over 10 years but was not widely adopted by the community due in part to the practice of severing sensory nerves at the time of implantation to permanently abolish the bladder reflexes. This study, however, is modulating the nervous system and observing functional improvements without purposefully damaging sensory nerves. Promisingly, the device allowed urination without catheterization and continence without medication for the first time in 41 years for a recent participant, illustrating for the first time that this technology can be utilized in spinal cord injury patients without permanent and purposeful nerve damage.

PARTNERS/COLLABORATORS

Leland Stanford Junior University and VA Palo Alto HC System; MetroHealth Medical Center; Santa Clara Valley Medical Center; University of New Mexico School of Medicine

AWARD NUMBER: W81XWH-14-2-0132

IMPACT: Using electrical stimulation to restore both bladder continence and emptying without destructive surgery is a game changer for the field and has the potential to significantly change clinical practice, allowing for a less invasive, non-destructive method to restore bladder function in individuals with a spinal cord injury.

Implantable Device Restores Upper Limb Function and Sense of Touch

IMPACT: This technology can help people with chronic spinal cord injuries regain reach and grasp abilities to restore functional independence.

DESCRIPTION

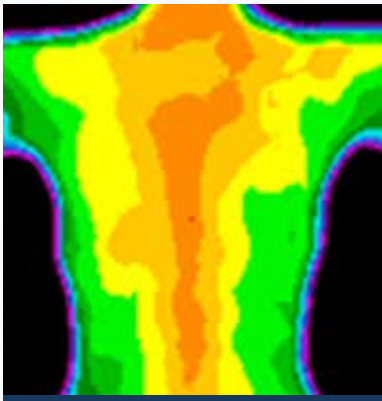
A SCIRP-funded clinical trial is testing the efficacy of a new device to restore hand and arm movements as well as the sense of touch in individuals with cervical spinal cord injuries. This device combines a brain implant with electrical stimulators in the arm to bypass the point of injury, mimicking the lost connections between the hand, arm, and brain. Early results are promising; not only can the first participant voluntarily move his paralyzed arm to offer a firm handshake and feed himself, but he is also able to feel the sensation of touch on his hand for the first time since his injury six years ago.

PARTNERS/COLLABORATORS

Case Western Reserve University; Brown University; Massachusetts General Hospital

AWARD NUMBER: W81XWH-19-1-0707

Near-Infrared Spectroscopy Sensor



DESCRIPTION

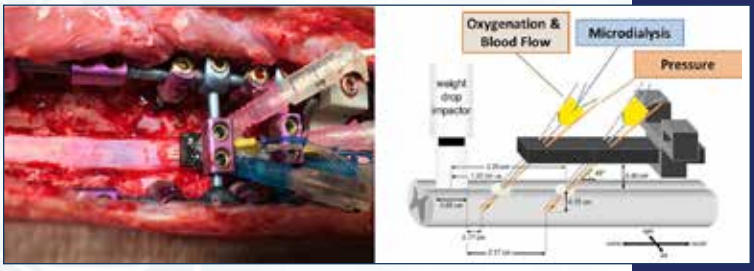
The Near-Infrared Spectroscopy system uses sensors to monitor the oxygenation, blood flow, pressure, and metabolism within the spinal cord and surrounding tissue in real time immediately after spinal cord injury. Researchers have shown that the system works in large animal models to detect local tissue changes within the injured spinal cord that reflect systemic hemodynamic changes, i.e., blood pressure, over the first seven days post-injury. They are now extending the work with support from SCIRP to a human clinical trial as well as developing advanced parameters that can help guide hemodynamic management in acute spinal cord injury to improve outcomes.

PARTNERS/COLLABORATORS

University of British Columbia

AWARD NUMBERS: W81XWH-16-1-0602, W81XWH-21-1-0388, HT9425-23-1-0777

IMPACT: The Near-Infrared Spectroscopy system is a monitoring tool that can provide clinicians with real-time data about how their interventions are affecting the tissue within the injured spinal cord, delivering previously unavailable information that is needed for evidence-based clinical practice guidelines to optimize management of acute spinal cord injury and improve neurologic recovery.



Intraparenchymal monitoring of the acutely injured spinal cord of the pig; probes for measuring oxygenation/blood flow, hydrostatic pressure, and microdialysis.

TRACK-SCI: Leveraging Fundamental Clinical Discoveries to Guide Treatment and Improve Recovery after Spinal Cord Injury

IMPACT: This database of patient treatments and outcomes is helping to inform evidence-based clinical care strategies to improve care in the acute phase of injury when decisions need to be made quickly and can have huge impacts on outcome and recovery.

DESCRIPTION

TRACK-SCI (Transforming Research and Clinical Knowledge in Spinal Cord Injury) is a SCIRP-funded collaborative effort that collects patient demographics, treatment, and outcomes data across multiple sites to establish crucial evidence-based standards of care for early treatment of spinal cord injury. Data from this long-term patient database is leveraged across multiple research sites to change clinical care for blood pressure management and surgical decompression post-injury. Machine learning approaches were also recently applied across the patient database to identify an optimal blood pressure range that correlates with improved recovery post-injury. Moreover, the TRACK-SCI patient database is being leveraged in additional SCIRP funded studies to examine novel drug candidates for improved neuroprotection, spinal plasticity, and pain reduction after injury.

PARTNERS/COLLABORATORS

University of California, San Francisco Brain and Spinal Injury Center; University of California, Fresno; Ohio State University Wexner Medical Center

AWARD NUMBERS: W81XWH-13-1-0297, W81XWH-16-1-0497, W81XWH-20-1-0245, W81XWH-21-1-0505, W81XWH-21-1-0505

Stentrode™, a Brain-Computer Interface to Facilitate Independence After Paralysis

DESCRIPTION

The Stentrode device, a blending of "stent" and "electrode," is a novel brain-computer interface technology that is unique in its minimally invasive delivery method: the thin, flexible device is implanted within a blood vessel of the brain without the need for invasive brain surgery. A SCIRP-funded project provided development, optimization, and biosafety testing of the Stentrode in a large animal model, which was integral for an industry-funded first-in-human clinical trial in individuals with motor deficits and severe paralysis. In the clinical trial, participants regained their ability to perform independent activities of daily living such as communication, using the Stentrode to control computers remotely with their minds in order to text, send emails, and shop online. TIME magazine named the Stentrode one of the 100 Best Inventions of the 2021. Synchron, the company developing the Stentrode, received FDA approval to commence human trials in the U.S. Other CDMRP programs are investing in this technology for additional indications as the device can be implanted in multiple locations to access different regions of the brain.

PARTNERS/COLLABORATORS

University of Melbourne

AWARD NUMBER: W81XWH-17-1-0210

IMPACT: The Stentrode's method of implantation via the vascular system allows the device to record from the brain without the need for invasive brain surgery, greatly increasing the safety and accessibility of the technology for users and providing real hope for individuals living with neurological disorders or injuries of regaining meaningful independence and autonomy.

SeePain

DESCRIPTION

SeePain is a comprehensive guide to understand and treat chronic spinal cord injury-associated neuropathic pain for those who have spinal cord injuries and their caregivers. This SCIRP-funded educational tool was developed with input from people living with spinal cord injury, their families, care partners, and health care providers. The SeePain guide considers many factors in pain control, including barriers to successful pain management. SeePain provides individuals with neuropathic pain, their family members, and caregivers a better understanding of the underlying mechanisms and external factors that affect pain management to encourage more effective communication regarding pain management plans.

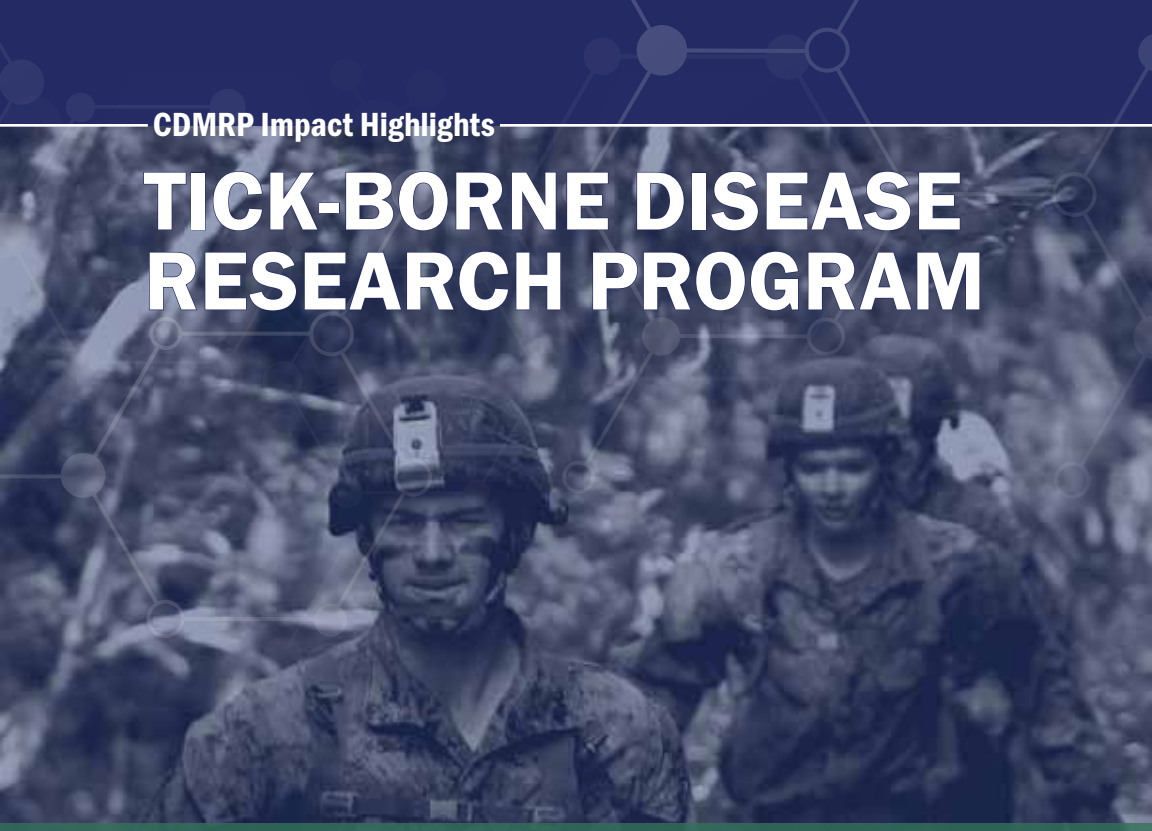
IMPACT: The SeePain guide provides individuals with spinal cord injury, their family members, and health care providers with knowledge and tools to discuss pain and pain management more effectively.

