CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS

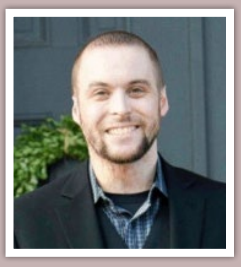
Military Burn Research Program

Developing and Delivering Burn Care Capabilities for the Warfighter

For more information, please visit
cdmrp.health.mil/mbrp

Congressionally Directed Medical Research Programs

Established in 1992, the CDMRP found its beginning through a powerful grassroots effort led by the breast cancer advocacy community. Their tireless work led to a Congressional appropriation that would mark the first research program at CDMRP. A unique partnership developed among the public, Congress, and the military. Since then, the CDMRP received over $20 billion in appropriations for multiple targeted programs through fiscal year 2023, to include the Military Burn Research Program, or MBRP.



"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."

SSG James West,
U.S. Army, Retired,
MBRP Programmatic Panel Member
Consumer Advocate, FY17-FY23

MILITARY BURN RESEARCH PROGRAM

VISION: Advancing combat burn trauma care for the Warfighter.

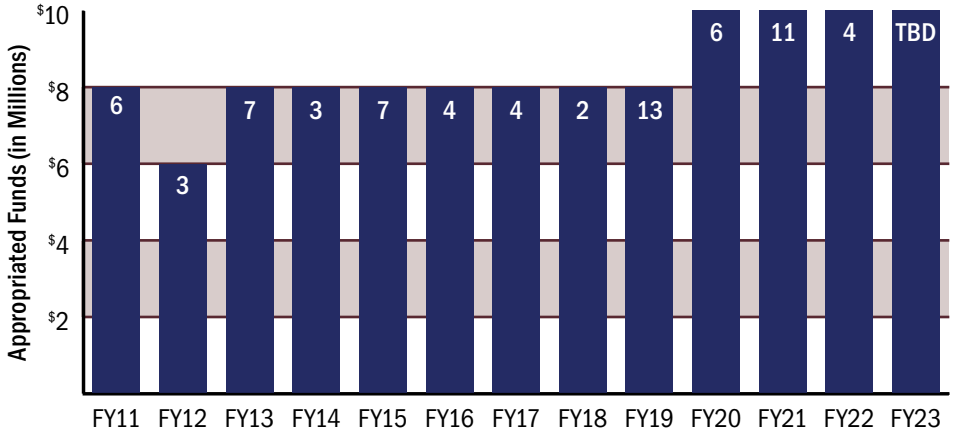
MISSION: Identify and address gaps in combat burn trauma care through military-focused research.

PROGRAM HISTORY

Burn injuries sustained by military service members while in the line of duty, whether on the battlefield, or in a military training environment, represent a continuous health burden on both the injured service member and the Department of Defense (DOD) health care systems in which they receive care. Historically, burn injuries afflicted some 5% to 20% of casualties during post-World War II conflicts.[1] In recent years, burns sustained during Operation Iraqi Freedom/Operation Enduring Freedom affected nearly 9% of combat-related casualties.[2] While flame burns represent the most common cause of burn injury, other less common burns such as frostbite, high-voltage electrical, chemical, directed energy, and radiation represent an additional formidable threat to the health and well-being of service members. Regardless of the injury mechanism, combat-associated burn injuries are devastating due, in part, to the high incidence of concurrent severe traumatic injuries. In addition, burns sustained in a deployed environment are often larger and deeper and more often lead to complications than those sustained in the civilian setting. The majority of combat burns in recent conflicts resulted from explosive device detonation, leading to a greater Injury Severity Score, an increase in inhalation injuries, and a larger, full-thickness burn size.[3]

The first appropriation by Congress to the MBRP occurred in 2011 to address combat-related and trauma-induced burn injuries, as well as to improve health and performance outcomes for burn injured service members, veterans, and the general public. Since FY11 through FY23, $110 million (M) has been appropriated to the program by Congress. Through FY22, MBRP has funded 70 research projects that have provided key research insights in advancing therapies for burn-injured patients and impacting standard practice.

Congressional Appropriations and Number of Awards, FY11-FY23



1 Kauvar DS, Wade CE, and Baer DG. 2009. Burn hazards of the deployed environment in wartime: Epidemiology of noncombat burns from ongoing United States military operations. Journal of the American College of Surgeons 209(4):453e460.

2 Escolas SM, Archuleta DJ, Orman JA, et al. 2015. Postdischarge cause-of-death analysis of combat-related burn patients. Journal of Burn Care and Research: Official Publication of the American Burn Association 38(1):e158-e164.

3 Kauvar DS, Cancio LC, Wolf SE, et al. 2006. Comparison of combat and non-combat burns from ongoing U.S. military operations. The Journal of Surgical Research 132(2):195-200.

PROGRAMMATIC PANEL:

The Programmatic Panel is a multi-functional panel composed of scientists, clinicians, and consumers. CDMRP Programmatic Panel members contribute to the program's vision and mission, assist in the development of an investment strategy, and make funding recommendations. Panel Members are recruited based on their expertise, community involvement, and/or organizational appointment.

