OXFORD INTERDISCIPLINARY BIOSCIENCE
Doctoral Training Partnership

Industrial CASE Studentship Advertisement – 2023 Entry

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Project Title:	Non-invasive phenotyping of muscle function using multi-nuclear MR

Brief description of project:

Short teaser: This interdisciplinary project combines biology, physics and engineering to uncover exciting information about skeletal muscle metabolism during ageing, through the development of innovative technology. It is built around a collaboration between The University of Oxford and Rapid Biomedical (industrial partner) giving the applicant possibility to experience working within friendly teams of internationally recognized experts in both "worlds". For a more detailed description continue reading and contact the supervisory team.

Ageing is often associated with a decline in mitochondrial metabolism, which leads to deterioration of muscle function, constitutes a severe burden on the quality and length of life of the elderly. Exercise programs, in particular those that include functional training, are often recommended for preventing and delaying late-life disability, however, they often do not yield significant benefits, which is very discouraging. **To improve the quality of life in older age, we need to improve our limited understanding of the rules of life governing muscle metabolism and our ability to non-invasively monitor it.**

Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique capable of assessing the chemical composition and metabolic processes of muscle tissue *in vivo*. In particular, hydrogen (^{1}H)-MRS provides insights into lipid metabolism and pH buffering through intramyocellular lipids, acetyl-carnitine and carnosine content quantification, respectively. In addition, tissue oxygenation and perfusion can be assessed using ^{1}H-MR imaging. Mitochondrial metabolism can then be probed using phosphorus (^{31}P)-MRS through the acquisition of phosphocreatine dynamics during and after exercise. In a complementary way, carbon (^{13}C)-MRS provides insights into glucose metabolism and glycogen production and storage capacity in muscle. **Hence, a combination of ^{1}H-, ^{31}P- and ^{13}C- MRS could provide a comprehensive assessment of a tailored muscle metabolic phenotype advancing our understanding of healthy ageing.**

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Using currently available MR technology, particularly the so-called "dual tuned" radio-frequency (RF) coils, capable of signal excitation and acquisition for two different nuclei, we were able to recently show that muscle carnosine levels (using ^{1}H-MRS) and metabolic fluxes during exercise (using ^{31}P-MRS) were particularly impaired in the elderly population even though their overall activity levels were similar to those of younger volunteers. To enable assessment of muscle glycogen (using ^{13}C-MRS) in the same scan, **requires the development of a novel transformative technology, namely a "triple tuned" RF coil**. Such a "triple tuned" RF coil will be capable of excitation and acquisition of MR signal at three different frequencies (one for each nucleus).

RAPID Biomedical GmbH is the market leader for the design and construction of dedicated multi-nuclear RF coils, with several major MR manufacturers offering RAPID RF coils as a standard with a new MR system purchase. Still, designing a triple tuned coil is not trivial, as a proper balance between coil coverage, signal-to-noise ratio (SNR) performance and channel coupling needs to be maintained.

The student will be given time to travel to the Rapid Biomedical GmbH headquarters in Rimpar Germany to work alongside Dr Lanz and his team, learning about multi-nuclear RF coil design (required for the in-depth knowledge of RF coil design needed in this project) and gaining insight into industrial practice. ***Combining the MR physics and physiology expertise of Professors Valkovič and Tyler with the in-depth RF engineering knowledge of Dr Lanz, this project provides a perfect interdisciplinary environment to develop a wide range of skill and design this transforming technology to further our understanding of the rules of life.***

The objectives of this collaborative interdisciplinary project are:

1) *Design and construct an efficient triple tuned RF coil for comprehensive assessment of muscle metabolism.*
2) *Use the novel coil to phenotype muscle metabolism in a group of elderly participants enrolled to an exercise programme, and look for potential association between their muscle phenotype and the intervention outcome.*

This will include the design of an efficient technique to avoid any "cross-talk" between the three channels through simulations and modelling of electromagnetic fields around the new RF coil designs, as well as construction and testing for performance and safety. The final coil design will be optimised for an interventional study. The examination protocol would ideally include: i) measurement of intramyocellular lipids, acetyl-carnitine, creatine and carnosine by ^{1}H-MRS, pre and post exercise; ii) interleaved acquisition of ^{31}P and ^{13}C MRS during exercise for assessment of metabolic fluxes and glycogenolysis rates; and iii) interleaved ^{31}P and ^{1}H MR during recovery for mitochondrial metabolism and tissue perfusion assessment.

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The combination of these metabolic measures will provide an unparalleled insight into muscle metabolism *in vivo* and will allow identification of an individualized muscle metabolism phenotype. This will be applied in an interventional study of healthy elderly individuals enrolled to a general exercise programme.

Attributes of suitable applicants:

We are looking for motivated students with a background in physics, chemistry, electrical engineering or a related field, interested in the development and application of imaging technologies for biological applications, as well as in metabolic processes and their assessment.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council UKRI-BBSRC. UKRI-BBSRC eligibility criteria apply (https://www.ukri.org/files/funding/ukri-training-grant-terms-and-conditions-guidance-pdf/). Successful students will receive a stipend of no less than the standard UKRI stipend rate, currently set at £17,668 per year.

This project is supported through the Oxford Interdisciplinary Bioscience Doctoral Training Partnership (DTP) studentship programme. The student recruited to this project will join a cohort of students enrolled in the DTP's interdisciplinary training programme, and will participate in the training and networking opportunities available through the DTP. For further details, please visit www.biodtp.ox.ac.uk. The DTP and its associated partner organisations aim to create a community that is innovative, inclusive and collaborative, in which everyone feels valued, respected, and supported, and we encourage applications from a diverse range of qualified applicants.