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Study identifies potential drug targets for muscular dystrophy treatments

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Myotonic dystrophy type I (MD1) is a common form of muscular dystrophy associated with muscle wasting, weakness, and myotonia. These symptoms are linked to the accumulation of toxic gene transcripts in muscle cells that result from abnormal gene splicing.

Recent studies have indicated that muscle cell health and function depend critically on the pathways that support energy balance and autophagy, a process that helps degrade and recycle cellular debris.

This week in the *JCI*, a study led by Perrine Castets at the University of Basel has demonstrated that pharmacological treatments targeting AMPK and mTOR signaling pathways, which regulate energy balance and autophagy in cells, improve the symptoms of MD1 in a mouse model. They initially observed that AMPK and mTORC1 pathways were disrupted in muscle tissue from the MD1 model mice.

Further investigation revealed that autophagy was also impaired in MD1 muscle, and this impairment contributed to dystrophy-like symptoms in the mice. When MD1 mice were treated with a drug that activated AMPK signaling, they displayed improvements in muscle function as well as reductions in abnormal gene splicing. Treating MD1 mice with rapamycin, a clinically-approved drug that activates mTORC1 signaling, also reduced signs of muscle pathology.

These findings identify targets in the AMPK and mTORC1 pathways that may be potential therapies for MD1.

More information: Marielle Brockhoff et al, Targeting deregulated AMPK/mTORC1 pathways improves muscle function in myotonic dystrophy type I, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI89616