PARTNERS/COLLABORATORS

Case Western Reserve University

AWARD NUMBERS: W81XWH-12-1-0465, W81XWH-15-1-0602, W81XWH-21-1-0497

TICK-BORNE DISEASE RESEARCH PROGRAM



Vision: To prevent the occurrence, better diagnose, and resolve or minimize the impact of Lyme disease and other tick-borne illnesses, with emphasis on burden of disease

Mission: To understand the pathogenesis of Lyme disease and other tick-borne illnesses, to deliver innovative solutions to prevent, diagnose, and treat their manifestations for the benefit of U.S. Service Members and the American public, and to disseminate this knowledge

Years Program Appropriated: FY16-FY23

Total Appropriations: $48M

The Tick-Borne Disease Research Program (TBDRP) seeks to reduce the significant burden of Lyme and other tick-borne diseases on the health and welfare of civilian and military populations by funding innovative and impactful research to better understand disease processes and thereby develop improved diagnostic methods, prevention measures, and treatment regimens. The program supports the development of innovative new ideas to advance basic research on tick-borne disease pathogenesis and development of improved methods of prevention with a view toward improving patient care, as well as hypothesis-driven therapeutic and diagnostic development research with translational potential, and career development to help grow the field of tick-borne disease researchers. The program encourages research focused on persistent Lyme disease and other tick-borne diseases and conditions endemic to the U.S. Applications submitted to this Program must address at least one of the following Focus Areas: diagnosis, pathogenesis, prevention, and treatment.

IMPACT: Because there is currently no vaccine or prophylaxis for the prevention of ehrlichiosis, a human vaccine would significantly improve care in both military and civilian populations.

Vaccine Candidate for Ehrlichiosis

DESCRIPTION

In the U.S., the bacteria *Ehrlichia chaffeensis,* known as Ech, is responsible for the majority of cases of ehrlichiosis, a tick-borne illness that, if left untreated, can be fatal. Researchers developed a potential vaccine for Ech and demonstrated that antibodies generated from this candidate limit bacterial spread from tick to human cells in cell culture models of infection. In preclinical tick-bite animal infection studies, the vaccine candidate limits *ehrlichia* replication, elicits an immune response, and facilitates pathogen clearance.

PARTNERS/COLLABORATORS

The Ohio State University

AWARD NUMBER: W81XWH-17-1-0519

IMPACT: A cost-effective, safe, efficacious vaccine against Lyme disease would protect the general public and Service Members from acute illness and possible severe complications.

Multitarget-Display Virus-Like Particle-Based Vaccine to Combat Lyme Disease

DESCRIPTION

Current Lyme disease prevention strategies include spatial and contact tick repellents that require reapplication and user compliance. This cost-effective Lyme disease vaccine candidate expresses outer membrane surface protein(s) of *Borrelia burgdorferi*, the bacteria that causes Lyme disease. The vaccine uses a plant-based system for the scalable production of virus-like particles that can easily be produced, purified, and formulated. In preclinical studies, lead vaccine candidates demonstrated an appreciable antibody response that correlated with protective efficacy in animal infection models.

PARTNERS/COLLABORATORS

Fraunhofer USA Center for Molecular Biotechnology; Tufts University

AWARD NUMBER: W81XWH-17-1-0604

Pathogen-Host Molecular Biosignature Lyme Disease Diagnostic Assay

DESCRIPTION

Diagnostic tests for all tick-borne illnesses, particularly the most common tick-borne disease, Lyme disease, have significant limitations. Researchers are working to develop a Lyme disease diagnostic assay capable of accurately differentiating acute Lyme disease from other acute illnesses that may present with similar symptoms, such as influenza or sepsis. Toward this assay, genes that are differentially expressed in acute Lyme disease patients, as compared to non-Lyme and healthy controls, were identified, leading to the discovery of a Lyme disease-specific biomarker signature. Using machine learning analysis of this signature, a predictive model was developed for distinguishing the blood samples of acute Lyme disease patients from healthy patients or those suffering from other acute illnesses.

PARTNERS/COLLABORATORS

University of California San Diego; Johns Hopkins University; Bay Area Lyme Foundation, Lyme Disease Biobank; Boston Children's Hospital; American Red Cross

AWARD NUMBER: W81XWH-17-1-0681

IMPACT: The ability to diagnose Lyme disease at all stages of infection using a noninvasive, specific, sensitive, rapid test would improve overall patient care and result in prompt treatment that could mitigate disease progression and limit severity.

Pre-Exposure Prophylaxis for the Prevention of Lyme Disease

IMPACT: A stable human antibody against *Borrelia burgdorferi* that could be administered prior to peak tick season would protect both civilians and Warfighters and substantially reduce the number of Lyme disease cases each year.

DESCRIPTION

Currently, no approved vaccine or prophylaxis exists for the prevention of Lyme disease and as a result, prevention relies on avoidance and compliance with the application of tick repellent. Researchers are working to develop a bactericidal, long half-life, human monoclonal antibody as a pre-exposure prophylaxis for Lyme disease. This human antibody against the outer membrane surface protein of *Borrelia burgdorferi*, a causative agent of Lyme disease, is stable in animal models of infection and capable of protecting 80% of animals from tick-bite transmitted *Borrelia* infection in preclinical studies.

PARTNERS/COLLABORATORS

MassBiologics, University of Massachusetts Medical School; Tufts University; New York State Department of Health, Wadsworth Center

AWARD NUMBER: W81XWH-18-1-0375

Warfighter Adaptive Barrier Controlled-Release Device (AB-CRD) for Active Protection Against Ticks

DESCRIPTION

Currently, there are 18 infectious tick-borne pathogens, 20 conditions, and 13 illnesses known to result from tick bites. As tick populations continue to increase and expand geographically, the threat to Service Members in the field is significant. Current prevention strategies rely on the permethrin treatment of Service Member uniforms, which wanes over time, and/or the frequent application of tick repellent, which may not always be practical. Researchers are developing a device that uses micro-electro-mechanical systems technology to provide controlled and sustained release of a low toxicity spatial repellent. The device design includes remote wireless control and programming and allows for receipt of device updates. The AB-CRD is compact so one or more devices can be worn by the Soldier or affixed to mobile infrastructure.

PARTNERS/COLLABORATORS

GearJump Technologies, LLC; Instituto Technológico de Buenos Aires; University of Pennsylvania; University of Massachusetts Amherst; U.S. Department of Agriculture; U.S. Army Combat Capabilities Development Command-Soldier Center

AWARD NUMBER: W81XWH-19-2-0028

IMPACT: The AB-CRD, worn as an ankle bracelet or incorporated into the uniform or unit infrastructure, provides the Warfighter with an additional line of defense against tick bites, thus reducing tick-borne disease incidence.

Early prototype of AB-CRD attached to standard issue Army boot.

Highly Sensitive and Specific Acute Diagnostic Test for Tick-Borne Rickettsioses

IMPACT: This assay will allow for diagnosis and treatment for patients with rickettsial disease and aid physicians in differentially diagnosing infections with symptoms similar to rickettsioses, thus reducing misdiagnoses and failure to treat.

DESCRIPTION

Currently, there is no timely, specific diagnostic evaluation for tick-borne rickettsioses. As a result, it is difficult to give antibiotics early enough to control infection. This increases morbidity and mortality. Researchers have made progress in developing a rapid, easy-to-perform lateral flow test to detect and quantify the rickettsial diagnostic marker RC0497 that was measured in experimental animal models. Test validation is underway using human serum samples obtained from the Centers for Disease Control and Prevention and other locations.

PARTNERS/COLLABORATORS

University of Texas Medical Branch, Galveston; University of Houston

AWARD NUMBER: W81XWH-20-1-0834

Longitudinal Systems-Level Analysis of the Human Immune Response During Lyme Disease

IMPACT: This research will contribute to improved host-based diagnostic biomarkers of Lyme disease to accurately diagnose infection earlier, and to new treatments that are milder than broad spectrum antibiotics like doxycycline.

DESCRIPTION

10-20% of Lyme disease patients develop post-treatment Lyme disease syndrome, characterized by persistent symptoms for six or more months after antibiotic treatment; however, its etiology remains unclear. Researchers examined the acute immune response to Lyme disease and explored if or how immune dysregulation may contribute to post-treatment Lyme disease syndrome development. Using serum samples from longitudinal patient cohorts, the team identified distinct immune cell populations and assessed differential immune system activity in acute versus long-term Lyme disease.