STAKEHOLDERS MEETING:

In May 2022, the MBRP held a Stakeholders Meeting to engage scientific, clinical, and military burn experts as well as lived-experience subject matter experts in an open dialogue forum to identify critical issues and underfunded areas of military burn research and care. Representatives from burn injury-related non-profit organizations, academia, government institutions, and the public contributed broad perspectives on potential barriers in research and patient outcomes, key knowledge or scientific gaps, and potential approaches for the treatment of burn injuries incurred while in the course of military service.

During the meeting, stakeholder participants discussed and created a prioritized list of gaps in four broad categories: (1) emergency/POI/field care, (2) acute/intensive care unit hospital care, (3) subacute burn care/rehabilitation, and (4) long-term challenges (Table 1). Outcomes and gaps identified by the stakeholders were considered by the Programmatic Panel during the development of program goals. The FY22 Stakeholders Booklet and Meeting Summary, including presentation materials, can be found at https://cdmrp.health.mil/mbrp/default.

Table 1: Prioritized Gaps from the FY22 MBRP Stakeholders Meeting

Emergency/POI/ Field Care Gaps	Acute/ICU Hospital Care	Subacute Burn Care/Rehabilitation	Long-Term Challenges
• Atypical Burns • Burn Wound Conversion • Improved/Novel Dressings • Infection Control • Inflammation Control	• Burns and Polytrauma • Infection Control • Inhalation Injuries • Burn Wound Closure • Resuscitation	• Tissue Regeneration/Repair • Novel and/or Improved Strategies of Dressing • Burn Wound Closure and Injury Progression/Conversion • Infection & Inflammation Control • Rehabilitation/Clinical Care (emphasizing mobility and exercise)	• Behavioral Health, Functional Recovery and Holistic Well-being • Functional Skin and Scar Prevention/ Treatment • Pain/Neuropathic Pain/Itch • Clinical Care, Rehabilitation • Burns and Polytrauma

STRATEGIC PLANNING MEETING:

In FY22, the Programmatic Panel members worked collaboratively to identify unanswered research questions in the burn field in order to develop a multi-year strategic investment plan for the program that aligns with the vision, mission, and congressional intent of the program. The strategic plan provides a framework within which the short- and long-term investments will be executed. The Programmatic Panel will revisit the plan annually to review the state of the science, military priorities, and clinical needs; ensure that the topic areas and capability gaps are still relevant; and refine the plan as necessary. The MBRP established four priorities around which it will build its funding efforts in the next years and beyond:

- Development of military-relevant interventions to improve survival from combat-associated burn and/or burn inhalation injuries. Burn inhalation injuries addressed through MBRP are separate from the inhalation of airborne toxins and smoke from burn pits. The health consequences of chronic exposure to burn pits is addressed through the CDMRP Toxic Exposures Research Program (TERP). Proposed interventions should be usable on the battlefield for prolonged (i.e., greater than 72 hours) medical care in resource-limited environments. The program will focus on thermobaric burns, however, management of sequelae from other types of burns will be considered.
- Development of interventions to accelerate or optimize burn wound healing to minimize scarring and contractures in later phases of recovery. Preference will be given to solutions that could be used in the military theater of operations.
- Development or refinement of interventions or technologies that will enable non-burn specialists, such as a field medic/corpsman/paramedic, to provide effective burn care closer to the point of injury, allowing for better survival and long-term outcomes.
- Development of interventions or advancement of standard-of-care practices addressing fluid resuscitation, inflammatory response, and complications of severe burn injuries including infection and sepsis of atypical burns (e.g., frostbite, nuclear, radiation, chemical) and/or burns with concomitant polytrauma.

The MBRP will continue its commitment to funding exploratory research, clinical studies and trials, and expansions on prior/early-stage research investments. The Programmatic Panel members emphasized a need for innovative, paradigm-shifting research in future investments.

APPLICATION REVIEW PROCESS:

