

Support \$10 Million Myotonic Dystrophy Research Request in House FY23 Department of Defense Congressionally Directed Medical Research Program (CDMRP)

Request

The Myotonic Dystrophy Foundation asks that the House Appropriations Committee provide \$10 million in research funding to study myotonic dystrophy as part of the fiscal year (FY23) Department of Defense Congressionally Directed Medical Research Program (CDMRP). Thanks to bipartisan Senate support, myotonic dystrophy has been an eligible condition under the Peer Reviewed Medical Research Program (PRMRP) for the past five years. This has enabled many researchers from across the country to successfully compete for peer review grants totaling nearly \$8 million. We respectfully ask our Representatives to include our request in their letters of support to the committee as part of the fiscal year 2022 appropriations process.

Background

Myotonic dystrophy is a multi-systemic inherited genetic disease that affects at least 1 in 2,300 people or over 150,000 individuals in the United States. The disease is caused by a mutation in a gene required for normal muscle function, which prevents the gene from carrying out its function properly and can impact multiple body systems. Individuals affected by myotonic dystrophy may have skeletal muscle problems, heart function abnormalities, breathing difficulties, cataracts, issues with speech and swallowing (dysarthria and dysphagia), cognitive impairment, excessive daytime sleepiness, or diabetic symptoms. It causes disability and can reduce life expectancy. There are currently no Food and Drug Administration (FDA) approved treatments for myotonic dystrophy, and federal funding for myotonic dystrophy has lagged other similar genetic disorders. Continued PRMRP eligibility is vital to advancing science in this neglected field and improving the quality of life for American military personnel and civilians living with myotonic dystrophy.

Examples of PRMRP Funded Myotonic Dystrophy Research

- **Massachusetts General Hospital:** Extracellular Vesicles as Therapeutic Vehicles for Myotonic Dystrophy



- **University of Illinois, Champaign/Urbana:** Role of Neuron-Specific Giant Ankyrins Isoform in Developing Cardiac Arrhythmia for DM Type 1
- **Scripps Research Institute/University of Florida:** Design and Study of Small Molecules That Cleave the RNA That Causes DM Type 1

The Myotonic Dystrophy Foundation (MDF) was founded in 2007 by families seeking answers and support. The MDF mission, "Community, Care and a Cure," is to enhance the quality of life of people living with myotonic dystrophy (DM) and accelerate research focused on finding treatments and a cure. Through direct services, research, education, and advocacy, MDF empowers the DM community, improves access to effective healthcare, and eliminates barriers to drug development. MDF is the leading global advocate helping individuals and families navigate the DM disease process and is often the first resource contacted by newly diagnosed patients, their families, their social workers, and their physicians around the world. To learn more visit: www.myotonic.org.

Support the NIH Repeat Expansion Disease Initiative (REDI) to Accelerate Discoveries in Myotonic Dystrophy and Related Genetic Diseases

Repeat expansion diseases include over 40 distinctive disorders caused expansions in DNA repeats. Myotonic dystrophy (DM1 and DM2) is one of these repeat expansion diseases and has served as paradigm for a class of diseases caused by toxic RNA, which includes amyotrophic lateral sclerosis/frontotemporal dementia (C9ORF72), Huntington's disease, and most common forms of dominantly inherited ataxia including Friedreich ataxia. Over the past several decades, researchers have begun to understand these causative mutations that drive pathogenesis in many these diseases.

According to the National Institutes of Health's Human Genome Research Institute, gene alterations in two genes - CNBP and DMPK - cause myotonic dystrophy. DM1 is caused by a mutation in the DMPK gene, and DM2 is caused by a mutation in the CNBP gene. These mutations involve a short segment of DNA that is abnormally repeated many times, which form an unstable region of the gene. These changes keep cells in the muscles and other body tissues from functioning normally, leading to signs and symptoms of myotonic dystrophy. Affecting as many as 1 in 2,100 individuals, myotonic dystrophy is the most common form of adult muscular dystrophy and is considered the most variable of all known conditions, yet there is currently no cure and there are no approved treatments.

While U.S. based researchers at the University of Florida, University of Rochester, and Stanford University are making progress studying gene regulation and how its dysregulation causes symptoms in repeat expansion diseases, federal funding and coordination have been limited. Recognizing the potential to make major advances in the field of repeat expansions diseases and accelerate new treatments, the Myotonic Dystrophy Foundation and our Scientific Advisory Committee urges Congress and the NIH to establish a new trans-NIH Repeat Expansion Disease Initiative (REDI) within the Office of the NIH Director to fund new research and accelerate scientific discovery in this important new field.

For example, we believe new federal research investments in the use of deep sequencing technologies, such as RNA-Seq and CLIP-Seq, in combination with molecular & cell biological techniques, will help scientists to better understand how the repeating RNAs cause a myriad of symptoms in virtually all tissues of the body, including skeletal, cardiac, and smooth muscle, and tissues of the central nervous system. We believe that new



investments in studies of DM pathogenesis and RNA regulation will accelerate efforts to identify treatments and eventually cures for DM and other related diseases.

Therefore, the Myotonic Dystrophy Foundation is asking Congress to include report language in the fiscal year 2023 Labor, Health and Human Services Appropriations legislation to establish a trans-NIH Repeat Expansion Disease Initiative (REDI) within the Office of the Director to increase federal funding for research on repeat expansions and consider new funding mechanisms across multiple institutes to support scientific discoveries that will lead to treatments and cures for these genetic disorders and related conditions.

***Repeat Expansion Diseases.** —The Committee recognizes the rapidly emerging science on DNA repeat expansions, which causes over 40 distinct diseases. Myotonic dystrophy (DM1 and DM2) is one of these repeat expansion diseases and has served as paradigm for a class of diseases caused by toxic RNA, which includes amyotrophic lateral sclerosis/frontotemporal dementia (C9ORF72), Huntington’s disease, and most common forms of dominantly inherited ataxia including Friedreich ataxia. Due to recently developed sequencing technologies, a common thread has recently emerged, that repeat expansions may underlie multiple neurodegenerative conditions. The Committee encourages NIH to establish a trans-NIH Repeat Expansion Disease Initiative (REDI) within the Office of the Director to increase federal funding for research on repeat expansions and consider new funding mechanisms across multiple institutes to support scientific discoveries that will lead to treatments and cures for these genetic disorders and related conditions. The Committee requests an update on these activities in the fiscal year 2024 Congressional Budget Justification.*

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