PARTNERS/COLLABORATORS

Institute for Systems Biology

AWARD NUMBER: W81XWH-21-1-0664

Live Attenuated Powassan Virus Vaccine

DESCRIPTION

Symptoms of Powassan virus infection range from fever and headache to severe infections of the brain, encephalitis; or of the spinal cord, meningitis. Both can be lethal. There are currently no treatment options to eradicate Powassan virus once it is contracted and researchers are developing a live attenuated vaccine against the virus. Recently published study results were significant, showing that a chimeric YFV-17D-POWV vaccine candidate protected mice from Powassan virus with 70% survival in a two-dose regime and 100% survival through a prime-boost vaccination. The prime-boost strategy included initial vaccination, a boost of a protein associated with flavivirus attachment to increase host recognition and binding, and targeting of neutralizing antibodies to stimulate further protection.

IMPACT: This novel vaccination strategy lays the groundwork for further development of a potential Powassan virus prophylactic treatment in humans to mitigate the risk of Powassan virus infection and long-term symptoms.

PARTNERS/COLLABORATORS

The Rockefeller University

AWARD NUMBER: W81XWH-19-1-0409

Maj. Anders Karlsen, U.S. Air Force, TBDRP Consumer Peer Reviewer

"I'm incredibly grateful for the innovative and cutting-edge research CDMRP enables. This critical research provides hope and ultimately solutions for DOD members and their Families as they face medical challenges comparable to combat."

Tech. Sgt. Vera Roddy, U.S. Air Force, Retired, TERP Programmatic Panel Member,

"I am incredibly grateful to the Vietnam Veterans who welcomed me home from Desert Storm. They spoke out on our behalf when we came back with undiagnosed illnesses now understood as Gulf War Illness. More recently, I have welcomed home a new generation of Veterans and listened to their concerns about toxic exposures, including airborne hazards, open burn pits, and other particulate matter exposures. It is my hope that the Toxic Exposures Research Program will expand the knowledge of and discover interventions for the many conditions and health concerns that Veterans experience and that the outcomes of the program will contribute to a better quality of life."

TOXIC EXPOSURES RESEARCH PROGRAM

Vision: Minimize and mitigate the impact of military-related toxic exposures and improve the health and quality of life of those affected

Mission: Support impactful research aimed at identifying the cause and understanding the health outcomes, comorbidities, and pathological mechanisms associated with military-related toxic exposures to facilitate the prevention, diagnosis, and treatment of the visible and invisible diseases and symptoms impacting Service Members, Veterans, and the American public

Years Program Appropriated: FY22-FY23

Total Appropriations: $60M

Congress initiated the Toxic Exposures Research Program (TERP) in FY22 as a broad program dedicated to improving the scientific understanding of the pathobiology of toxic exposures, more efficiently assessing comorbidities, and speeding the development of treatments, cures, and preventions. The TERP supports military-related toxic exposure research across four major Topic Areas: neurotoxin exposure, Gulf War illness and its treatment, airborne hazards and burn pits, and other military service-related toxic exposures in general, including prophylactic medications, pesticides, organophosphates, toxic industrial chemicals, materials, metals, and minerals.

Prior to FY22, the CDMRP received congressional support for other programs aimed at providing health care solutions for diseases or conditions associated with toxic exposures, including the Gulf War Illness Research Program, the Peer Reviewed Medical Research Program's Burn Pits and Metals Toxicology Topic Areas, and the Neurotoxin Exposure Treatment Parkinson's Research Program.

The TERP coordinates with similar activities in the VA and encourages collaborations between military and/or VA institutions with non-military/non-VA research institutions to leverage the knowledge, infrastructure, and access to military and Veteran populations.

Safeguarding Military Lives and Health via Superior Monitoring of Environmental and Personal Chemical Exposures

IMPACT: The Xcel+ has the potential to detect chemical toxic exposures, aid with decisions on protecting the force, and help clinicians diagnose and treat those that may have been exposed to harmful chemicals.

DESCRIPTION

The research team at XploSafe LLC is developing the Xcel+ sampler, a device that will sample a wide range of volatile chemicals including, but not limited to, pesticides, fuels, and toxic industrial chemicals. This device is intended to be worn or placed in environments to monitor personal or general exposure to potentially harmful ambient chemical vapors. Xcel+ could help prevent exposures, identify compounds Service Members are exposed to, and encourage timely diagnoses and intervention.

PARTNERS/COLLABORATORS

XploSafe, LLC

AWARD NUMBER: HT9425-23-1-1012

A Novel and Practical Intervention for Detoxification of PFAS in Humans

IMPACT: This study will test dietary fiber as a non-invasive, cost-effective intervention to reduce the burden of PFAS in the body, thus reducing the potential for PFAS toxicity and improving the health of those exposed.

DESCRIPTION

Per- and poly-fluoroalkyl substances, or PFAS, are common chemicals used in water- and stain-repelling products, as well as in firefighting foams, which has led to long-lasting contamination of water supplies. This contamination poses a considerable threat to military and civilian populations due to increased risk of cancer, liver damage, increased cholesterol in the blood, and links to impaired vaccine response. The research team aims to use dietary fibers to prevent the absorption of and accelerate the elimination of ingested PFAS in animal exposure models. If successful, the results from this study will serve as the foundation for follow-up studies in humans.

PARTNERS/COLLABORATORS

Boston University Medical Campus; University of Massachusetts, Lowell

AWARD NUMBER: HT9425-23-1-0690

Identification of Metabolic Biomarkers of Gulf War Exposures and Gulf War Illness Using the DOD Serum Repository

DESCRIPTION

This study intends to identify Gulf War-related toxic exposures by identifying chemical fingerprints left by small molecules called metabolites in pre- and post- deployment serum samples from Veterans living with Gulf War illness and comparing them to healthy controls. Serum samples will be obtained from the DOD Serum Repository. Veterans will be identified using data collected by the Boston Biorepository and Integrative Network patient cohort, an effort supported by the CDMRP's former Gulf War Illness Research Program (GWIRP). The team will employ a technique called high-resolution metabolomics to identify Gulf War-era environmental exposures and endogenous metabolites that can be used as biomarkers for diagnosis and as putative therapeutic targets.

PARTNERS/COLLABORATORS

Henry M. Jackson Foundation; Uniformed Services University of the Health Sciences; Emory University

AWARD NUMBER: HT9425-23-2-0052

IMPACT: Upon successful completion of the project, the team will have identified new biomarkers that can aid in understanding the metabolic changes associated with Gulf War illness. These biomarkers will promote diagnostics, as well as an improved understanding of susceptibility and therapeutics for Veterans with Gulf War illness.

The Role of Adaptive Immune Activation in Solvent-Induced Parkinson's Neurodegeneration

IMPACT: The study will determine whether specific immune cell populations (T cells) become dysregulated following trichloroethylene exposure, thus contributing to cognitive impairment. Successful completion of this study may identify existing drug candidates that could be repurposed to prevent or slow the cognitive decline associated with the progression of parkinsonism.

DESCRIPTION

Trichloroethylene is a chlorinated solvent and one of the previous water contaminants at Camp Lejeune. Environmental factors and exposures, such as trichloroethylene, are believed to play a significant role in many cases of parkinsonism — the spectrum of Parkinson's disease, including Parkinson's disease dementia and dementia with Lewy bodies — though the mechanisms remain unclear. Increasing evidence suggests that dysregulation of the adaptive immune system, including the T cell response, may impact cognitive function in Parkinson's disease, and trichloroethylene is a well-known T cell activator. The research team hypothesizes that trichloroethylene may drive dementia with Lewy bodies pathogenesis and progression by activating the T cells, thus having specific effects on cognitive impairment. Using animal models, the research team will evaluate the effects of trichloroethylene exposure on T cell activation and determine whether blocking this activation limits neurodegeneration and cognitive decline. Furthermore, the team will determine if they can measure changes to adaptive immune cell populations in the blood. Upon completion, these studies will demonstrate whether trichloroethylene influences cognitive impairment by dysregulating the adaptive immune response, accelerating cognitive decline in parkinsonism, and influencing the outcomes of dementia with Lewy bodies.

PARTNERS/COLLABORATORS

University of Alabama at Birmingham

AWARD NUMBER: HT9425-23-1-0788

Advanced Phenotyping Improves Diagnostic, Longitudinal Assessment, and Treatment Strategies for Deployment-Related Respiratory Disease

IMPACT: This project will define a trajectory of deployment-related respiratory disease and demonstrate how quantitative computer tomography imaging methods are an effective, noninvasive means to diagnose and predict deployment-related respiratory disease.

DESCRIPTION

Deployment-related respiratory disease refers to a spectrum of respiratory conditions experienced by Service Members and Veterans that were previously deployed. In efforts supported by CDMRP's former GWIRP and the VA, researchers used parametric response mapping, a quantitative computer tomography imaging approach, to detect constrictive bronchiolitis and other respiratory conditions. They concluded that Service Members and Veterans have increased functional small airway disease relative to healthy subjects and those with mild chronic obstructive pulmonary disease. In this TERP-funded study, the research team will use noninvasive parametric response mapping imaging in subjects with functional small airway disease to determine if the condition changes over time in Service Members and Veterans with suspected deployment-related respiratory disease, and if there are subtypes of the disease. The team will also use molecular and functional imaging in an animal model of constrictive bronchiolitis and pulmonary fibrosis to determine whether specific treatments are effective at preventing disease.

