

27 September 2021

MEMORANDUM FOR RECORD

SUBJECT: Fiscal Year 2021 (FY21) Peer Review Orthopaedic Research Program (PRORP) Stakeholders Meeting

1. The PRORP held a stakeholders meeting on 27 September 2021. The meeting was intended to provide an opportunity for scientific, clinical, and military experts, as well as lived-experience subject matter experts, to engage in an open-forum dialogue to identify critical knowledge and capability gaps, as well as underfunded areas, in orthopaedic research and care. Representatives from non-profit organizations, academia, industry, government institutions, and the public shared broad perspectives on potential barriers in research and patient outcomes, key knowledge and scientific gaps, and potential approaches for addressing orthopaedic needs. A list of stakeholder participants, invited speakers, and other attendees are included in [Appendix A](#).
2. Welcome and Overview of the Congressionally Directed Medical Research Programs (CDMRP)

Dr. Akua Roach, Program Manager for the PRORP, began the meeting and introduced COL Sarah Goldman, the CDMRP Director. COL Goldman welcomed the participants and emphasized the importance of stakeholders meetings for informing the strategies of new and established programs managed by the CDMRP. Dr. Walter Lee Childers offered a moment of silence. Dr. Roach described the purpose of the meeting as identifying knowledge gaps to inform future PRORP research funding and strategic directions. Ms. Elizabeth Guman provided an overview of the meeting agenda and explained her role as the meeting facilitator. Last, Ms. Ayad provided some administrative remarks before Dr. Roach began her introductory comments.

Dr. Roach provided an overview of the CDMRP and described its history, starting with the Breast Cancer Research Program established in 1992. She emphasized the role that consumers play throughout the CDMRP processes, including at peer and programmatic review. She outlined the traditional programmatic cycle for CDMRP programs, noting that stakeholders meetings are held for new programs as well as established programs as needed. She also highlighted the CDMRP's focus on maximizing the impact of research spending and transitioning research findings into knowledge and tangible products.

3. Overview of the PRORP

Dr. Roach described the funding history and research portfolio of the PRORP. She emphasized the role that injuries play in impeding the readiness of Service Members and how the research funded by the PRORP is also relevant to civilian and Veterans populations. She highlighted several challenges in conducting orthopaedics research, including patient enrollment and retention and the impacts of polytrauma on injury complexity. When describing the program's portfolio, she noted a nearly equal distribution of research projects funded in the developmental

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stages versus translational and clinical research areas, with more recent investments focused on clinical research.

4. Topic Area Presentations

a. Military Operational Medicine Research Program (MOMRP)/Joint Program Committee 5 (JPC-5) (Dr. Richard Shoge)

Dr. Richard Shoge described the MOMRP's focus on solutions and capabilities to support Warfighters in multi-domain operations. He also reiterated Dr. Roach's assessment of injuries, particularly musculoskeletal injuries that substantially reduce Warfighters' readiness. He noted the MOMRP's efforts in identifying risk factors of multi-domain environments and reducing the risk to Warfighters through optimizing fitness and human performance. Further, he appreciated the alignment and coordination between the MOMRP and PRORP in addressing gaps for rehabilitation following neuromusculoskeletal injuries. He closed by describing some recent MOMRP investments addressing both injury prevention and rehabilitation.

b. Combat Casualty Care Research Program (CCCRP)/JPC-6 (Dr. Therese West)

Dr. Therese West's recorded presentation described the scope of the CCCRP as encompassing point of injury through definitive care for injured Warfighters. She noted the potential for prolonged care scenarios, which would require additional care capabilities closer to the battlefield (e.g., Role of Care 1) in order to best support an injured Warfighter. She identified many priorities for both basic and applied research, including treating physiological injuries, supporting return to duty decision-making, and managing triage. She closed by highlighted several foci of the CCCRP strategic plan for mitigating extremity injuries in far-forward environments.

c. U.S. Department of Veterans Affairs (VA) (Dr. Brian Schulz)