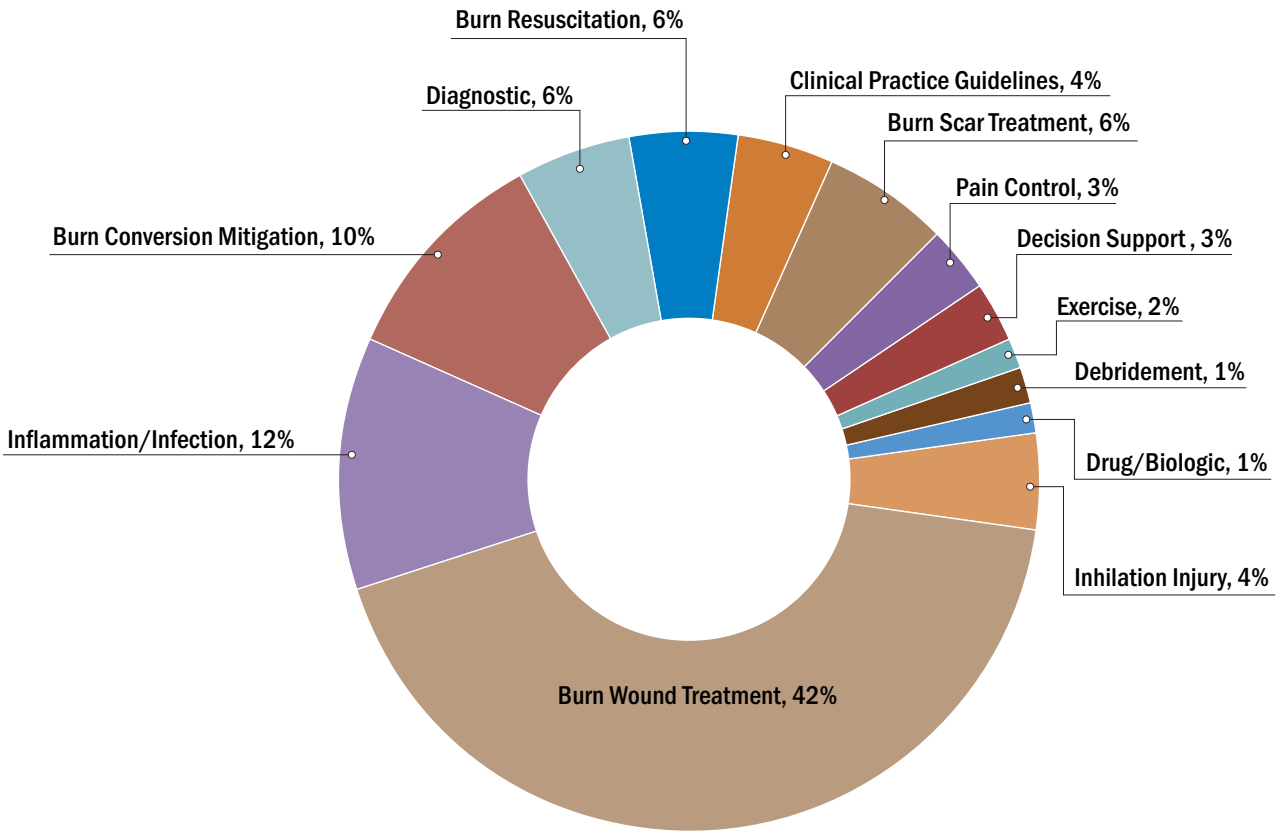
The CDMRP uses a two-tier review process for evaluating applications, with both tiers involving dynamic interaction between scientists, consumers from advocacy organizations, clinicians, members of the military and other specialists as applicable. The first tier of evaluation is a scientific peer review of the applications, measured against established criteria for determining scientific merit. The second tier is a programmatic review conducted by the Programmatic Panel, comparing applications to each other and making recommendations for funding based on scientific merit, potential impact, adherence to the intent of the award mechanism, relevance to program goals, and portfolio composition.

RESEARCH PORTFOLIO:

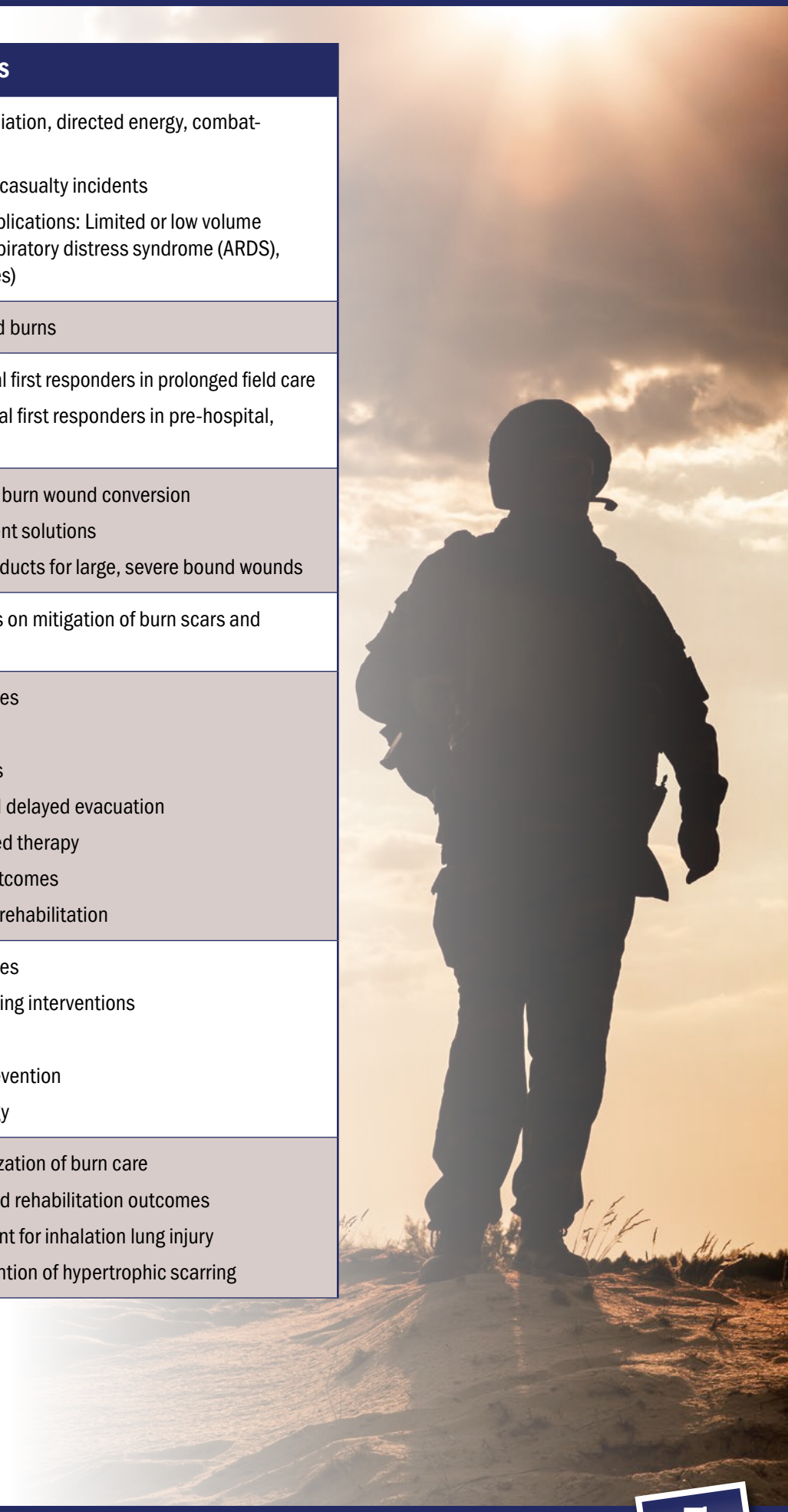
MBRP-funded projects seek innovative approaches that close close current gaps in military-focused burn trauma care through clinical and translational research. The knowledge and technology achieved through the funded studies promise to deliver new standards of care for the treatment of burn injuries. Funded research focuses on the care of burn-injured service members, however civilian burn casualties can also expect to benefit from knowledge and products developed through this program.

