University of Leicester

The Leicester Lifestyle and Health Research Group (LLHRG) PhD studentship

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| **First Supervisor** | Professor Leigh Breen |
| **School/Department** | Diabetes Research Centre, College of Life Sciences |
|  | cls-pgr@le.ac.uk  |

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| **Second Supervisor** | Dr Tom Wilkinson |
| **School/Department** | Diabetes Research Centre, College of Life Sciences |
| **Email**  | t.j.wilkinson@leicester.ac.uk  |

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| **Additional Supervisor** | Dr Emma Watson emma.watson@leicester.ac.uk  |

**Section 2 – *Project Information***

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| **Project Title** | ***Novel nutritional and pharmacological interventions to optimise healthy weight loss in older adults with obesity.*** |
| **Project Summary**  |
| **Project Highlights:**

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| 1.  | In vitro cell culture and ex vivo analysis of biological samples from patient cohorts to understand the muscle anabolic properties and underlying mechanisms of candidate compounds. |
| 2.  | Application of cutting-edge stable isotope tracer and mass spectrometry methods to measure muscle protein synthesis, gene expression and multi-omics outcomes.  |
| 3.  | Opportunities to work in outstanding research environments across DRC/UoL and with external collaborators (isotope tracer analysis) with scope for engagement opportunities with industry collaborators and Patient and Public Involvement and Engagement groups. |

***Aim:*** To determine the efficacy of novel nutritional and/or pharmacological compounds for attenuating the loss of skeletal muscle mass and function with weight loss (WL) interventions in older adults with obesity; through pre-clinical mechanistic cell-to-human experimental approaches. This will aid the development of intervention studies to optimise healthy weight loss and wider metabolic health benefits in older adults with obesity.***Background:*** Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and combination therapies can achieve weight loss (WL) that approaches magnitudes achieved with surgery 1, 2. However, as more WL is achieved, there is concern for potential adverse effects on lean mass and function 1, 3, with implications for sarcopenia and frailty progression in older adults 4-6. Strategies to preserve muscle mass and function during WL interventions are critical to support long-term metabolic health outcomes and the prevention or worsening of sarcopenia and frailty. To date, the potential for nutritional and/or pharmaceutical combination therapies to spare muscle mass and function in older individuals during WL intervention is unknown. Interestingly, a number of candidate nutraceutical and pharmaceutical compounds show promise in enhancing muscle growth and cellular energetics in older adults but have not been investigated in the context of WL 7-9. There is great potential across the Diabetes Research Centre (DRC) and NIHR Leicester BRC to exploit newly developed facilities for investigating muscle metabolic physiology, clinical trial infrastructure and expertise in cell culture to investigate the muscle anabolic properties of novel nutra- and pharmaceutical compounds in WL models/settings. This PhD application is designed to harness this potential.***Methods:*** The PhD will include the following components. **Months 0-18: Identification and screening:** Following a scoping review of the literature to determine the biological feasibility of candidate compounds, the muscle anabolic properties selected compounds will be screened using ex vivo biopsy and blood analysis from well phenotyped cohorts and in vitro experimental models. Efforts will be expedited by biological samples and preliminary data collected by the supervisors. **Months 18-36: Human mechanistic studies:** Stable isotope tracer and muscle biopsy applications will be used to measure muscle protein synthesis with supplementation of the selected compound(s). This will be combined with proteomic and transcriptomic analysis to uncover detailed mechanistic insights. Progress will be expedited through recruitment of patients from approved clinical trials at the DRC and NIHR BRC.***Expected outcomes and impact:*** This studentship will provide crucial proof-of-principle evidence in the development of novel therapeutics to protect muscle mass during WL in older adults with obesity. Outputs will inform the development of future larger-scale clinical trials to determine efficacy and acceptability, through collaboration across UoL, NHS and industry. |
| **References** |
| 1. Sargeant, J.A., et al., Endocrinol Metab (Seoul), 2019. **34**(3): p. 247-262.2. Karakasis, P., et al., Metabolism, 2025. **164**: p. 156113.3. Chaston, T.B., et al., Int J Obes (Lond), 2007. **31**(5): p. 743-50.4. Prado, C.M., et al., Lancet Diabetes Endocrinol, 2024. **12**(11): p. 785-787.5. Belfield, A.E., et al., Age Ageing, 2024. **53**(5).6. Linge, J., et al., Circulation, 2024. **150**(16): p. 1288-1298.7. D'Amico, D., et al., Trends Mol Med, 2021. **27**(7): p. 687-699.8. Idris, I., Diabetes Obes Metab, 2024. **e109**.9. Deane, C.S., et al., Am J Physiol Endocrinol Metab, 2017. **312**(4): p. E282-E299. |