Dr. Brian Schulz introduced the VA Health Care System as the largest integrated health care system in the United States. In addition to health care priorities, he noted several crosscutting research priorities that aligned with the PRORP's mission and goals, including those related to pain and opioid use. However, he clarified the VA's funding opportunities are specific to VA researchers and driven by an investigator-driven approach. He highlighted several areas where the VA and PRORP collaborate on research and care, including funding complimentary research areas that address both organization's goals and objectives. Last, he addressed several emphasis areas of special interest to the VA related to orthopaedics research, including prosthetic and assistive technology and exoskeleton research.

d. National Institute for Arthritis Musculoskeletal and Skin Disorders (NIAMS) Portfolio (Dr. Chuck Washabaugh)

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Dr. Chuck Washabaugh introduced the NIAMS, the primary institute or center for orthopaedics research at the National Institutes of Health (NIH), although he noted the interconnected nature of research at the NIH allows funding of orthopaedics-related research through other institutes focused on other aspects of musculoskeletal injuries or aging. He also described the NIH model of research as highly investigator-driven, which does not allow for prioritization outside of specific mission areas. Dr. Washabaugh described current NIAMS-funded research efforts in orthopaedic device and joint replacement, preclinical testing of devices and implants, and musculoskeletal biomechanics. In closing, he emphasized outreach and collaborative efforts with other funding organizations, including the PRORP and professional societies.

5. Pre-Meeting Data Review

Dr. Roach briefly described the information available to the meeting participants in the read-ahead materials, including the PRORP's mission, focus on consumer involvement, award mechanisms offered in FY16–FY21, and portfolio assessments. Ms. Guman provided an overview of the data gathered before the meeting from various stakeholders. The majority of survey respondents identified Emerging Areas in Preclinical and Clinical Orthopaedic Research as the most impactful topic area. Ms. Guman also noted that each topic area would be the focus for a breakout session later in the meeting. When ranking the top gaps by topic area, Ms. Guman highlighted regenerative medicine, “other” topics, and decision aids as the top three. She suggested that the prevalence of “other” topics would facilitate good discussion points in the breakout sessions. Finally, when assessing the demographic profiles of the respondents, she identified academic researchers as the majority of respondents, although clinicians, patient advocates, and others also contributed significantly.

6. Breakout Sessions

Participants discussed specific topic areas in six concurrent breakout sessions according to those they identified as most important in their responses to the pre-meeting data collection instrument. During these discussions, they identified and ranked primary (and in some cases secondary and tertiary) gaps for future consideration.

- a. Care for Return to Duty (Within 1 Year of Injury) for Military Service Members (Chairs: Drs. Jessica Goetz and James Irrgang)

Primary Gaps

1. Identification and reduction of reinjury risks
2. New quantitative tools to predict military-relevant outcomes
3. Leveraging of existing and emerging technologies to optimize musculoskeletal injury care
4. Optimization of rehabilitation strategies
5. Patient-specific functional and qualitative assessments

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Secondary Gaps

- Care coordination among various providers and interested parties (e.g., patients, commanders, units)
- Chronic pain
- Return to duty testing as different from physical fitness testing
- Development of innovative prosthetics, orthotics, and robotics
- Long-term, large-scale clinical trials of individual orthobiologics

- b. Diagnosis and Acute Care of Prehospital Musculoskeletal Trauma Injuries in Military and Civilian Populations (Chairs: Drs. Constance Chu and Aksone Nouvong)

Primary Gaps

1. Preservation/restoration of musculoskeletal function
2. Point-of-care decision-making aids (e.g., artificial intelligence wearables, assessment tools, pain assessments)
3. Wound management (e.g., tissue preservation, infection management)
4. Optimization of the pre-hospital continuum of care (e.g., stabilization, transport, artificial intelligence wearables)
5. Fracture care

Secondary Gaps

- Muscle, soft tissues, and joint injuries
- Pain assessment and management (including cognitive function)
- Fluid loss and replacement
- Acute inflammation
- Prevention of secondary injuries and complications

- c. Emerging Areas in Preclinical Orthopaedic Research (Chairs: Dr. Luis Alvarez and COL Leon Nesti)