PARTNERS/COLLABORATORS

The University of Michigan; Veterans Affairs Ann Arbor Health Care System

AWARD NUMBERS: HT9425-23-1-0697, HT9425-23-1-0698; prior funding under GWIRP W81XWH-17-1-0575 and VA support 01BX004740-01A1

Pre-Diagnostic Serum Concentrations of Per- and Polyfluoroalkyl Substances and Risk of Testicular Germ Cell Tumors Among Active-Duty Servicemen

IMPACT: Completion of this study will provide evidence of whether elevated serum concentrations of PFAS are associated with an increased risk of testicular germ cell tumors in Service Members. The results could impact regulations limiting PFAS exposures, and aid in the diagnosis, prediction, and prevention of testicular cancers in Service Members and the American public.

DESCRIPTION

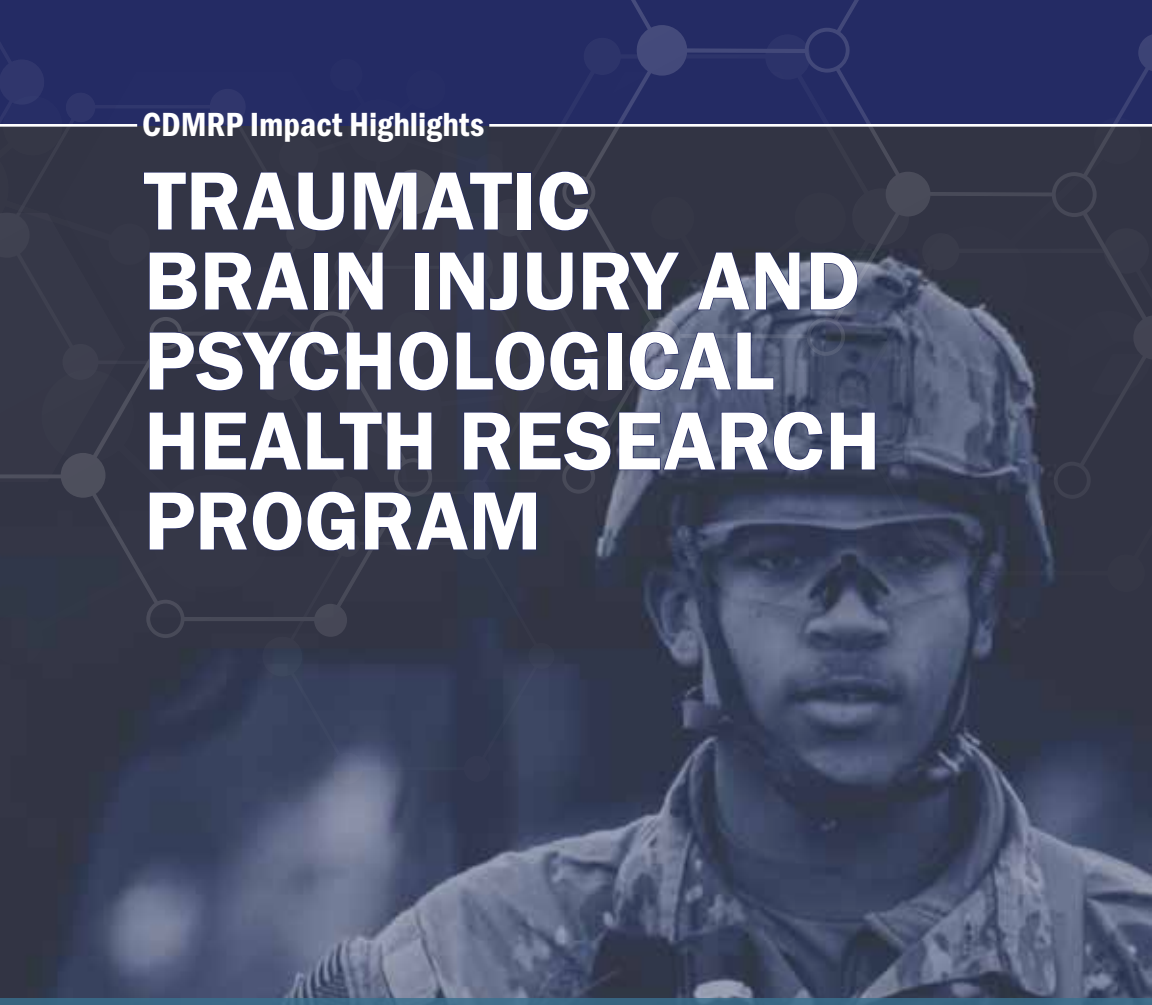
PFAS are found in everyday products like nonstick cookware and firefighting foams. These substances are detected in the blood of many Americans, persist for many years, and are believed to be associated with adverse health effects. However, their exact effects, particularly in Service Members, are largely unknown. In an FY18 PRCRP-funded study, the research team found that Air Force Service Members diagnosed with testicular germ cell tumors were more likely than controls to have high serum levels of perflourooctane sulfonate, a type of PFAS. In this TERP-funded study, the research team will perform a larger study, again using banked serum from the DOD Serum Repository, to perform a similar evaluation across other service branches, including the Army, Navy, and Marine Corps. The team will measure PFAS levels in pre-diagnostic serum samples from those diagnosed with testicular germ cell tumors and cancer free controls to determine whether increased PFAS levels suggest increased risk for testicular cancer.

PARTNERS/COLLABORATORS

The Geneva Foundation; The National Cancer Institute; Henry M. Jackson Foundation; Uniformed Services University of the Health Sciences

AWARD NUMBERS: HT9425-23-1-0968; prior funding under PRCRP W81XWH-19-1-0444

TRAUMATIC BRAIN INJURY AND PSYCHOLOGICAL HEALTH RESEARCH PROGRAM



Vision: Optimize the prevention, assessment, and treatment of psychological health conditions and/or traumatic brain injuries

Mission: Fund research to understand, prevent, and treat psychological health conditions and/or traumatic brain injuries that accelerates solutions to improve the health and health care of Service Members, their Families, Veterans, and the American public

Years Program Appropriated: FY07; FY09-FY23

Total Appropriations: $2.3B

The Traumatic Brain Injury and Psychological Health Research Program (TBIPHRP) is dedicated to advancing research to understand, prevent, assess, and treat traumatic brain and/or psychological health conditions. The TBIPHRP solicits and funds research across the research continuum including epidemiology, translational research, clinical trials, and services research. Program strategy is informed by congressional intent and the medical research needs of Service Members, their Families, Veterans, and the American public.

IMPACT: This study will address the unmet need for point-of-care treatments for TBI.

Developing the Use of Intranasal Insulin for On-Field Treatment of Traumatic Brain Injury

DESCRIPTION

The sooner a traumatic brain injury is treated, the better the effect on long-term outcomes. There is an unmet need for stable, portable, easy-to-administer, and immediately effective treatments for TBIs, both on the battlefield and in the civilian world. To address this unmet need, the investigators propose to use intranasal insulin. Compared to traditional intravenous injections, nasal delivery provides faster onset of action and allows for higher bio-availability in a smaller dose. Using both blast-related and rotational head injury animal models of TBI, the study will determine the ideal intranasal insulin dosing paradigm. Information gained from this research is critical to moving closer to effective treatments that can help mitigate the effects of traumatic brain injury.

PARTNERS/COLLABORATORS

Uniformed Services University of the Health Sciences; Henry M. Jackson Foundation

AWARD NUMBER: W81XWH-22-2-0048

Randomized Controlled Trial of Intensive Multi-Couple Therapy for PTSD versus Relationship Education in Military Couples

DESCRIPTION

When a Service Member or Veteran experiences PTSD, it does not only affect the individual, but also the relationship with their intimate partner. With funding from the TBIPHRP, this study will compare two couple-based PTSD interventions: abbreviated, intensive, multi-couple group format of cognitive-behavioral conjoint therapy (AIM-CBCT) versus the widely used Prevention and Relationship Enhancement Program (PREP). If successful, the two-day AIM-CBCT for PTSD could be implemented within the Military Health System and Veterans Health Administration and help military and veteran families maintain strong, healthy relationships.

PARTNERS/COLLABORATORS

Pennsylvania State University

AWARD NUMBER: W81XWH-22-1-0985

IMPACT: The AIM-CBCT for PTSD has the potential to promote PTSD functional recovery and support and maintain healthy military families. The intervention's abbreviated two-day delivery facilitates treatment program completion and can be scaled up for implementation within the Military Health System and Veterans Health Administration.

Preventing Suicide Among Survivors of Military Sexual Violence: Identifying Critical Risk Periods and Factors That Attenuate and Exacerbate Risk

IMPACT: The research is expected to lead to a better understanding of periods when military sexual trauma survivors are at increased risk for suicidal thoughts and behaviors and may lead to the development and implementation of more holistic and inclusive suicide prevention approaches.

DESCRIPTION

There is a clear link between military sexual trauma and suicide ideation, suicide attempt, and suicidal mortality, but knowledge is limited regarding when suicide risk is most elevated among sexual trauma survivors. This study will evaluate the roles of perceived stigma from others, self-stigma, and the military's institutional response to sexual trauma in suicidal ideation and suicide attempt among active duty and Veteran survivors of military sexual violence. It will assess whether gender, sexual orientation, and military status (active duty vs. Veteran) alter a survivor's experiences, perceptions, and needs regarding optimal suicide prevention strategies. The research is expected to lead to better understanding of periods when survivors are at increased risk for suicidal thoughts and behaviors and may also lead to the development and implementation of more holistic and inclusive suicide prevention approaches that are trauma-informed and gender-sensitive. This study will also take into account military sexual trauma survivors' varied backgrounds, experiences, and needs.

