How muscle cells deteriorate with age, hampering recovery from injury

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A team at Nottingham Trent University analyzed the full set of more than 11,000 gene transcripts inside muscle cells, finding that the 'development pathways'—the different ways in which genes work

together to regenerate muscle—become weakened in aged cells.

The study may help to shed some light on why muscle damage take longer to recover from as we age. The study is published in the *Journal of Tissue Engineering and Regenerative Medicine*.

The researchers developed a new approach to examine muscle cells in vitro in the laboratory to enable them to observe the different molecular mechanisms that drive muscle aging.

They were able to study muscle cells from donors, chemically injuring cells after they had been donated and isolated, then assessing how they heal and regenerate back to their pre-injury baseline levels

Looking at cell lines derived from a 20 and 68-year-old donor, there were distinct differences in the development pathways of the younger and older cells, the researchers found.

While younger muscle cells fully recovered from the injury, the team found that in older cells the pathways linked to muscle development and regeneration were all 'downregulated.'

This means that the genes are expressing less of what they need to, leaving the cells no longer able to perform in the way they should.

This contributes to reduced regeneration capacity leading to thinner, less robust 'myotubes'—a type of cell that can fully develop into a muscle fiber.

Muscle regeneration is a complex and finely balanced biological process and is known to deteriorate with aging, leading to the decline of musculoskeletal health and in some cases metabolic and genetic diseases.

"This goes some way towards explaining why muscle injures may take longer to recover as we get older," said lead researcher Dr. Lívia Santos, an expert in musculoskeletal biology in Nottingham Trent University's School of Science and Technology.

She said, "We know that healthy muscle regenerates after we've had an injury, but aging impairs that regeneration potential and recovery gets harder the older we get. What we've observed, in terms of what happens inside the cells, helps us to better understand why we don't heal as well or as quickly in older age.

"The pathways that control cell processes and development work differently in older cells and are downregulated, meaning regeneration is impacted the older we get. If we can understand these pathways, however, we could potentially identify new therapies and interventions to mitigate the problem."

Janelle Tarum, another researcher on the study, said, "We've been able to develop a new approach to assess muscle regeneration which involves a state-of-the-art technique called RNA-sequencing.

"There's a very clear reduced regeneration capacity and weakened recovery of aged cells and we have been able to further understand the factors underlying this impairment.

"Our work enables us to examine muscle cell regeneration across the lifespan and this in turn could be key for future drug discovery for disease related to muscle aging."

The study, which also involved Manchester Metropolitan University, Liverpool John Moores University is published in the Journal of Tissue Engineering and Regenerative Medicine.

More information: Janelle Tarum et al, Modelling Skeletal Muscle Ageing and Repair In Vitro, *Journal of Tissue Engineering and Regenerative Medicine* (2023). DOI: 10.1155/2023/9802235