Primary Gaps

1. Development of biologics, implants (devices), combination products, pharmacologic, or non-pharmacologic interventions to improve regeneration of bone, cartilage, muscle, nerve, tendon and ligament, and/or adipose tissues
2. Development of pharmacologic or non-pharmacologic interventions or knowledge products to prevent development of post-traumatic osteoarthritis (PTOA) at the time of injury or to treat PTOA
3. Development of interventions to prevent or treat infection, inflammation, and/or pathological immune response in the context of orthopaedic repair
4. Development of tools to enable decision-making, including discovery and validation of predictive biomarkers
5. Validation of animal models for specific mechanisms that underlie orthopaedic regeneration, infection control, and prevention of PTOA and are more predictive of outcomes in humans than current models

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Secondary Gaps

- Development of rehabilitation protocols that complement regenerative interventions
- Understanding origins and strategies to treat musculoskeletal pain
- Development of powered orthotics and prostheses, including smart orthotics and prostheses (i.e., with sensory and active components)
- Development of protocols for better “first-time fit” of prosthetics
- Understanding multi-tissue crosstalk in repair
- Understanding the effects of secondary factors on musculoskeletal outcomes (e.g., smoking, obesity, diabetes, lifestyle factors, genetics)
- Development of strategies to apply and model multidimensional musculoskeletal data to treat disease (e.g., molecular profiling, omics)
- Development and validation of organ-on-a-chip or organoid system for musculoskeletal tissues

Tertiary Gaps

- Understanding the role of mechanobiology in tissue injury and repair
- Understanding the role of COVID-19 in the etiology of musculoskeletal diseases and conditions
- Understanding how human variability (e.g., host, microbiome) plays a role in the outcomes of musculoskeletal treatments
- Justifying the differences between animals models and human systems

d. Emerging Areas in Clinical Orthopaedic Research (Drs. Stephen Goldman and Mike Hahn)

Primary Gaps

1. Prioritization of precision medicine, surgery, and rehabilitation, informed by biomarker, biosensor, imaging, and omics data, to deliver the right preventative and/or remediative treatment to the right patient at the right time
2. Development of novel musculoskeletal imaging capabilities for diagnosis of underlying pathology and efficacy of interventions measurements
3. Development of rehabilitation clinical assessments that are sensitive to differences in gender and race differences and address the need for increase equity in populations with limb loss and other complex orthopaedic and multi-system pathology/disabilities
4. Development of novel surgical techniques for enhancing limb restoration
4. Development of therapies to modulate the immune-inflammatory response to musculoskeletal trauma

Secondary Gaps

- Development of biomaterials for improved tissue-implant interface
- Development of sensors for longitudinal monitoring of musculoskeletal healing and functional recovery
- Development of technologies for enhanced ability to diagnose osteoarthritis
- Development of novel interventions that prevent and/or mitigate osteoarthritis
- Development of pre- and perioperative technologies for enhanced surgical outcomes

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- Development of novel control strategies for prosthetics
 - Development of technologies for early and/or enhanced detection of musculoskeletal infections
 - Development of novel techniques/modalities for management of musculoskeletal infections across the continuum of care
- e. Knowledge Gaps in Surgical Care for Musculoskeletal Combat Casualties (Chairs: Drs. Jessica River and Robert O'Toole)

Primary Gaps

1. Therapies and techniques that decrease and treat complications following high-energy extremity trauma, with a focus on fracture-related infections and fracture nonunion
2. Therapies and techniques with improved outcomes following high-energy extremity trauma, with a focus on improving wound healing, neuromuscular recovery following composite tissue loss, and segmental bone loss
3. Solutions of traumatic tissue loss, with a focus on nerve gaps and nerve healing with successful innervation, volumetric muscle loss, and protection or restoration of limb and wound vascularity
4. Surgical techniques and technologies to improve high-energy extremity trauma care
5. Regenerative capability of traumatic tissue loss including nerve gaps, volumetric muscle loss, segmental bone loss, and vascularity