PARTNERS/COLLABORATORS

Arizona State University, Tempe; Denver Research Institute

AWARD NUMBERS: W81XWH-22-1-1102, W81XWH-22-1-1103

Validating a New Algorithm to Diagnose Traumatic Brain Injury in Far-Forward Settings

DESCRIPTION

When Service Members and civilians suffer a mild TBI in remote locations or during sporting events, first responders lack an objective way to diagnose and assess injury severity. With funding from TBIPHRP, in conjunction with a collaborative, nonoverlapping study by CRRP, this study combines two mild-TBI assessments to develop a diagnosis algorithm for mild TBI: blood-based biomarkers and pupillary light reflex, a measure of symptom severity. The test will be the first to combine blood-based biomarkers of brain injury with a marker of symptom severity in order to create a diagnostic algorithm and prediction model for symptom severity and length of care after mild TBI. The goal is to incorporate the assessments into a single hand-held device that can be used at the point of injury to provide information regarding symptom severity and inform return-to-duty/work/play decisions.

IMPACT: These biomarkers, if usable at the point of injury, could inform triage and evacuation decisions and directly improve health care for those experiencing a mild TBI.

PARTNERS/COLLABORATORS

Uniformed Services University of the Health Sciences; Henry M. Jackson Foundation

AWARD NUMBERS: W81XWH-22-2-0066, W81XWH-22-2-0049

Glecaprevir/Pibrentasvir for the Treatment of PTSD

IMPACT: If successful, results of this trial could lead to the development of a new class of therapeutics for treatment of post-traumatic stress disorder.

DESCRIPTION

PTSD is a condition that can develop as a result of exposure to a traumatic situation. This TBIPHRP award will investigate the repurposing of Mavyret® (glecaprevir/pibrentasvir), an FDA-approved antiviral used to treat hepatitis C viral infections, as a PTSD therapeutic in the absence of hepatitis C. Through a randomized, double-blind, placebo-controlled clinical trial, the study will determine whether Mavyret is an effective, tolerable treatment for PTSD. Unlike current FDA-approved PTSD drugs, Mavyret demonstrates a lower side-effect profile, and is not known to act directly on the brain. If successful, the results of the trial will identify a novel use for an FDA-approved drug and could lead to the development of a new class of PTSD therapeutics.

PARTNERS/COLLABORATORS

White River Junction Veterans Affairs Medical Center; Veterans Education and Research Association of Northern New England, Inc.

AWARD NUMBER: W81XWH-22-C-0147

Swoop® Portable Imaging Device

DESCRIPTION

Swoop is a portable magnetic resonance imaging device developed by Hyperfine, Inc., and cleared by the FDA for brain imaging in neonatal through adult patients. The device is intended to complement conventional high-field brain imaging that is typically limited to specific hospital settings. This study funded the development of low-magnetic field imaging technologies and techniques that would enable the use of brain imaging in non-hospital settings. The device can be used on patients with imbedded metal fragments or devices and patients on ventilator support in complex clinical environments.

PARTNERS/COLLABORATORS

Harvard University; Massachusetts General Hospital; Hyperfine, Inc.

AWARD NUMBER: W81XWH-11-2-0076

IMPACT: Availability of a less expensive, portable, low-field magnetic resonance imaging expands use outside of controlled hospital imaging facilities and into bedside and field-based applications.

(Photo Courtesy of Dr. Kevin Sheth, Yale University)

The portable magnetic resonance imaging, Dr. Matthew Rosen (l), and Dr. W. Taylor Kimberly (r)
(Photo courtesy of Dr. Matthew Rosen)

NCAA-DOD Grand Alliance: Concussion Assessment Research Education (CARE) Consortium

IMPACT: The work of the CARE Consortium is answering critical questions about head impact exposures and concussions, filling important knowledge gaps, and leading to changes in clinical practice guidelines that are improving care for those suffering from concussions. The vast amount of information gathered by this research team will continue to provide scientific and clinical advancements for years to come.

DESCRIPTION

The CARE Consortium is a joint DOD and National Collegiate Athletic Association research effort dedicated to studying concussion to better understand the development of injury and trajectory of recovery utilizing a multi-site, longitudinal investigation of concussive and repetitive head impacts. The study also allows for more advanced research projects, such as testing impact sensors, studying potential biomarkers, and evaluating concussions with advanced neuroimaging. Since initially receiving funding in 2014, the CARE Consortium has enrolled over 50,000 student athletes and service academy cadets at 30 sites. The CARE Consortium will allow development of evidence-based approaches to understanding the risks, management, and possible treatment strategies for concussion.

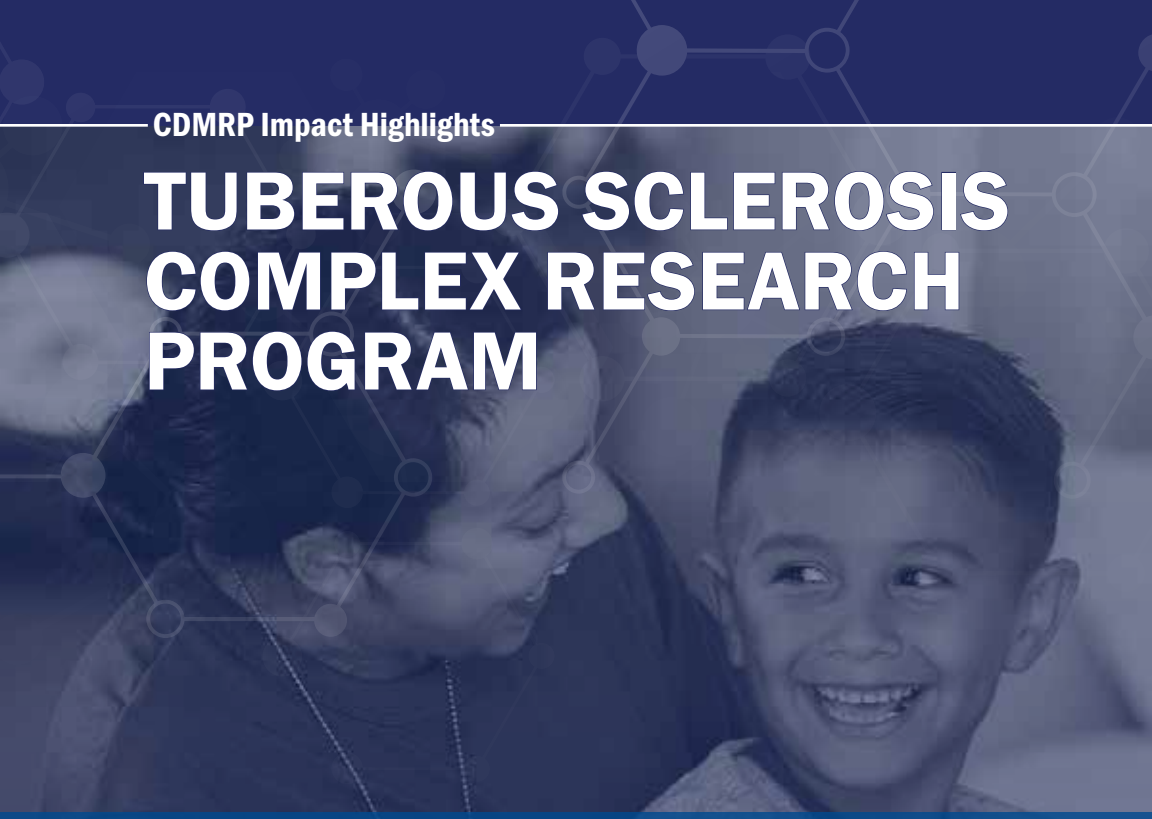
PARTNERS/COLLABORATORS

Indiana University; National Collegiate Athletic Association; University of Michigan; Medical College of Wisconsin; Uniformed Services University of the Health Sciences; U.S. Military Academy; U.S. Air Force Academy; U.S. Coast Guard Academy; U.S. Naval Academy; University of North Georgia; University of California, San Francisco; Datalys Center for Sports Injury Research and Prevention; The Mind Research Network; NIH; University of Oklahoma; University of Delaware; Humboldt State University;* University of Wisconsin; University of California, Los Angeles; University of Washington; Wilmington College; Princeton University; University of Pennsylvania; Virginia Tech; University of North Carolina; Wake Forest University; University of Miami; University of Pittsburgh; University of Georgia; University of Florida; University of Rochester; Temple University; Bloomsburg University; California Lutheran University; University of Chicago; Azusa Pacific University; Winston-Salem State University

AWARD NUMBERS: W81XWH-14-2-0151, W81XWH-18-2-0047; additional funding and support provided by the Combat Casualty Care Research Program, NCAA, and NIH

* California State Polytechnic University as of January 2022

TUBEROUS SCLEROSIS COMPLEX RESEARCH PROGRAM



Vision: Improve prevention strategies and treatments to lessen the impact of tuberous sclerosis complex while striving for a cure

Mission: Support innovative and high-impact research that promotes discoveries in tuberous sclerosis complex, from mechanistic insights to clinical application across all ages, by fostering new ideas and investigators for the benefit of Service Members, their beneficiaries, and the American public

Years Program Appropriated: FY02-FY06; FY08-FY23

Total Appropriations: $113M

Tuberous sclerosis complex (TSC) is a rare genetic disorder that is caused by a spontaneous genetic mutation in the *TSC1* or *TSC2* gene. It affects approximately 50,000 individuals in the U.S. and 1 to 2 million individuals worldwide. TSC causes non-malignant tumors in many different organs, primarily in the brain, eyes, heart, kidneys, skin, and lungs. It presents itself in a variety of clinical manifestations; the most severe impact is associated with the brain, which causes seizures, developmental delay, intellectual disability, and autism. Currently, there is no cure.

