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Scientists studying fatal muscle wasting disease make significant discovery

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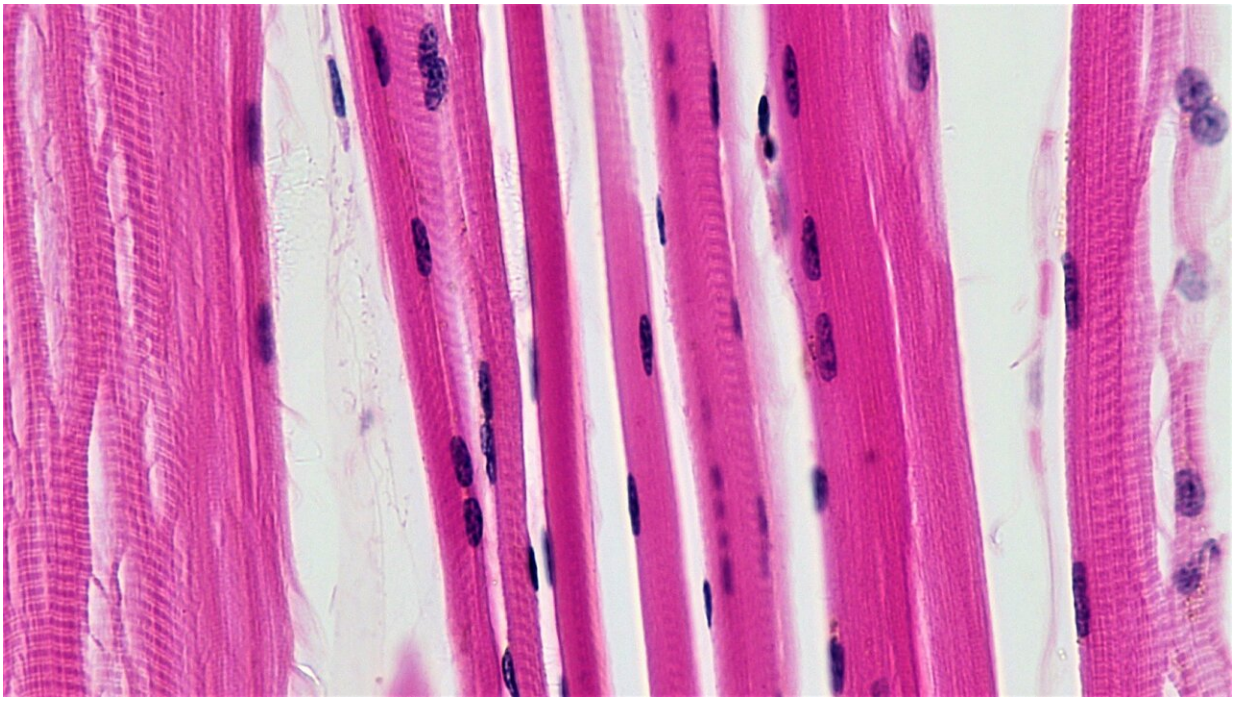

Skeletal muscle fibers. Credit: Berkshire Community College Bioscience Image Library / Public domain

Duchenne muscular dystrophy (DMD) is caused by a genetic mutation and affects one in every 5,000 boys born. Because the affected gene is on the X chromosome, girls are carriers of the mutant gene but develop the disease only very rarely (one in about 50 million).

Children with the condition will need a wheelchair by their teenage years , and most will die in or before they reach their 30s.

Previously, it was widely believed DMD starts in myofibers—cells involved in contraction, which make up the bulk of any muscle. As a result, the search for a treatment had long been focused on these cells and how to deliver therapeutics to them.

New research has revealed the disease begins much earlier in cells destined to become muscle fibers, known as myoblasts.

The study, published in *eLife*, is part of an ongoing collaboration between scientists at the University of Portsmouth, CNRS, I-STEM, AFM in France and Maj Institute of Pharmacology of the Polish Academy of Sciences

Senior author, Professor Darek Gorecki from the School of Pharmacy and Biological Sciences at the University of Portsmouth, said: "The findings are significant because they change the way we understand the disease. We discovered the functions of myoblasts are severely affected by the absence of dystrophin, and these cells are critically important for normal muscle growth but also regeneration.

"Because these myogenic cells malfunction, damaged muscle can't be repaired effectively. And any repaired myofiber will eventually need to be replaced, which will not happen without myogenic cells, so it becomes a vicious circle."

Last year, the team published results of modeling DMD to look at its development, from its initial trigger and first manifestation. They found evidence of abnormalities even before birth in the embryo. Most boys with DMD are diagnosed between two and five years old by which time the damage to their bodies is already significant. This delay in

identifying the condition may be preventing therapeutic interventions that could help slow, if not stop, disease progression.

"At the moment we're targeting the late stage of this disease by treating patients in their teens when muscle degeneration has already taken its toll", added Professor Gorecki.

"Instead, if we try to correct cells that are at the beginning of the pathological process we might be able to delay muscle degeneration and extend a patient's lifespan. We can do this by identifying and treating DMD newborns and targeting myogenic cells."

The paper says new technologies could be the key to producing effective therapies for this devastating disease.

More information: Maxime RF Gosselin et al, Loss of full-length dystrophin expression results in major cell-autonomous abnormalities in proliferating myoblasts, *eLife* (2022). DOI: 10.7554/eLife.75521

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