Secondary Gaps

- Amputation/osseointegration
- f. Knowledge Gaps in Surgical Care for Musculoskeletal Non-Combat Casualties (Chairs: Drs. Jon Dickens and Ida Gitajn)

Primary Gaps

1. Development of new or leveraging of existing technologies and/or precision medicine approaches (including tissue engineering and scaffolds) to augment or aid surgical care, monitor/follow recovery, assess return to activity/duty, or identify early predictors of failure
2. Determination of biological and mechanical causes, predictors (including biomarkers), and treatment approaches following trauma (including bone, joint, cartilage, and soft tissue) and development of subsequent sequelae (e.g., PTOA)
3. Research to evaluate primary and secondary injury prevention strategies for common overuse tendon and ligament injuries, fractures (including stress fractures), and/or joint instability
4. Development of avenues to bridge outcomes research across platforms (e.g., Department of Defense, VA, civilian care), leveraging of existing outcomes platforms, and assessment of outcomes that best predict return to activity/duty
5. Development of effective engagement and management strategies around optimizing patient resiliency, mental health, and/or psychosocial factors that contribute to outcomes after orthopaedic surgery and rehabilitation

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Secondary Gaps

- Prediction, prevention, and treatment of complications following surgical treatment of musculoskeletal non-battle injuries
- Research to determine patient-specific rehabilitation strategies and best utilization of therapies as compared to home exercise programs (i.e., value-based care)
- Efforts to assess the broad impacts of injury, including financial, employment, and mental health impacts
- Development of tissue engineering and scaffolds to augment, accelerate, or improve musculoskeletal injury treatments
- Instability, chronic low back pain, anterior cruciate ligament injury, ankle sprain/fracture, stress fracture, fragility fracture, bone health

Tertiary Gaps

- Identifying balance of standardization of care versus precision medicine
- Value-based care assessment of common non-battle injury treatments
- Standardization of orthobiologic treatment to include development of an orthobiologics repository
- PTOA
- Point of injury and temporizing strategies

7. Adjournment

Dr. Roach described how gaps identified during the Stakeholder meeting will be used to inform PRORP investment strategy discussions, strategic planning discussions, and shared with internal and external collaborators. She also noted that outcomes of the meeting would be posted on the CDMRP webpage for public dissemination. Dr. Roach thanked the participants for their time and careful consideration of the gaps to be addressed by the PRORP. Ms. Guman also thanked the participants for their attention and adjourned the meeting.

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Appendix A: Meeting Attendees

The following individuals were present for the teleconference:

Invited Speakers

Dr. Brian Schulz, VA
Dr. Richard Shoge, MOMRP
Dr. Chuck Washabaugh, NIAMS, NIH
Dr. Therese West, CCCRP

Stakeholders

Dr. Devendra Agrawal, Western University of Health Sciences
Dr. Adil Akkouch, Western Michigan University School of Medicine
Dr. Farshid Alambeigi, University of Texas at Austin
Dr. Abass Alavi, University of Pennsylvania
Dr. Tamara Alliston, University of California, San Francisco
Dr. Luis Alvarez, Theradaptive
Dr. Conrado Aparicio, Universitat Internacional de Catalunya, Barcelona
Dr. Ravi Balasubramanian, Oregon State University
Dr. Brian Barlow, Naval Medical Center San Diego
Dr. George Bittner, University of Texas at Austin
Dr. Kath Bogie, Case Western Reserve University
COL William (Bill) Brown, Landstuhl Regional Medical Center
Dr. Steven Buchman, University of Michigan
Dr. Linda Cendales, Duke University
Dr. Walter Lee Childers, Extremity Trauma and Amputation Center of Excellence (EACE)
Dr. Constance Chu, Stanford University
Dr. Daniel Clifton, Uniformed Services University of the Health Sciences (USU)
Dr. David Dean, The Ohio State University
LTC Jon Dickens, Walter Reed National Military Medical Center
Dr. John Elias, Cleveland Clinic Akron General
Dr. Dave Ewart, Minneapolis VA Medical Center
Dr. Michael Francis, Asante Bio
Dr. Theresa Freeman, Thomas Jefferson University
Dr. I. Leah Gitajn, Dartmouth-Hitchcock Medical Center
Dr. Jessica Goetz, University of Iowa
Dr. Stephen Goldman, EACE
Dr. David Grainger, University of Utah
Mr. Lee Grossman, Orthopaedic Research and Education Foundation
Dr. Fernando Guastaldi, Massachusetts General Hospital/Harvard Medical School
Dr. Ranjan Gupta, University of California, Irvine
Dr. Michael Hahn, University of Oregon
Dr. Brian Hatzel, Grand Valley State University
Dr. Nick Heebner, University of Kentucky
Dr. He (Helen) Huang, University of North Carolina at Chapel Hill