The MBRP manages awards in numerous burn care focus areas with the largest percentage of awards in burn wound treatment (29 awards, 42.0%), followed by inflammation/infection control (8 awards, 11.6%) and burn conversion mitigation (7 awards, 10.1%).

FY11-FY22 MBRP Investment by Focus Area



FISCAL YEAR	RESEARCH FOCUS AREAS
FY22-FY23	• Atypical burns (cold, radiation, directed energy, combat-related electrical) • Burn injury during mass casualty incidents • Burn injury-related complications: Limited or low volume resuscitation, acute respiratory distress syndrome (ARDS), sepsis, inhalation injuries)
FY21	• Complex combat-related burns
FY20	• Burn care by non-medical first responders in prolonged field care • Burn care by non-medical first responders in pre-hospital, not prolonged field care
FY19-FY20	• Interventions to prevent burn wound conversion • Non-surgical debridement solutions • Temporary coverage products for large, severe bound wounds
FY17-FY18	• Clinical research studies on mitigation of burn scars and contractures
FY15-FY16	• Fluid resuscitation studies • Organ failure studies • Wound healing solutions • prolonged field care and delayed evacuation • Clinical impact of delayed therapy • Delayed care patient outcomes • Functional outcomes of rehabilitation
FY13-FY14	• Fluid resuscitation studies • Accelerated wound healing interventions • Organ support studies • Sepsis and infection prevention • Rehabilitation physiology
FY11-FY12	• Checklists for standardization of burn care • Intensive care unit-based rehabilitation outcomes • Device/drug development for inhalation lung injury • Management and prevention of hypertrophic scarring



69
Awards

49
Drugs, biologics, or devices

79
Publications

4
Patents

253
Abstracts/ scientific dissemination

4
Follow on Funding

MBRP RESEARCH OUTCOMES

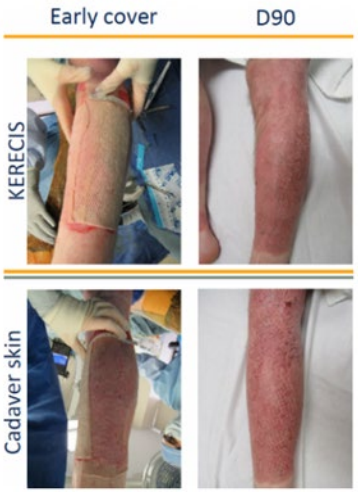
FY11-FY22 MBRP research funding resulted in:

Kerecis™ Fish Skin

Hilmar Kjartansson, Ph.D., Kerecis Limited

Temporary coverage for acute burns

- A mesh product made from Kerecis fish skin that is stable at room temperature and usable in remote settings as opposed to traditional burn cover made from cadaver skin that requires a hospital environment
- 90-day outcomes show healed skin and improved skin appearance versus traditional treatments



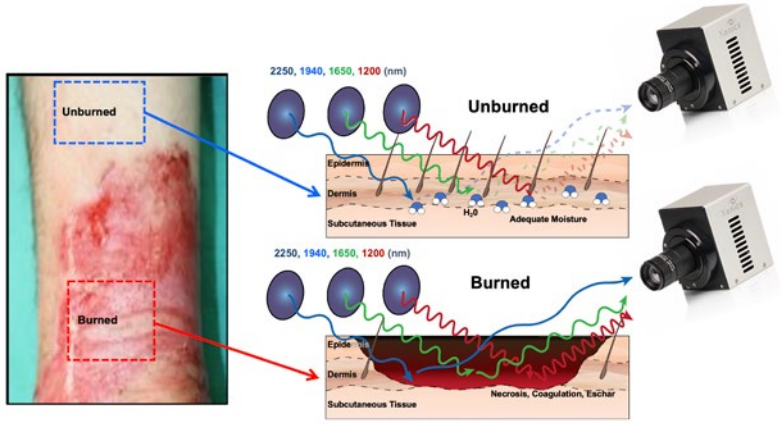
images provided by Hilmar Kjartansson

Short Wave Assessment Tool (SWAT)

