New research may help older adults stay physically capable for longer

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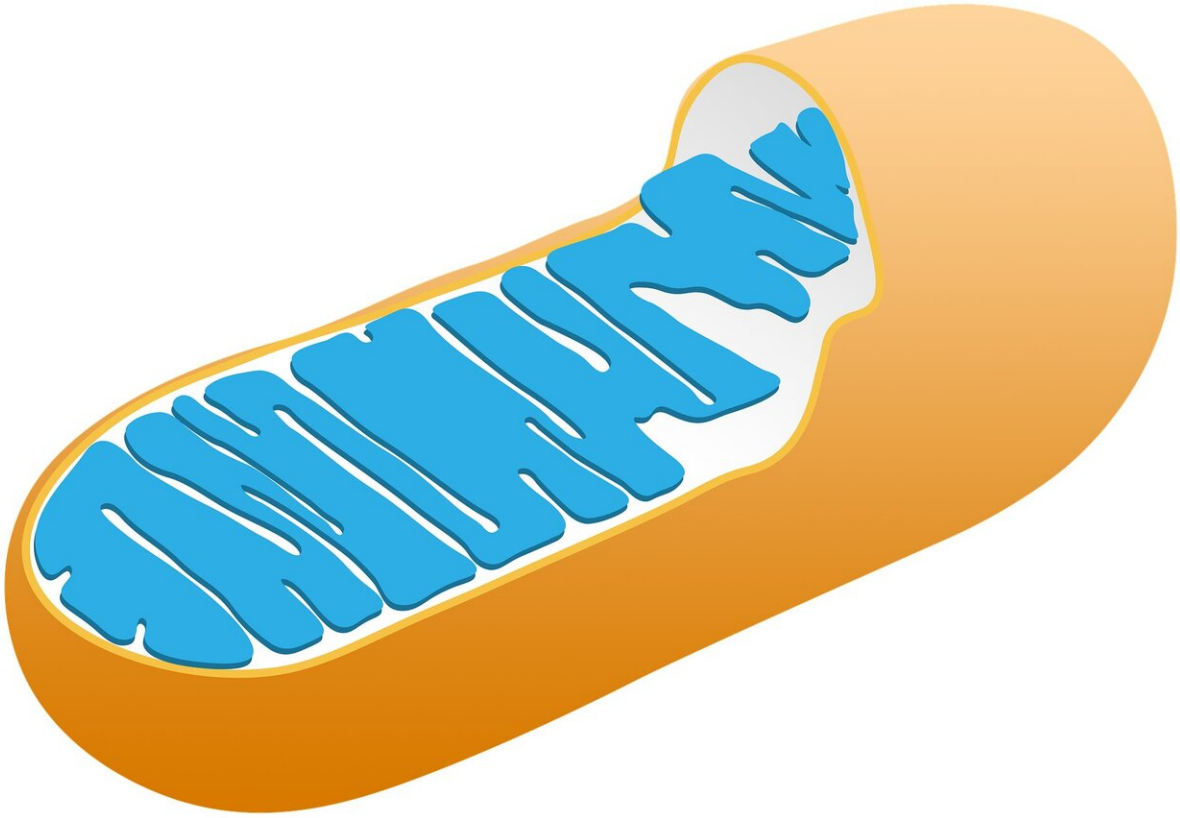

Drug therapies that help older adults maintain their skeletal muscle mass and physical function for longer could be a step closer after researchers at the University of Birmingham identify a key mechanism that drives the clearance of damaged mitochondria.

A team in the University's School of Sport, Exercise and Rehabilitation Sciences are well-versed at investigating dynamic machinery within cells called mitochondria. Mitochondria act as the power plant in every cell and help to supply energy for all living things.

Because mitochondria are so important to energy supply, they constantly undergo synthesis and break down to match energy demands. However, in older people, the way that mitochondria are naturally broken down in cells starts to change, leading to a build-up of damaged mitochondria or old mitochondria that are not functioning as well. It is thought these changes might contribute to the decline in the function of older people's muscles, which in turn reduces their physical capabilities. The team wanted to find out more about mitochondrial break down in muscle and the factors controlling it. Their results are published today in the *FASEB Journal*.

The lead researcher Alex Seabright (Ph.D. candidate in the Lai lab) developed a new tool that uses fluorescent tags to study the mitochondria in muscle cells. In healthy cells, networks of mitochondria appear gold in colour, but turn red when undergoing break down. Using this experimental set up, they discovered that activating a master energy sensor molecule, called AMP-activated protein kinase (AMPK), helps to stimulate mitochondrial break down. These exciting findings suggest that other well-known AMPK activators, such as exercise, may stimulate the

clearance of damaged mitochondria, thus keeping mitochondria in muscle healthy and prolonging older people's physical capabilities.

Project Leader Dr. Yu-Chiang Lai says: "The idea of targeting AMPK with drugs is not new. Many studies, including some of our previous work, demonstrate that AMPK activation in muscle elicits many beneficial effects for treating type 2 diabetes. As a consequence, many pharmaceutical companies are currently working to develop pre-clinical compounds that activate AMPK. We hope that our new discovery will accelerate targeted drug development to help identify new and safe compounds to activate this key molecule in muscle.

Alex Seabright adds: "We know that exercise and diet regimes can be used to help people maintain their muscle mass and physical capabilities in later life. But, improving our understanding as to why muscle loss occurs with ageing, will aid the development of targeted pharmacological interventions to help people to stay physically capable for longer."

More information: Alex P. Seabright et al. AMPK activation induces mitophagy and promotes mitochondrial fission while activating TBK1 in a PINK1-Parkin independent manner, *The FASEB Journal* (2020). DOI: 10.1096/fj.201903051R

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