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Dr. James Irrgang, University of Pittsburgh
Dr. Sean Kelly, Tripler Army Medical Center
Dr. Amanda Koh, University of Alabama
Dr. Krishna Kolan, MediCarbone, Inc.
Dr. Patricia Kramer, University of Washington
Dr. Peter Le, Naval Medical Research Unit-Dayton
Dr. Timothy Mauntel, EACE
Capt (U.S. Air Force, Ret.) Darcy Mortimer, U.S. Air Force Research Laboratory
Dr. Gustavo Nader, Pennsylvania State University
Dr. Leif Nelson, VA
COL Leon Nesti, USU
Dr. Aksone Nouvong, University of California, Los Angeles
Dr. Robert O'Toole, University of Maryland School of Medicine
Mr. Gautam Parthasarathy, GE Research
Dr. Thuvan Piehler, MOMRP
Dr. Sarah Pixley, University of Cincinnati College of Medicine
Dr. Jashvant Poeran, Icahn School of Medicine at Mount Sinai
Dr. Doug Powell, University of Memphis
Dr. Carmen Quatman, The Ohio State University
Dr. Kara Radzak, University of Nevada, Las Vegas
Dr. Sampath Rangasamy, Translational Genomics Research Institute
Dr. Joseph Rappold, Tufts University
Dr. Jennifer Richards, Washington University in St. Louis
CDR (U.S. Navy, Ret.) Jaden Risner, Family Proud
Dr. Jessica Rivera, Louisiana State University Health Science Center
Dr. Craig Roberts, University of Louisville School of Medicine
Dr. Joseph Roche, Wayne State University
Mr. Stan Sansone, 911 Medical Devices
Dr. Brian Schulz, VA
Dr. JoEllen Sefton, Auburn University
Dr. Steven Segal, University of Missouri
Mr. John Shero, EACE
Dr. Dmitriy Sheyn, Cedars-Sinai Medical Center
Dr. Michael Shuler, Athens Orthopedic Clinic
Dr. Richard Shoge, MOMRP
Dr. Michael Shuler, Athens Orthopedic Clinic
Dr. Amy Silder, Naval Health Research Center
Dr. M. Gerard-Paul Slobogean, University of Maryland School of Medicine
Dr. Sang-Eun Song, University of Central Florida
Dr. Abiraman Srinivasan, MediCarbone, Inc.
Dr. Wesley Thayer, Vanderbilt University
Dr. Randy Trumbower, Harvard Medical School
Dr. Sami Tuffaha, Johns Hopkins University School of Medicine
Dr. Charles Wade, McGovern Medical School
Dr. Sam Ward, University of California, San Diego

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Dr. Chuck Washabaugh, NIAMS
Dr. Brian Waterman, Wake Forest Baptist Health
Dr. Richard Westrick, U.S. Army Research Institute of Environmental Medicine
Dr. Therese West, CCCRP
Dr. Richard Westrick, U.S. Army Research Institute of Environmental Medicine
Dr. Fletcher White, Indiana University School of Medicine
Dr. Shane Wurdeman, American Orthotics and Prosthetics Association
Dr. Xu Yang, Hospital for Special Surgery
Dr. Xiaoning (Jenny) Yuan, USU
Dr. Damiano Zanotto, Stevens Institute of Technology

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