The Tuberous Sclerosis Complex Research Program (TSCRP) was established in FY02 with a congressional appropriation of $1M. It is the second largest government funding source supporting TSC research in the U.S. Since its inception, the TSCRP has played a critical role in supporting high-impact research, fostering new ideas, encouraging innovation, and bringing new investigators into the TSC field.

Immunotherapy for Tuberous Sclerosis Complex Tumors

IMPACT: Immunotherapy has the potential to become a novel therapy for TSC tumors and could have long-lasting and significant effects on tumor burden and therefore, improve the overall prognosis and quality of life for those living with tuberous sclerosis.

DESCRIPTION

Blood vessel-filled tumors called angiomyolipomas occur in the kidneys of most children and adults with TSC. Current therapies only partially decrease the size of the tumor, and the angiomyolipomas regrow when treatment is stopped. Taking a novel approach called immunotherapy, which has been successful in treating a number of cancers, this study is using the body's own immune system to treat angiomyolipomas. In a mouse model of tuberous sclerosis, individual treatment using antibodies to block one of two key proteins was successful in decreasing tumor growth, and pre-treatment with combined antibodies led to tumor rejection.

PARTNERS/COLLABORATORS

Brigham and Women's Hospital

AWARD NUMBER: W81XWH-17-1-0150

HYFTOR® (Sirolimus Topical Gel) for Facial Tumors

DESCRIPTION

HYFTOR was approved by the FDA in 2022 to treat facial angiofibromas in adults and children six years of age and older. Facial angiofibromas are benign skin tumors on the face. Seventy-five percent of patients with TSC will develop this condition, which causes notable disfigurement and impacts the patient's quality of life.[1] Previously, there was no effective method for treating this condition. In 2011, researchers received a Clinical Research Award to conduct a phase 2 randomized clinical trial to study the safety and efficacy of topical rapamycin to treat tuberous sclerosis-related facial angiofibromas. The study was highly successful, which paved the way for HYFTOR to treat facial angiofibromas.

IMPACT: The drug is now readily available for TSC patients to treat their facial tumors. The TSC community has very positive responses to this new drug, which greatly enhances their quality of life.

PARTNERS/COLLABORATORS

University of Texas Health Science Center at Houston; additional clinical sites: Clinic Without Walls, Minnesota Epilepsy Group; University of Alabama at Birmingham; Texas Scottish Rite Hospital for Children and University of Texas Southwestern Medical Center; Massachusetts General Hospital; Cincinnati Children's Hospital; Kennedy Krieger Institute and Johns Hopkins University; Children's Hospital UCLA; Children's Hospital and Research Center at Oakland; Sydney Children's Hospital

AWARD NUMBER: W81XWH-11-1-0240

[1] Koenig MK, Bell CS, et al. 2018. TREATMENT Trial Collaborators. Efficacy and Safety of Topical Rapamycin in Patients with Facial Angiofibromas Secondary to Tuberous Sclerosis Complex: The TREATMENT Randomized Clinical Trial. *JAMA Dermatology* 154(7):773-780.

JASPER: Early Behavioral Intervention to Improve Social-Communication Skills

IMPACT: This behavioral intervention could improve the developmental delays such as social communication skills, which is a common to children with TSC.

DESCRIPTION

TSC-associated neuropsychiatric disorders includes a wide range of cognitive, behavioral, developmental, and neuropsychiatric manifestations and is considered as one of the most unmet needs of the TSC community. Joint Attention, Symbolic Play, Engagement, and Regulation (JASPER) is an early behavioral play-based intervention aimed to improve the social communication skills for infants with TSC. TSCRP funded a pilot trial to investigate whether JASPER would improve the developmental skills of infants with tuberous sclerosis. Combining behavioral and brain-based measures to study outcomes with this early intervention, the study showed the infants made substantial gains in their social and communication skills at a rate not seen in infants who did not receive this targeted early intervention. This project led to a large randomized, controlled clinical trial, which could be adopted by the TSC community in the near future.

PARTNERS/COLLABORATORS

University of California, Los Angeles; Boston Children's Hospital

AWARD NUMBER: W81XWH-15-1-0183

Tuberous Sclerosis Complex Remote Assessment and Intervention (TRAIN)

DESCRIPTION

Even before the COVID-19 pandemic, there was a tremendous need for expanding access to high quality care for children with TSC via telehealth. In 2019, TSCRP funded a pilot trial called TRAIN that aims to fill this unmet need. TRAIN is designed to provide remote training and give families the skills they need to make impactful and lasting improvements for their child with tuberous sclerosis. The team will adapt the caregiver training version of JASPER, which was initially designed to improve social communication skills for children with the disorder, and deliver it through telehealth platforms. Eighteen participants from 12 states participated in this trial and received the intervention remotely. None of these participants would have been able to participate without the telehealth delivery platforms.

IMPACT: This telehealth-based intervention will expand health care access to the TSC community and empower families to gain essential skills to help their child with tuberous sclerosis.

PARTNERS/COLLABORATORS

University of California, Los Angeles

AWARD NUMBER: W81XWH-20-1-0085

Matt Bolger, TSCRP Consumer Peer Reviewer

"There have been great leaps in the research and treatment options due to the work that we look to advance through the TSCRP. I am confident, when looking at what has been accomplished in this short time that we can, and will, have a significant, positive impact on those who struggle with the effects of TSC every day."

Donald Overton, Vision Research Program Programmatic Panel Member and Consumer

"Military combat medics are charged with saving life, limb, and eyesight. Thanks to the emerging research from the VRP portfolio, their available tools are continually expanding, and increasingly impactful rehabilitative opportunities realized."

VISION RESEARCH PROGRAM

Vision: Transform visual system trauma care for our armed forces and the nation

Mission: To address clinical needs through innovative research targeting the mechanism, effects, and treatment of Service-connected eye injuries and vision dysfunction

Years Program Appropriated: FY09-FY23

Total Appropriations: $184.95M

The Vision Research Program (VRP) is the nation's primary funder of visual system trauma research. The VRP aims to transform visual system trauma care by advancing the understanding of visual system trauma, advancing therapeutic development, and expanding forward care capability. VRP-funded research covers injuries across the visual pathway, from the cornea to the visual cortex, and spans the continuum of care from battlefield to chronic care.

iNexin™ Regenerative Eye Drops

IMPACT: Existing corneal injury treatments address secondary symptoms such as irritation or itching. iNexin aims to reset the eye's injury response and promote regenerative healing.

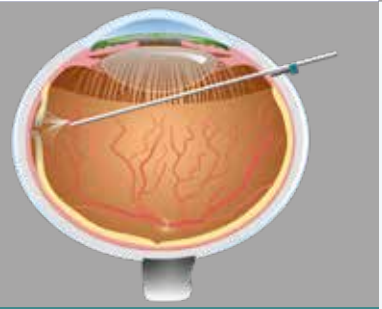
DESCRIPTION

iNexin eye drops' peptide aims to regulate the eye's inflammatory response to injury to promote healing. A phase 1b clinical trial demonstrated iNexin's safety, tolerability, and efficacy in dry eye patients with a corneal injury. These positive results supported Xequel Bio's successful application for further VRP funding and iNexin's continued clinical development to phase 2 trials.

PARTNERS/COLLABORATORS

Xequel Bio, Inc.

AWARD NUMBERS: W81XWH-20-1-0879, W81XWH-22-1-1113



Retinal Thermofusion

IMPACT: Retinal thermofusion is a new procedure that will improve care by reducing surgical time and post-surgery complications.

DESCRIPTION

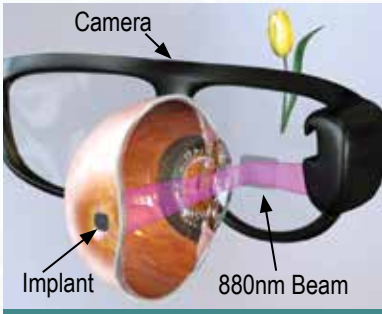
Retinal thermofusion is a novel procedure that seals retinal tear margin during retinal detachment repair surgery and prevents intraoperative fluid flow through the retina break into the subretinal space. The traditional method of sealing is via gas tamponade, which may expand during air evacuation. In comparison to gas tamponade, retinal thermofusion is expected to reduce surgical time, reduce recovery time, reduce potential complications, and enable immediate post-operative aeromedical evacuation. The procedure has been tested in two large animal models and on ex vivo human donor eye tissue with promising results, and a first in human trial of retinal thermofusion has been planned.

PARTNERS/COLLABORATORS

Centre for Eye Research Australia Limited

AWARD NUMBERS: W81XWH-16-1-0787, W81XWH-21-1-0730

Photovoltaic Subretinal Prosthesis



DESCRIPTION

The photovoltaic subretinal prosthesis is a wireless, easy-to-implant device that holds the promise to restore sight up to 20/80 and maybe even 20/40 in patients blinded by the loss of photoreceptors. The modular design of the photovoltaic arrays allows scalability to thousands of pixels. Visual information is projected onto the retina by augmented-reality goggles using pulsed near-infrared light. Light is converted into pulsed electric current in each pixel, stimulating the nearby neurons. The prosthesis is being tested in an externally funded clinical trial. Efforts are also ongoing to advance this technology to enable visual acuity at a level that supports highly functional restoration of sight (e.g., reading and face recognition).

PARTNERS/COLLABORATORS

Stanford University

AWARD NUMBERS: W81XWH-15-1-0009, W81XWH-19-1-0738, W81XWH-22-1-0933

IMPACT: The photovoltaic subretinal prosthesis is a new technology that will improve care by restoring functional vision in retinal blind patients.

IMPACT: Retinal ganglion cell transplantation holds the potential to restore vision to patients of optic nerve injury.

