

Published in the *Journal of Biological Chemistry*, Jonathan Memme et al., show that the importance of p53 is most evident under stress conditions where the maintenance of mitochondrial function is essential. Since its discovery in the late 1990s, p53 has been a focal point of research and lauded for its role in regulating the metabolic programming of the cell. While p53 is often studied in the context of cancer as a potent tumor suppressor protein, researchers in the MHRC have focused on understanding how p53 regulates mitochondria in muscle, the organelles responsible for providing energy to muscle cells.

Previous research has indicated that p53 plays a role in mediating the mechanisms that regulate mitochondrial quality in muscle, such as synthesis of new mitochondria (termed biogenesis), as well as elimination of dysfunctional mitochondria that may become toxic to the cell. However, the degree to which p53 is essential to regulating these mitochondrial adaptations, to this point, has remained controversial. Until now, there have been no studies that examine the role of p53 under conditions of chronic muscle disuse in which mitochondrial dysfunction is evident as part of the atrophy and muscle weakening process.

In this [study](#), York researchers set out to determine the necessity of p53 in maintaining mitochondrial content and function in muscle, both basally as well as following acute and chronic muscle disuse. Using RNA-sequencing technology, among other biochemical assessments of mitochondrial content and function, researchers assessed the effect of p53 ablation from muscle on more than 20,000 genes.

The inquiry led to convincing evidence to suggest that p53 is perhaps not required for basal maintenance of mitochondrial health in muscle; however, under stress conditions such as with chronic disuse, the absence of p53 contributes to exacerbated declines in mitochondrial function brought about by defects in the mitochondrial quality control machinery, particularly mitochondrial clearance via mitophagy.

These results address a decades-worth debate about the role of p53 in muscle metabolic health and show that the true importance of p53 is most evident under stress conditions where the maintenance of mitochondrial function is essential.