

The Explore-CKD study (Exploring the mechanisms of muscle wasting in CKD) sought to investigate how having Chronic Kidney Disease (CKD) influences aspects of skeletal muscle biology, ultimately leading to loss of muscle mass and function. This loss has been shown to significantly contribute to reduced quality of life and poor outcomes for people with CKD. Understanding the underlying biology of this process is key to development of effective interventions. In this study we collected blood samples and skeletal muscle biopsies from 25 people with CKD and 46 without CKD (controls), and analysed them in the lab to explore how the muscle biology of the two groups differs. We studied whole muscle and cells extracted from the samples to look at details of the structure and proteins, which helps us to understand potential avenues for reducing the negative effect of CKD on skeletal muscle.

The main findings were as follows :

1. People with CKD have higher levels of inflammation in the muscle tissue itself. Higher levels of inflammation have been shown to be one of the reasons for poor muscle mass and function in those with CKD. We were also able to show that exercise doesn't exert the same anti-inflammatory effect in those with CKD as it does in those without CKD. Future work will investigate why this is the case and what we can do to alter this response so that those with CKD can get the same biological benefits of exercise as those without CKD ([link to manuscript below \(1\)](#))
2. People with CKD have a reduced amount of mitochondria in their muscle tissue. Mitochondria are often called 'the powerhouse of the cell' and play a vital role in cellular energy production. The fact that those with CKD have a reduced number in their muscle tissue may contribute to the muscle fatigue and weakness noted in these people. This was also not altered with exercise and future work will seek to work out why this is and what we can do to improve mitochondrial number and function in CKD ([link to manuscript below \(2\)](#))
3. The muscle cells of people with CKD are more sensitive to a factor called chemerin than the muscle cells of those without CKD, which contributes to the high level of muscle tissue inflammation noted above. We have also shown how chemerin affects muscle in CKD and future work will look to understand how we can intervene in this process to improve muscle mass and function in CKD (manuscript currently in preparation)
4. When grown in the lab, muscle cells from people with CKD retain many of the characteristics that they show in the living muscle. This

is an important and exciting discovery as it means we can use lab-grown cells to model the intricacies of CKD muscle wasting, dysfunction and fatigue, and test potential therapeutic agents in the lab before giving them to patients. (link to manuscript below (3))

Links to Publications

1. [Inflammation and physical dysfunction: responses to moderate intensity exercise in chronic kidney disease | Nephrology Dialysis Transplantation | Oxford Academic \(oup.com\)](#)
2. [Reductions in skeletal muscle mitochondrial mass are not restored following exercise training in patients with chronic kidney disease - Watson - 2020 - The FASEB Journal - Wiley Online Library](#)
3. [Primary skeletal muscle cells from chronic kidney disease patients retain hallmarks of cachexia in vitro - Baker - 2022 - Journal of Cachexia, Sarcopenia and Muscle - Wiley Online Library](#)