Retinal Ganglion Cell Transplantation as a Treatment for TBI-Related Optic Nerve Injury

DESCRIPTION

This multidisciplinary project aims to synergistically advance four critical elements needed for sucessful development of a cell replacement therapy for optic nerve regeneration: (1) improving differentiation and survival of stem cell-derived tissues, (2) improving retinal integration and synaptic function of transplanted human retinal ganglion cells, (3) optimizing the microenvironment to boost cell survival, and (4) translating these findings into two clinically relevent models of traumatic optic neuropathy. If successful, these complementary efforts will provide a strong foundation to advance this viable vision restorative therapy toward clinical implementation.

PARTNERS/COLLABORATORS

Johns Hopkins University; Schepens Eye Research Institute; Stanford University

AWARD NUMBER: HT9425-23-0589

Outer Retina Reconstruction for Combat Afflictions (ORRCA)

DESCRIPTION

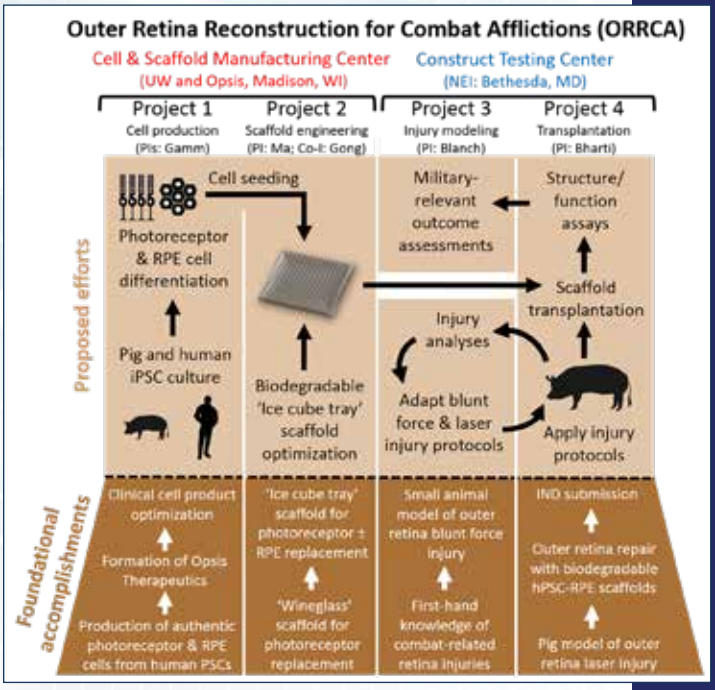
ORRCA is a precision-based outer retinal cell replacement therapy that reconstructs areas within the central outer retina that are irreversibly damaged by blunt force trauma or laser exposure. The retinal cells have demonstrated an ability to create synaptic connections with other cells, which is necessary for communication between the retina and the brain. ORRCA showcases an international team effort that combines stem cell-based production of retinal cells, bioengineering of outer retina scaffolds, and the development and optimization of surgical techniques into one therapy. ORRCA holds the potential to fill a gap in the treatment of blinding retinal injuries caused by blunt force trauma or laser exposure.

IMPACT: ORRCA is a new therapy that will fill a gap in the treatment of blinding retinal injuries.

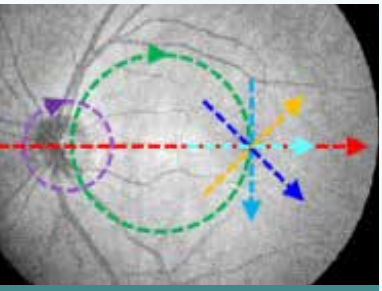
PARTNERS/COLLABORATORS

University of Wisconsin, Madison; National Eye Institute; University of Birmingham, UK

AWARD NUMBER: W81XWH-20-1-0655



UW - University of Wisconsin
NEI - National Eye Institute
RPE - Retinal Pigment Epithelium
PSCs - Pluripotent Stem Cells
hPSC -Human Pluripotent Stem Cell



IMPACT: The portable optical coherence tomography system is expected to improve forward care for military personnel affected by eye injury or visual dysfunction.

Portable Eye Imaging System

DESCRIPTION

Optical coherence tomography is a non-invasive infrared imaging technique widely used in ophthalmology clinics. This portable diagnostic device will bring optical coherence tomography to the forward environment, greatly enhancing forward care capability. It is compact, telemedicine-compatible, automated, and can be operated by trained non-specialists. Successful development and deployment will enable early responders to assess ocular trauma and intraocular inflammation in austere/remote conditions.

PARTNERS/COLLABORATORS

Duke University

AWARD NUMBERS: W81XWH-16-1-0498, W81XWH-20-1-0660

Topical Application of Losartan: An Effective Treatment for Injury-Related Scarring

IMPACT: Losartan, an FDA-approved topical inhibitor of TGF-β, prevents scarring and reduces corneal haze post-injury.

DESCRIPTION

Myofibroblasts, cells that aide in wound healing, cause corneal scarring when continually stimulated by the signaling protein, TGF-β. Researchers used animal models to assess the effects of topical application of Losartan, an FDA-approved TGF-β inhibitor, typically prescribed to treat high blood pressure and other conditions. Results indicated that Losartan prevents scarring and reduced corneal haze post-injury. This work led to a provisional patent and provided scientific rationale for a successful follow-on clinical evaluation of Losartan for treating corneal scarring.

PARTNERS/COLLABORATORS

Cleveland Clinic Foundation

AWARD NUMBERS: W81XWH-19-1-0846, W81XWH-22-1-0745

Small Molecule Therapeutics Protects from Trauma-Induced Vision Loss

IMPACT: HIFN is a promising new pharmaceutical treatment for ocular blast injury and other forms of traumatic optic neuropathy that can be administered on the battlefield, in field hospitals, or in ambulances.

DESCRIPTION

Retinal damage caused by traumatic blast-related injury or blunt force trauma to the eye is a risk factor for vision loss. Studies of blast injury models identified a lead small molecule compound that can be administered by systemic injection, get into the retina and brain from the blood stream, and protect from trauma-induced vision loss. Out of 28 derivatives of the lead compound, researchers identified the therapeutic compound HIFN as having the highest activity and superior penetrance into the retina and brain. Systemic administration of HIFN, started within three hours of trauma and continued daily for one week, preserves visual function for at least four months in mice exposed to ocular blast injury. Preliminary toxicological studies found no detectable acute or chronic toxicity in treated animals.

PARTNERS/COLLABORATORS

Emory University

AWARD NUMBERS: W81XWH-12-1-0255 (co-funded by VRP and PHTBIRP), W81XWH-18-1-0700

DOD-NEI Vision Research Collaborative (VRC)

DESCRIPTION

Established in 2018, the VRC is a joint initiative between the National Eye Institute (NEI) and the VRP. Through the VRC, the NEI participates in selected VRP funding opportunities and has the option of selecting meritorious VRP proposals for independent funding consideration. The VRC provides additional funding opportunities for VRP proposals, enhances current NEI program portfolios, expands the scope of research supported by the NEI, and provides support for high-quality projects addressing critical gaps in civilian and military vision research.

PARTNERS/COLLABORATORS

National Eye Institute

AWARD NUMBERS:

NIH 1-R01-EY031144, A Stem Cell-Based Treatment Strategy for Laser-Induced Permanent Retinal Damages;
NIH 1-R01-EY031167, The Role of Perinuclear cAMP in Retinal Ganglion Cell Neuroprotection and Optic Nerve Regeneration;
NIH 1R01EY033652, Develop Regenerative Therapies for Neurological Vision Loss;
NIH 1R01EY034716, Engineered Extracellular Vesicles for Mild TBI-Induced Retinal Injury;
NIH 1R01EY034715, Reduction of Vision Loss with Early Interventions After Optic Nerve Injury;
NIH 1R01EY035947, Inhibiting p38 to Prevent and Restore Corneal Scarring

IMPACT: The VRC promotes synergy and collaboration between federal funding agencies and coordination in the pursuit of the common goals in funding research that (1) prevents and treats the degeneration or injury of critical components of the eye and (2) restores impaired or lost vision.

1st Sgt. Tomas Cruz, U.S. Army Retired,
TBIPHRP Ad Hoc Programmatic Reviewer and Consumer

"As a combat Veteran that has been diagnosed with multiple mental health disabilities, I think this program is impacting the military and general public greatly with innovative and "out-of-the-box" thinking that will provide support in so many ways to the Soldiers and civilians for years to come while incorporating their Families and communities."

Patricia Horan, ERP Programmatic Panel Member and Consumer

"The ERP honors my husband's Service and sacrifice by its mission; to better understand how trauma transforms the brain and disturbs cognitive function. This program is tasked to find and eliminate mechanisms that start the epileptogenic process, which means a better chance for survival, rehabilitation, and quality of life for the next generations of Veterans."

Appendix A

PREVIOUSLY FUNDED RESEARCH PROGRAMS

Gulf War Illness Research Program

Vision: Improved health and lives of Veterans who have Gulf War Illness

Mission: Fund Gulf War Illness research that expeditiously identifies effective treatments and accelerates their clinical application, improves definition and diagnosis, and results in better understanding of pathobiology and symptoms of disease

Years Program Appropriated: FY06, FY08-FY21

Total Appropriations: $236M

The Gulf War Illness Research Program (GWIRP) prioritized innovative, competitively peer-reviewed research to develop and accelerate clinical application of treatments for the complex of Gulf War Illness symptoms and their underlying causes. Identification of objective markers for improved definition, diagnosis, and therapeutic efficacy was also a program focus area. Beginning in FY22, funding opportunities for Gulf War Illness research are within the Toxic Exposures Research Program and not as a separate research program.