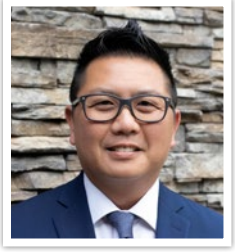
Benjamin Levi, Ph.D., and Caroline Park, Ph.D., University of Texas Southwestern Medical Center at Dallas

Portable burn wound assessment

- A portable handheld, camera-based system that helps to objectively assess burn wound depth and predict wound health outcomes
- Guides more precise treatment debridement



images provided by Benjamin Levi and Caroline Park



"It is an honor and a privilege to serve CDMRP as a panelist to support the mission in advancing military burn care research. During the process, I quickly recognized how diverse the panelists are strategically, by leveraging different subject experts to create a high-impact body of work. I see CDMRP providing a vital step in bridging burn care gaps in the battlefield to protect our men and women in uniform, while many research projects will undeniably benefit the civilians of this country and the world."

Dr. Peter Yen,
Joseph M. Still Burn Centers, Inc.,
Programmatic Panel Member FY21-FY23

Novel Use of TXA

Damien Carter, Ph.D., Maine Medical Center

Tranexamic acid (TXA) to limit burn injury severity

- FDA-approved to treat heavy menstrual bleeding and hemorrhage prevention in hemophilia patients
- Currently being tested in a preclinical animal model as a novel treatment to reduce burn wound progression

4F EnteroResus

Barclay Stewart, M.D., Ph.D.,
University of Washington

Augmenting intravenous fluid resuscitation for burn casualties

- Enteral resuscitation with World Health Organization oral rehydration salts and clean water via drinking and/or a nasogastric tube
- Operationally advantageous intervention to restore blood volume and prevent hypovolemic shock

image provided by Barclay Stewart

TP509

Celeste Finnerty, Ph.D.,
The University of Texas Medical Branch-Galveston

Burn conversion prevention product

- A thrombin-derived peptide (in topical or injection formulation) used to accelerate wound healing and wound closure after burn and lethal radiation exposure
- Field-accessible product may prevent the progression/conversion of burns from deep-partial to full-thickness burns

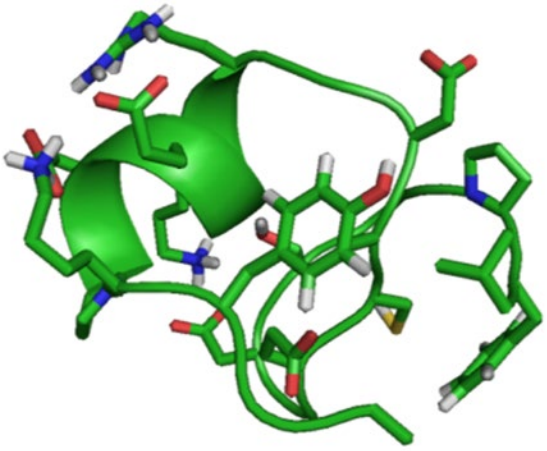
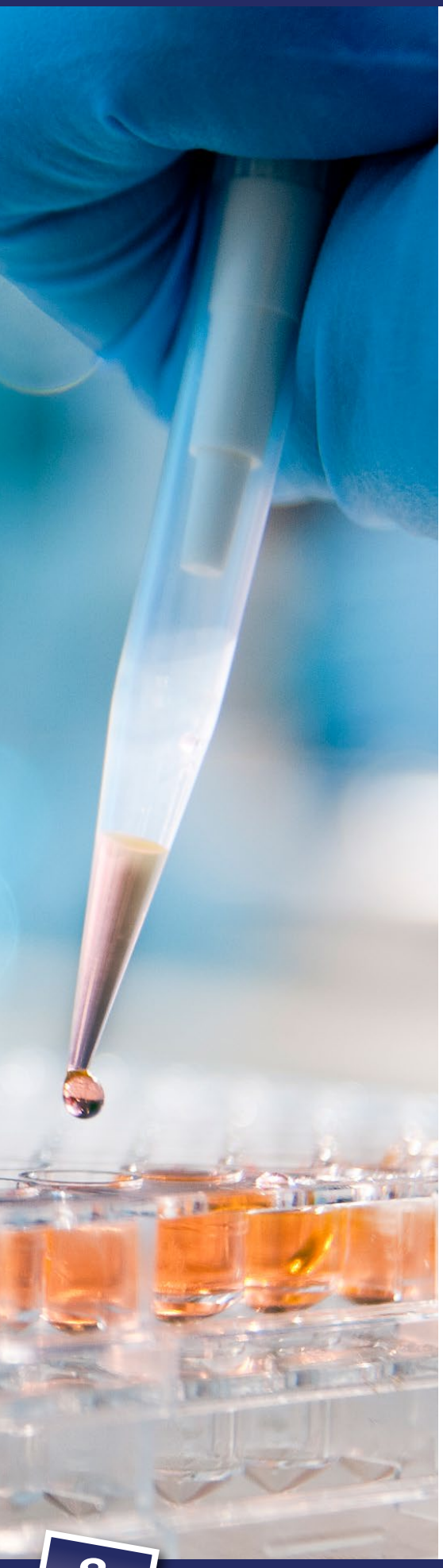


