Cell Stem Cell: Researchers at CNIC, UPF, ICREA, CIBERNED and CIBERFES identify a mechanism that maintains mitochondria function in muscle stem cells and that can be stimulated in old age

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The finding provides a basis for mitigating the loss of muscle regenerative capacity in elderly people

Researchers at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), Universidad Pompeu Fabra, ICREA, Centro de Investigación Biomédica de Enfermedades Neurodegenerativas (CIBERNED) and Centro de Investigación Biomédica en Red Fragilidad y Envejecimiento Saludable (CIBERFES) have identified a physiological mechanism that sustains the regenerative capacity of muscle stem cells, and that fails at old age. This failure can be overcome genetically and pharmacologically, hence restoring old stem cell regenerative functions.

Skeletal muscle regeneration depends on a muscle stem cell population (satellite cells) in a dormant or quiescent state, a situation that can be triggered by damage or stress to form new muscle fibres and expand in new stem cells.

The regenerative functions of these stem cells are known to decline with ageing. Dr. Pura Muñoz-Cánoves, senior investigator at the National Centre for Cardiovascular Research (CNIC) in Madrid, and ICREA professor at the MELIS Department at Pompeu Fabra University (UPF) in Barcelona, and Ciberned, and Dr. José Antonio Enríquez, senior investigator at CNIC and CIBERFES, and their colleagues, have found in experiments with mice that mitochondrial dynamics are required for tissue regeneration. Mitochondrial fission facilitates muscle stem cell function via OXPHOS and mitochondrial autophagy (mitophagy) regulation.

Xiaotong Hong, the PhD student that has conducted the study, together with her colleagues, has shown that genetic loss of the mitochondria fission regulator DRP1 in muscle stem cells (or during aging) blunts their proliferation and regenerative capacity, whereas its reestablishment rescues these defects.

According to the results presented in *Cell Stem Cell*, normalizing mitochondrial dynamics (or increasing OXPHOS and mitophagy) in aged muscle stem cells restores tissue regeneration. This opens the way to improve the health of elderly people who are debilitated by the loss of muscle regenerative capacity.

This scientific study has also involved the collaboration of researchers at the University of Cordoba and the University of Padua (Italy). The study was funded in part by grants from the European Research Council (ERC), the Spanish Ministry of Science and Innovation, La Caixa-Health, Human Frontier Science Program and Leduq Foundation (LeduqRedox).

Mitochondrial dynamics maintains stem cell regenerative competence throughout adult life by regulating metabolism and mitophagy. Xiaotong Hong et al (2022). Cell Stem Cell, 2022

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identify-mechanism