DUCHENNE MUSCULAR DYSTROPHY RESEARCH PROGRAM

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

IMPROVING FUNCTION, QUALITY OF LIFE, AND LIFE SPAN

FY24 Appropriation $10M

PROGRAM PRIORITIES

- Accelerate discovery and development of therapeutics with a path to clinical applications
- Advance understanding of the effect of Duchenne muscular dystrophy on the body, e.g., skeletal muscle, heart, bone, central nervous system, gastrointestinal
- Enhance DMD research capacity

FY24 Funding Mechanisms

Pre-Application (Letter of Intent)	Application:	Peer Review:	Programmatic Review:
August 1, 2024; 5:00 p.m. ET	August 22, 2024; 11:59 p.m. ET	November 2024	February 2025

IDEA DEVELOPMENT AWARD

Supports high-impact, new ideas in early development **$350K**

- Established Investigators - At or above the level of Assistant Professor
- New Investigators – Early Stage: *within 10 years of first faculty appointment*
- New Investigators – Transitioning: *Bringing new expertise to the field via established investigators in an area other than muscular dystrophy*

FY24 Focus Areas:

Applications must address opportunities and challenges in the development of safe and effective therapies that focus on the primary pathology of DMD

CLINICAL/TRANSLATIONAL RESEARCH AWARD

Supports translational research to move DMD research into clinical applications

FUNDING LEVEL 1 - $650K

FUNDING LEVEL 2 - $1.35M

Early-Career Partnering PI Option

An Early-Career Partnering PI Option is offered to promote enhanced research capacity within the DMD field.

FY24 Focus Areas:

Applications must address at least one of the following focus areas:

Pre-Clinical Translational Research

- Extension or expansion of existing preclinical data in support of Investigational New Drug application-enabling studies.

Clinical Research

- Clinical studies designed to improve care and quality of life
- Prospective real-world data collection for combination or sequential therapies, and/or follow-up safety and efficacy studies
- Assessment of clinical trial tools and outcome measures
- Natural history studies in understudied systems or age ranges with an aim toward clinical trial readiness

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

For more information visit https://cdmrp.health.mil/dmdrp

DMDRP RESEARCH BREAKTHROUGHS – MAKING A DIFFERENCE

FDA-Approved Drugs

- **Exondys 51®** (eteplirsen) and **Viltepso®** (vitolarsen): antisense oligonucleotide treatments for skipping over/deleting dystrophin gene mutations

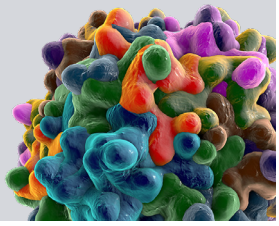
- **Agamree®** (vamorolone): a non-hormonal steroid drug that decreases muscle inflammation with reduced side effects compared to other corticosteroid-based treatments

Transitioned Tools to Industry

- Validation of motor function assessment using SMART device to track step/stride movement
- Validation of prognostic assay to measure levels of dystrophin in muscle biopsies

Treatment Approaches Now in Clinical Trials

- **Micro-Dystrophin Gene Transfer:** expression of micro-dystrophin produces functional dystrophin, leading to improved cardiorespiratory and skeletal muscle function



PROJECTS FUNDED IN FY22

ADVANCING EFFICACY, LONGEVITY, AND SAFETY OF GENE EDITING THERAPIES FOR DMD

Dr. Niclas Bengtsson, University of Washington

This study aims to advance gene editing for therapeutic use in DMD by developing specific approaches to maximize dystrophin editing in both existing muscle and muscle stem cells in a spatiotemporally controlled manner, including developing sensitive "switches" for turning gene editing on and off, with the purpose of reducing risks of unintended editing or development of immune responses within treated patient muscles.

EPIGENETIC LIQUID BIOPSY FOR DUCHENNE AND BECKER MUSCULAR DYSTROPHY

Dr. Yuval Dor, Hebrew University of Jerusalem

This project aims to establish and validate a dystrophinopathy cfDNA methylation biomarker assay for disease severity and response to therapy in patients with DMD and Becker muscular dystrophy.

ENGINEERING IPS-DERIVED MSCs WITH ENHANCED HOMING AND ANTI-INFLAMMATORY PROPERTIES FOR THE TREATMENT OF DMD

Dr. Christopher Rohde, Factor Bioscience, Inc.

This project aims to generate engineered induced pluripotent stem cell-derived-mesenchymal stromal cells that better home to damaged muscles, improve suppression of inflammation, and promote muscle regeneration for DMD.

PROTEIN SUPPLEMENTATION THERAPY TO INCREASE MEMBRANE REPAIR TO TREAT DUCHENNE MUSCULAR DYSTROPHY

Dr. Noah Weisleder, Ohio State University

This investigator plans to develop a novel protein therapeutic intervention, MyoTRIM, for the treatment of DMD. This intervention will enhance the repair capacity of muscle cell membranes of skeletal and cardiac muscle to compensate for the membrane fragility produced by mutations in the dystrophin/dystroglycan complex.

ENHANCED GENE THERAPY FOR DMD USING LARGER DYSTROPHINS AND LOWER VECTOR DOSES

Dr. Jeffrey Chamberlain and Dr. Julie Crudele, University of Washington

This project aims to refine a novel split intein, adeno-associated viral vector system, to deliver larger and more-functional dystrophins with improved AAV vectors at much lower doses than are currently used in the clinic. This new generation of gene therapy vectors could enhance the ability to treat both skeletal and cardiac muscles, enabling significant improvements in the quality of life and the life span of individuals with DMD.