image provided by Celeste Finnerty

"The dynamic nature of the MBRP and the passion its members have for supporting the Warfighter have allowed us to fundamentally drive burn research towards improving care from point of injury in a combat environment through rehabilitation. Though active duty and Veterans will always be the focus of our mission, the products of our program often readily translate to also benefit civilian burn patients. I'm so very proud of the research our awards have funded, and the direct impact it has had on burn care."

Capt. Zachary Brown,
Naval Medical Center Portsmouth,
Programmatic Panel Chair FY22-FY23; Programmatic Panel Member FY19-FY23



RESEARCH HIGHLIGHTS:

Novel Peptide Drugs to Improve Burn Care Outcomes

Richard Clark, M.D., NeoMatrix Formulations, Inc.

Burns are dynamic injuries that evolve over time in terms of depth and size of the burns. The burn research community describes this concept, burn wound conversion, as a cascade of events following the initial burn injury, specifically when superficial partial-thickness burns evolve to deep partial-thickness or full-thickness burns. The dynamic nature of burn wound conversion leads to treatment challenges, with patients frequently requiring multiple surgeries, skin grafting, longer hospital stays, and lengthy rehabilitation, along with pain, scarring, and other long-term complications that affect burn survivors.

The Military Burn Research Program seeks to fund research that advances novel products focused on arresting burn wound conversion. The MBRP issued an FY17 Clinical Trial Award to Dr. Richard Clark and his team at NeoMatrix Therapeutics, Inc. to advance the development of NeoMatrix's novel peptide drug called cP12, which the team demonstrated in a relevant animal model of burns to limit progressive tissue damage and promote burn wound closure when administered by intravenous (IV) infusion within 1-4 hours of the burn injury. cP12 derived from fibronectin, a naturally occurring protein involved in tissue healing and regeneration. Fibronectin degrades following a burn injury, and burn patients show low levels of the protein in blood and other bodily fluids. The clinical award funded the team to complete a randomized, double-blind, placebo-controlled phase 1 single ascending dose study to evaluate the safety, tolerability, dosing, and pharmacokinetics of cP12 in healthy individuals. Thirty healthy adults completed the trial with no serious adverse events observed. The investigators concluded that cP12 was well-tolerated in adults at the clinically effective optimal dose. NeoMatrix is currently designing a phase 2a clinical trial to evaluate the safety and efficacy of cP12 in patients admitted to burn centers with 5% to 20% total body surface area burns. The FDA has granted cP12 Orphan Drug status as well as "Fast Track" designation, a process intended to expedite review of drugs that treat a serious condition with little to no available treatments. Preclinical work on P12-related peptides, including cP12, was originally funded through the Armed Forces Institute of Regenerative Medicine.

In addition to the MBRP-funded award, the Combat Readiness Medical Research Program (CRRP) awarded NeoMatrix an FY19 Rapid Development and Translational Research Award for preclinical work on another fibronectin-derived peptide drug named cNP8. When faced with prolonged field care and delayed treatment beyond the 4-hour window for delivery of cP12, cNP8 may be given up to 24 hours after burn injury to prevent burn wound progression. The preclinical animal data derived from the CRRP-funded award facilitated submission of an Investigational New Drug application to the FDA for cNP8 clinical safety and efficacy testing.

With limited treatment options available for preventing burn wound conversion, the novel drugs cP12 and cNP8 could significantly reduce burn complications for the patient and ease the burden of clinical care associated with deep-partial and full-thickness burns.

Enzymatic Debridement for Prolonged Field Care of Military Burn Wounds

Matthew Smeichowski, Ph.D., Guild BioSciences

Following a burn injury, removal of damaged tissue is a critical step in wound healing. The process, known as debridement, involves the manual removal of infected or necrotic tissue, often through surgery, which allows the skin to better heal and repair as well as prevent life-threatening systemic infection. Timing of debridement is important; delays in this step of burn wound care can lead to poor burn recovery outcomes due to increased risk of infection and slower wound healing from the presence of necrotic tissue. While surgical debridement works well in a hospital setting, 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. Nonsurgical debridement methods use certain enzymes to break down infected or necrotic tissue and can be effectively utilized by nonmedical personnel in a prolonged field care environment.

The research team at Guild BioSciences, led by Dr. Matthew Smiechowski, received an FY19 Military Burn Research Program Idea Development Award to develop a nonsurgical burn wound debridement product suitable for use during prolonged field care. I-Debride™ is intended for field application at the point of injury by first responders, such as combat medics, with the potential for use by civilian paramedics and burn units. A single FDA-approved nonsurgical debridement product currently exists, but it has several drawbacks limiting its field use potential, including specific storage temperature requirements. Conversely, I-Debride™ is shelf-stable and has several other features that offer improvements over the currently FDA-approved product. I-Debride™ is based on Guild BioSciences' ImmobiZyme™ technology, which, as shown in the illustration, combines a mixture of enzymes with support matrix materials and a crosslinker to improve the enzyme performance. Results from this work may also offer the potential for application to nonburn wounds, such as diabetic wounds and pressure ulcers.