Select outcomes from GWIRP awards include:

- **Coenzyme Q10 (CoQ10) for Gulf War Illness.** The GWIRP funded both an early phase and a follow-on confirmation phase 3 double-blind, placebo-controlled trial of different doses of Ubiquinone, the oxidized form of the antioxidant CoQ10, in Veterans with Gulf War Illness to shed light on the relative merits of treatment and define the most effective dose. Because of its status as a dietary supplement with a known broad safety margin, CoQ10 may represent a safe and inexpensive treatment for Veterans with Gulf War Illness. Award Numbers: W81XWH-07-1-0667, W81XWH-20-1-0523
- **Repository for Gulf War Illness Biomaterials and Data.** The Boston Biorepository, Recruitment, and Integrative Network is a biorepository network that provides a centralized holding and cataloging of retrospective and prospective biological samples, specimens, and data related to Gulf War Illness research studies. This repository is an extension of a GWIRP research consortium that banked large numbers of specimens and developed large datasets. Award Number: W81XWH-18-1-0549
- **Neuronavigation-Guided Transcranial Magnetic Stimulation (NG-rTMS) for Gulf War Illness-Related Headaches and Pain.** NG-rTMS is currently an FDA-approved treatment for major depression and migraine. In a GWIRP-funded pilot trial, this treatment provided significant relief of muscle pain, concentration difficulties, and fatigue as well as improvements in joint pain and headache. A follow-on phase 2 trial of NG-rTMS was funded to confirm improvements in several Gulf War Illness symptom domains. Award Numbers: W81XWH-16-1-0754, W81XWH-19-1-0691

Scleroderma Research Program

Vision: To combat scleroderma through a partnership of scientists, clinicians, and consumers

Mission: To fund and facilitate the most promising, highest quality research aimed at understanding mechanisms, improving therapies, and ultimately curing scleroderma for Service Members, Veterans, and the American public

Years Program Appropriated: FY20-FY21

Total Appropriations: $10M

The Scleroderma Research Program (SRP) focuses on the prevention, detection, diagnosis, and treatment of scleroderma for the benefit of Service Members, their Families, Veterans, and the American public.

Research from previously funded awards is ongoing. The following selected outcomes are anticipated:

- **Patient Stratification for Precision Medicine.** Through a stratification method, this project aims to use blood samples to identify patients most likely to improve with a given treatment. Using cutting-edge technologies to analyze samples, researchers will compare skin and individual cells between various groups of patients. Identifying patient subsets will enable individualized, precision medicine approaches to treatment. This research could lead to new approaches to diagnosis and therapy. Award Numbers: W81XWH-21-1-0878, W81XWH-21-1-0880, W81XWH-21-1-0881
- **Biomarkers to Inform Therapeutic Choice.** Interstitial lung disease is the leading cause of disease-related mortality in systemic sclerosis patients. Employing advanced molecular techniques and prediction modeling with samples collected in a Scleroderma Lung Study, researchers identified serum protein and blood cell RNA markers. These markers predict the course of disease in patients treated with mycophenolate mofetil, the most commonly used medication for systemic sclerosis-related interstitial lung disease. The research team plans to use the clinical data and biospecimens collected from an observational, multicenter CONQUER study to confirm this discovery. The development of prediction tools could transform treatment for patients with systemic sclerosis. Award Numbers: W81XWH-22-1-0162, W81XWH-22-1-0163, W81XWH-22-1-0164

ACRONYMS

AB-CRD ..... Adaptive Barrier Controlled-Release Devices

A-BLOCKS... Antimicrobial Block Copolymers

ABRUPT ..... Acute Burn ResUscitation Prospective Multicenter Observational Trial

ACL..... Anterior Cruciate Ligament

AIM-CBCT .....Abbreviated, Intensive, Multi-Couple Group Format of Cognitive-Behavioral Conjoint Therapy

AKCI ..... Academy of Kidney Cancer Investigators

ALI.....Acute Lung Injury

ALS.....Amyotrophic Lateral Sclerosis

ALSRP .....Amyotrophic Lateral Sclerosis Research Program

ARDS.. Acute Respiratory Distress Syndrome

ARP ..... Autism Research Program

ASUDRP.....Alcohol and Substance Use Disorders Research Program

ATLAS ..... Adjuvant Tamoxifen Longer Against Shorter

B .....Billion

BAFF-R..... B Cell Activating Factor Receptor

BCRP .....Breast Cancer Research Program

BMFRP..... Bone Marrow Failure Research Program

CAR T.....Chimeric Antigen Receptor T Cells

CARE ..... Concussion Assessment Research Education

CDMRP .....Congressionally Directed Medical Research Programs

CoQ10..... Coenzyme Q10

COVID-19 ..... Coronovirus Disease 2019

CPMRP .....Chronic Pain Management Research Program

CRED ..... Combat-Ready Exposure Device

CRRP .....Combat Readiness–Medical Research Program

CT..... Computed Tomography

DECAMP ..... Detection of Early Lung Cancer Among Military Personnel

DEX .....Dexmedetomidine

DHA..... Defense Health Agency

DMDRP..... Duchenne Muscular Dystrophy Research Program

DMRDP..... Defense Medical Research and Development Program

DOD ..... Department of Defense

ERP..... Epilepsy Research Program

FDA..... U.S. Food and Drug Administration

[^{18}F] FTT .....[^{18}F] FluorThanatrace

GFAP..... Glial Fibrillary Acidic Protein

GWIRP .....Gulf War Illness Research Program

HER2 ..... Human Epidermal Growth Factor Receptor 2

HR+ ..... Hormone Receptor-Positive

HRF-NET .....Hearing Research Funding Network

HRRP ..... Hearing Restoration Research Program

ImPACT .....Improving Parents as Communication Teachers

IPASS .....Intracranial Pressure Assessment and Screening System

IRF5..... Interferon Regulatory Factor 5

JASPER .....Joint Attention, Symbolic Play, Engagement, and Regulation

JPC .....Joint Program Committees

JWMRP ..... Joint Warfighter Medical Research Program

KCRC ... Kidney Cancer Research Consortium

KCRP ..... Kidney Cancer Research Program

LCBRN ..... Lung Cancer Biospecimen Resource Network

LCRP..... Lung Cancer Research Program

M..... Million

mAGIC .....Mobile Application for Genetic Information on Cancer

MAPKi..... Mitogen-Activated Protein Kinase inhibitors

MBRP .....Military Burn Research Program

MIND-MCI.... Minds Navigating the Diagnosis of Mild Cognitive Impairment

MMP3.....Matrix Metalloproteinase 3

MRP.....Melanoma Research Program

MS..... Multiple Sclerosis

MSRP .. Multiple Sclerosis Research Program

NCI .....National Cancer Institute

NEI ..... National Eye Institute

NF ..... Neurofibromatosis

NFRP .. Neurofibromatosis Research Program

NFCTC.....Neurofibromatosis Clinical Trials Consortium

NG-rTMS..... Neuronavigation-Guided Transcranial Magnetic Stimulation

NIH ..... National Institutes of Health

OCRP .....Ovarian Cancer Research Program

OPORP.....Orthotics and Prosthetics Outcomes Research Program

ORRCA.....Outer Retina Reconstruction for Combat Afflictions

OTTA-SPOT..... Ovarian Tumor Tissue Analysis Consortium - Stratified Prognosis of Ovarian Tumours

PARP.....Poly ADP-Ribose Polymerase

PCARP .....Pancreatic Cancer Research Program

PCRP .....Prostate Cancer Research Program

PFAS... Per- and Poly-Fluoroalkyl Substances

PiPT .....Psychologically Informed Physical Therapy

PMC.....Pain Management Collaboratory

POIP .....Phases of Illness Paradigm

PRARP ..... Peer Reviewed Alzheimer's Research Program

PRCRP ..... Peer Reviewed Cancer Research Program

PRMRP .....Peer Reviewed Medical Research Program

PRORP .....Peer Reviewed Orthopaedic Research Program

PRP ..... Parkinson's Research Program

PS+ASD.....Project SEARCH Plus ASD

PTEN..... Phosphatase and Tensin Homolog

PTSD .....Post-Traumatic Stress Disorder

QTxI .....Quantitative Total Extensible Imaging

RANKLE ..... Receptor Activator of Nuclear Factor Kappa-B Ligand

RCRP ..... Rare Cancer Research Program

RS-tDCS .. Remotely Supervised Transcranial Direct Current Stimulation

RTRP..... Reconstructive Transplant Research Program

SBIR .... Small Business Innovation Research

SCD..... Selective Cytopheretic Device

SCIRP .. Spinal Cord Injury Research Program

SPRINT PNS ..... SPRINT Peripheral Nerve Stimulation System

SRP ..... Scleroderma Research Program

STRONG..... Support through Remote Observation and Nutrition Guidance

TARPIN.....To Auto-Release & Relock a PIN

TBDRP ..... Tick-Borne Disease Research Program

TBI..... Traumatic Brain Injury

TBIPHRP .....Traumatic Brain Injury and Psychological Health Research Program

TERP ..... Toxic Exposures Research Program

TRACK-SCI ..... Transforming Research and Clinical Knowledge in Spinal Cord Injury

TRAIN ..... Tuberous Sclerosis Complex Remote Assessment and Intervention

Tregs.....Regulatory T Cells

TSC..... Tuberous Sclerosis Complex

TSCRP..... Tuberous Sclerosis Complex Research Program

UCH-L1 .....Ubiquitin C-Terminal Hydrolase

VA.....U.S. Department of Veterans Affairs

VIRF.....Vision Injury Research Forum

VRC ..... Vision Research Collaborative

VRP .....Vision Research Program

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