

University of Leicester – PhD project

Funding Source: Self-funded / Applicants own Sponsor

Proposed start date: negotiable

Closing date for applications: open until filled

Eligibility: UK/International

Tuition fees for overseas: 2025/26 academic year: £23,650 - £38,300 per year

Department/School: Cardiovascular Sciences

Supervisors: Dr Emma Watson emma.watson@le.ac.uk, Dr Luke Baker, lab69@leicester.ac.uk

Project Title: The effect of glucagon-like peptide-1 receptor agonists on exercise adaptation

Project Description

Aim: To understand the impact of GLP-1 RA therapy on skeletal muscle adaptation to exercise

Background:

Obesity is a chronic disease associated with increased risk of multiple metabolic, and mental health related comorbidities. Recent advances in obesity pharmacotherapy, particularly glucagon-like peptide-1 (GLP-1) receptor agonists (RAs), have the potential to transform obesity and type 2 diabetes mellitus (T2DM) care by promoting marked weight loss, improving glycaemic control and addressing multiple obesity-related comorbidities, with added cardio-renal benefits. However, up to 40% of the weight lost with GLP-1 RAs comes from lean body mass, raising concerns about potential adverse effects on skeletal muscle function. It is likely that these drugs will be combined with lifestyle management including exercise delivery. It is therefore important to understand the interaction between these drugs and exercise. We have novel *in-vitro* data emerging from our laboratory to show that a range of GLP-1 RAs not only result in significant muscle atrophy, but also negatively impair skeletal muscle mitochondrial function. This may have important consequences for the ability of an individual to engage in an exercise programme and the benefits they are able to receive if effects persist.

Methods:

This project will utilise a combination of *in-vitro* models of exercise and *ex-vivo* biopsy analysis. We will use primary skeletal muscle cells from people with obesity to understand how a number of different GLP-1 RAs (e.g. semaglutide, trizapatide or cagrilintide) affect the response to simulated exercise. We will also utilise the on-going opal trial to collect muscle biopsies from the following time points with participants used as their own control:

- 1) Baseline
- 2) 24h post exercise prior to drug administration. This will provide information on the acute response to exercise before training
- 3) 24h post exercise after receiving the drug for 1 week. This will provide information on how the GLP-1 RA has affected this acute exercise response
- 4) 24h post exercise at the end of the exercise training period. This will provide information about how regular exercise training has modified this acute response to exercise.

Expected outcomes and impact: A clearer understanding of the interaction between GLP-1 RAs and the acute and chronic skeletal muscle response to exercise. This project offers significant impact in a novel and fast-moving field. Prescription rates of these drugs are on an upward trajectory and have become an integral part of obesity care along with more traditional diet and lifestyle interventions. The data from this study will help inform the way in which these drugs are used in combination with these traditional therapies informing and potentially changing clinical practice.

Entry requirements:

Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject.

The University of Leicester English language requirements apply where applicable.

Application advice:

To apply please refer to <https://le.ac.uk/study/research-degrees/research-subjects/cardiovascular-sciences>

With your application, please include:

- CV
- Personal statement explaining your interest in the project, your experience, why we should consider you in addition to confirmation of how you will pay your fees.
- Degree Certificates and Transcripts of study already completed and if possible transcript to date of study currently being undertaken
- Evidence of English language proficiency if applicable
- In the reference section please enter the contact details of your two academic referees in the boxes provided or upload letters of reference if already available.

In the funding section please specify that you wish to be considered for Ref Self funded Watson Project

In the proposal section please provide the name of the supervisors and project title (a proposal is not required)

Project / Funding Enquiries: Dr Emma Watson emma.watson@le.ac.uk

Application enquiries to cls-pgr@le.ac.uk