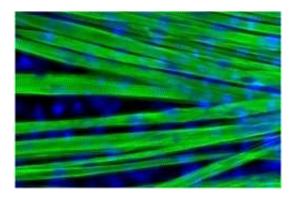


## Muscle fibers grown in the lab offer new model for studying muscular dystrophy

3 August 2015



Researchers have been able to grow differentiated muscle fibers (green) in the lab. Nuclei shown in blue. Credit: Olivier Pourquie, Brigham and Women's Hospital

Skeletal muscle is one of the most abundant tissue types in the human body, but has proven difficult to produce in large quantities in the lab. Unlike other cell types, such as heart cells, neurons and cells found in the gut, previous attempts to efficiently and accurately derive muscle cells from pre-cursor cells or culture have not been fruitful. In a new study published this week in Nature Biotechnology, investigators from Brigham and Women's Hospital (BWH) report that by identifying and mimicking important developmental cues, they have been able to drive cells to grow into muscle fibers, producing millimeter-long muscle fibers capable of contracting in a dish and multiplying in large numbers. This new method of producing muscle cells could offer a better model for studying muscle diseases, such as muscular dystrophy, and for testing out potential treatment options.

Previous studies have used genetic modification to create small numbers of muscle cells in the lab, but the research team, led by investigators from BWH and the Harvard Stem Cell Institute, wanted a technique that would allow them to grow large numbers of muscle cells efficiently for use in clinical applications.

"We took the hard route: we wanted to recapitulate all of the early stages of muscle cell development that happen in the body and recreate that in a dish in the lab," said corresponding author Olivier Pourquie, PhD, of BWH's Department of Pathology and the Department of Genetics at Harvard Medical School. "We analyzed each stage of early development, and generated cell lines that glowed green when they reached each stage. Going step by step, we managed to mimic each stage of development and coax cells toward muscle cell fate."

The team found that a combination of secreted factors that are important at early embryonic stages are also essential for stimulating differentiation - or the specialization of <u>stem cells</u> into particular cell types - in the lab. Using just the right recipe for differentiation, the team was able to produce long, mature fibers in a dish, derived from mouse or human pluripotent stem cells. They also cultured stem cells from the mouse model of Duchenne muscular dystrophy, observing the striking branched pattern that dystrophin-deficient muscle fibers show in the body.

The research team was also able to produce more immature cells known as satellite <u>cells</u> which, when grafted into a mouse model of Duchenne muscular dystrophy, produced <u>muscle fibers</u>. Further studies will be needed to determine if the new strategy could be optimized to develop cell therapies for treating degenerative diseases in humans.

In addition to developing a better model for Duchenne muscular dystrophy, the new protocol may also be useful for studying other muscle diseases such as sarcopenia (degenerative muscle loss), cachexia (wasting away of muscle associated with severe illness) and other muscular dystrophies.

"This has been the missing piece: the ability to produce <u>muscle cells</u> in the lab could give us the



ability to test out new treatments and tackle a spectrum of <u>muscle</u> diseases," said Pourquie.

More information: *Nature Biotechnology*, <u>DOI:</u> 10.1038/nbt.3297

Provided by Brigham and Women's Hospital

APA citation: Muscle fibers grown in the lab offer new model for studying muscular dystrophy (2015, August 3) retrieved 22 August 2015 from <u>http://medicalxpress.com/news/2015-08-muscle-fibers-grown-lab-muscular.html</u>

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