The effect of resistance training and acidosis correction on anabolic signals in skeletal muscle in Chronic Kidney Disease (CKD)

Application deadline: Applications accepted all year round

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Funding: Self-funding only

Summary

Patients with chronic kidney disease (CKD) suffer from skeletal muscle wasting which is associated with increased morbidity and mortality. A major factor in CKD driving muscle wasting is metabolic acidosis.

Exercise training can potentially reverse wasting, but effects of training may be limited by the patients’ acidosis, further aggravated by lactic acid generated in working muscle. We recently found serious depletion of intramuscular amino acids after 1-6 months of walking exercise in CKD, but exercise plus acidosis correction (oral bicarbonate) prevented this and had beneficial effects on muscle anabolic signals not seen with exercise or bicarbonate alone. In isolated muscle cells, acid strongly inhibits the key amino acid transporter SNAT2 [1], leading to depletion of intracellular amino acids and impaired anabolic signals.

The present project investigates resistance training which is a stronger stimulus for muscle hypertrophy. The hypothesis to be tested is that training combined with acidosis correction in CKD maintains intramuscular amino acids, stimulates anabolic signals and increases muscle mass, whereas training alone is limited by acidosis and amino acid depletion.

In collaboration with exercise researchers in the John Walls Renal Unit Leicester and Loughborough University, this will be tested by:

**In vitro** studying activity of the SNAT2 transporter and amino acid profiles and anabolic signals in response to mechanical stress with/without acid loading in the cultured muscle model that we used previously [1]

**In vivo** performing parallel studies in skeletal muscle biopsies drawn from patients undergoing resistance training with/without bicarbonate supplements

Full training and close supervision will be provided in the techniques of mammalian cell culture, *in vivo* muscle function studies, gene expression, and protein phosphorylation signalling that are required for this project.