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Researchers identify novel therapy to treat muscular dystrophy

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Researchers at Boston University College of Health & Rehabilitation Sciences: Sargent College have identified a combinatorial therapeutic approach that has proven effective in treating muscular dystrophy in a mouse model. The findings, published in *Human Molecular Genetics*, represent a paradigm shift for the treatment of muscular dystrophy as well as a host of other disabling and devastating muscle diseases.

The study was led by Mahasweta Girgenrath, PhD, assistant professor and director of the Muscle Disorders and Regenerative Biology Laboratory at BU Sargent College's Department of Health Sciences. Boston University (BU) researchers and postdoctoral fellows Jenny Yamauchi, Ajay Kumar, Lina Duarte, and Thomas Mehuron were collaborators on this study.

Muscular Dystrophy type 1A (MDC1A) is the second most common form of congenital muscular dystrophy. Patients with this disease have poor muscle tone at birth, extremely compromised neuromuscular function, and are rarely able to walk independently. Most patients with MDC1A succumb to a premature death due to either respiratory complications or failure to thrive. Although significant strides have been made towards understanding the molecular and biochemical mechanisms underlying MDC1A, there remains no effective therapy in place to combat this lethal disease.

The research team, led by Girgenrath, hypothesized that the complex pathology seen in MDC1A may be the result of dysregulation of multiple

cellular functions and processes, meaning that strategies which simultaneously target several of those mechanisms might lead to a reduction of symptoms.

"Very few studies have utilized the power of combinatorial therapy in the context of muscular dystrophy." said Professor Girgenrath, the study's corresponding author. "While most MD treatments are single-target therapies, we're delving into combinations of different therapies to target multiple pathways."

The research team studied the outcome of combining the following single mode treatments: increasing regeneration, by overexpressing muscle specific insulin like growth factor-1, IGF-1 and preventing cell death, by inhibiting the expression of Bax, a pro-apoptotic protein. In addition, to test the translational potential of this combination therapy, the researchers systemically treated Bax deficient dystrophic mice with recombinant human IGF-1 (IPLEX TM, manufactured by Insmed Inc).

By combining these two therapies, researchers found that in addition to increased body and muscle weight, mice showed enhanced locomotory capacities and remarkable improvement in muscle pathology. The most impressive outcome was the significant resolution of inflammation and fibrosis, not seen with single mode therapies. The research team concluded that the use of this combination therapy is an effective treatment for MDC1A, highlighting a compelling argument that a combinatorial approach has a synergistic benefit and could have the potential of treating patients with congenital muscular dystrophy.

Provided by Boston University

dystrophy.html