The MBRP-funded development of I-Debride™ addresses a critical gap in the burn care continuum by supporting the development of an enzymatic burn wound debridement product that could be used at the point of injury during prolonged field care of burn-injured service members.

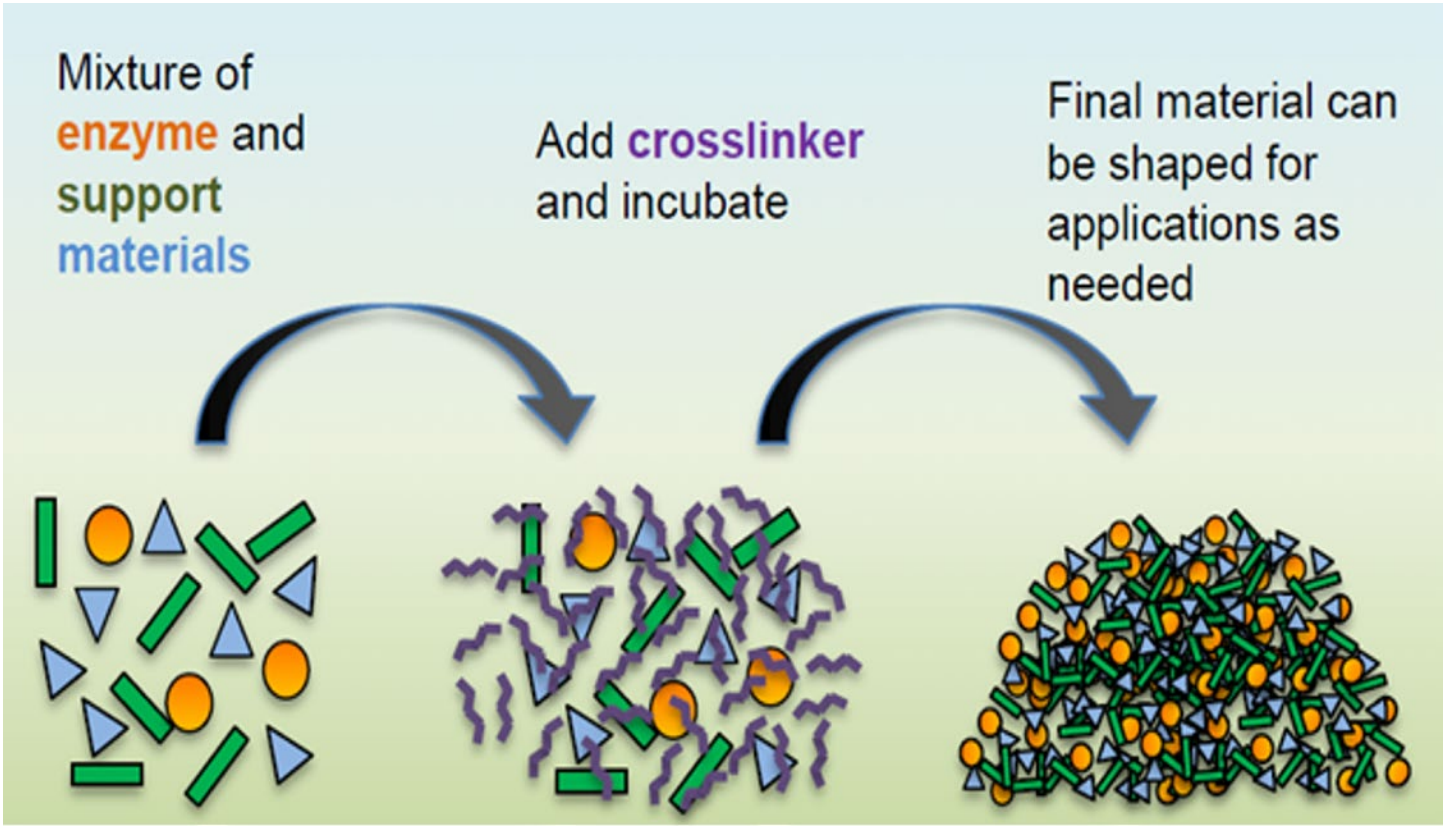


Figure 1: Debridement Illustration

image provided by Matthew Smeichowski

Pirfenidone-Containing Burn Wound Patch to Reduce Scarring

Kai Leung, Ph.D., United States Army Institute of Surgical Research

Burn wound scars result from a complex physiologic process. After healing from a severe burn wound, the damaged skin often forms hypertrophic scars, marked by raised, itchy, and inelastic skin, dark red- or purple-colored tissue, and hypersensitivity. Hypertrophic scars originate from excessive skin fibrosis and disordered layers of skin proteins, and areas of severe scars can develop into contractures, which decrease joint mobility and contribute to chronic muscle and joint pain.[1] Burn survivors may also feel self-conscious about severe scarring, especially facial scarring, and this can greatly reduce quality of life following an injury. For service members who suffer burn injuries, timely treatment of wounds to minimize or prevent scarring can be even more challenging in a prolonged field care environment with delayed access to a higher level of care. Burn-injured service members are also more likely to suffer severe burns than the general population, due to the nature of explosions during combat.[2] This can translate to larger total body surface area burn injuries with increased burn thickness and therefore higher risk for extensive hypertrophic scarring and contractures.

With an FY15 Military Burn Research Program Broad Agency Announcement for Extramural Medical Research, Dr. Kai Leung led a team of investigators at the U.S. Army Institute of Surgical Research through the development of an easily applied, drug-eluting burn wound patch as shown in the illustrations. The patch holds the drug pirfenidone, an anti-inflammatory and anti-fibrosis drug that is FDA-approved for the treatment of idiopathic pulmonary fibrosis. Experiments using profibrotic human dermal fibroblasts (produced by stimulation with Transforming Growth Factor Beta) demonstrated that direct contact of pirfenidone with these profibrotic fibroblasts significantly inhibited their proliferation and transformation into myofibroblasts in vitro. Increase in fibroblasts proliferation and their transformation into myofibroblasts are some of the key hallmarks of fibrosis. Excess myofibroblasts can also cause increased collagen accumulation and tissue contractures.

Investigators are testing the effectiveness of the pirfenidone burn wound patch as an early treatment to reduce dermal fibrosis (i.e., scarring) following deep partial-thickness burns in a preclinical animal model. As illustrated in the photographs, application begins with the removal of the clear release liner, exposing the silicone face of the patch, which is placed directly onto the wound. The paper liner is then removed, leaving behind the transparent patch adhering to the contours of the burn wound. The patch is stable at room temperature, can be easily carried, self-administered, and kept in place on the wound for 2 days before the next dressing change, thus allowing for use in a prolonged field care setting.

The MBRP-funded development of this pirfenidone-containing burn wound patch targets several critical gaps in burn care, including treatment options suitable for prolonged field care and improved quality of life following recovery from a burn injury through reduced hypertrophic scarring.

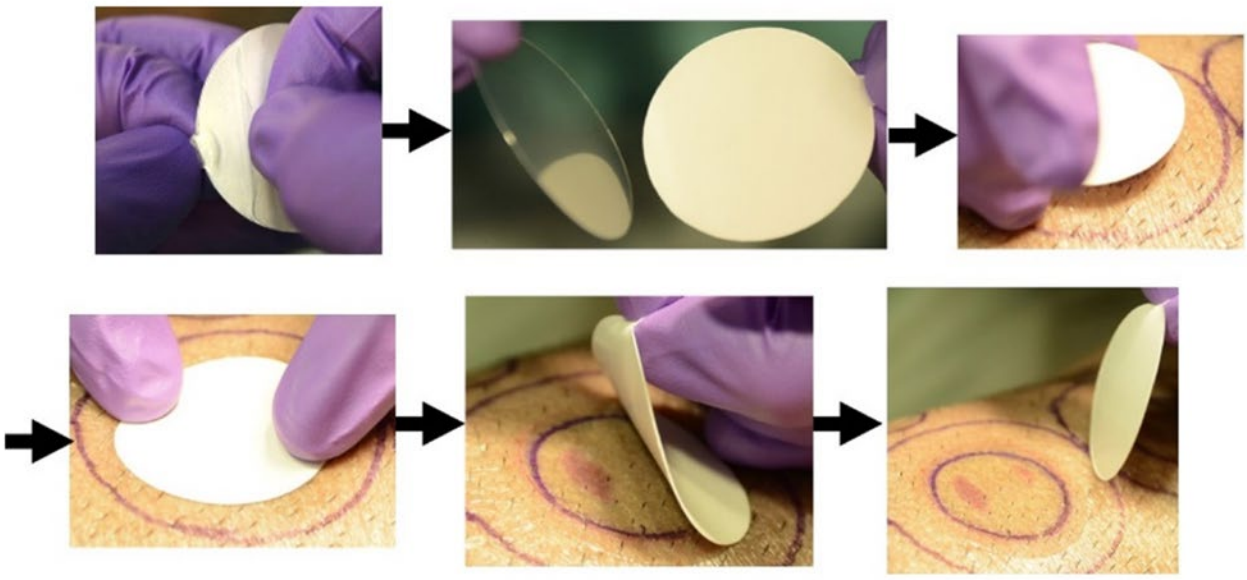


Figure 2: Application of the pirfenidone-containing burn wound patch to reduce dermal fibrosis (i.e., scarring) after deep partial-thickness burns in preclinical animal model. The patch is applied by first removing the clear release liner, exposing the silicone side of the patch, which is then placed directly onto the wound. The paper liner is then removed,

[1] Mony MP, Harmon KA, et. al. 2023. An Updated Review of Hypertrophic Scarring. Cells. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10000648/

[2] Engel CC, McBain RK, et al. 2020. The Effect of Blast-Related Burn Injuries from Prolonged Field Care to Rehabilitation and Resilience: A Review of the Scientific Literature. RAND Corporation. https:// www.rand.org/pubs/research_reports/RRA807-1.html.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12/2023
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The Congressionally Directed Medical Research Programs is a part of the U.S. Army Medical Research and Development Command, U.S. Army Futures Command.