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Precision Imaging Beacon of Excellence
Studentship Form

Supervisors	**Professor Guru Aithal** Nottingham Digestive Diseases Centre **Professor Paul Greenhaff** Division of Physiology, Pharmacology and Neuroscience, School of Life Sciences		
Co-supervisors	**Dr Stephen Bawden** **Professor Penny Gowland** Sir Peter Mansfield Imaging Centre **Collaborator: Prarthana Thiagarajan**		
Start date	September 2018	**Duration**	3 years
Project	**ECLIPSE: E**ffect of carnitine on **L**iver steatosis, **I**nsulin sensitivity, **P**lasma glucose, **S**keletal muscle metabolism and **E**nergetics - a pilot study		
Abstract	This ambitious project unites institutional research priorities in translational imaging, liver disease and musculoskeletal health. Through cross-cutting collaborations between the Schools of Medicine, Life Sciences and Physics, we will employ MR spectroscopy in combination with the euglycaemic hyperinsulinaemic clamp technique to explore the pathophysiology of non-alcoholic fatty liver disease (NAFLD). The study will hinge upon use of sophisticated MRS methods to quantitate the impact of chronic dietary supplementation with L-carnitine on hepatic and intramyocellular carnitine moieties, lipid content and hepatic mitochondrial metabolism. NAFLD presents a growing public health and economic challenge and is the leading cause of chronic liver disease in high-income economies. As there is **no licensed pharmacological treatment** for this condition, its clinical and economic burden are projected to rise dramatically in coming decades. L-carnitine is a naturally occurring amine located primarily in skeletal muscle tissue that plays a central role in mitochondrial fat oxidation. Accordingly, increasing muscle carnitine content, by targeting insulin mediated carnitine transport, has been shown to augment muscle fat oxidation and gene networks regulating this process in healthy volunteers. We hypothesise that increasing muscle carnitine content in NAFLD using a dietary mediated approach will increase muscle fat oxidation and reduce intramyocellular muscle lipid content, and secondary to this will reduce muscle and hepatic insulin resistance and hepatic fat content, thereby augmenting hepatic mitochondrial ATP flux. We will therefore highlight L-carnitine as a broadly-applicable and safe potential treatment option in a NAFLD population. This study affords abundant opportunities for development and validation of novel MR spectroscopic methods, including: 1. Refining and validating saturation transfer ^{31}P-MRS methodology at 3T to quantitatively determine hepatic ATP flux in NAFLD. 2. Developing ^{1}H-MRS methods to quantify carnitine moieties in muscle tissue. This will develop and validate a non-invasive protocol for determination of muscle free carnitine, as well as acylcarnitine moieties, by comparison against biopsy-determined values. 3. Use of ^{1}H-MRS at 3T to quantify intra- and extra- myocellular lipid fraction and determine its relationship to tissue-specific and whole-body insulin resistance. 4. Advanced 7T ^{1}H-MRS muscle imaging, proton spectroscopy and IMCL/EMCL lipid quantification. Each of these dimensions will add to the quality and depth of precision imaging capabilities at the University of Nottingham, enhancing its strategic value and enduring applicability across research priority areas worldwide. The project will		

	provide excellent training within a multidisciplinary team and address the obvious skills gap in the application of MR spectroscopy in metabolic disease. The project is in an area of priority for NIHR Nottingham Biomedical Research centre with two senior supervisors from Gastrointestinal and Liver disorder theme and musculoskeletal theme. This will permit the candidate to be involved in translational research and participate in N-Trans programme. This is an excellent research opportunity, as the successful candidate will be exposed to high quality research in an environment where they will interact on a day-to-day basis with clinicians, academic research staff, postdoctoral fellows and other PhD students. This experimental and philosophical approach will produce the highly skilled, integrative translational scientist that is acutely required to meet research needs. Applicants must have a minimum of UK 2.1 honours degree (or equivalent) in physics or a related area (e.g. mathematics, chemistry or computer science, depending on skills and interests).
Queries	Please contact **PI-Beacon@nottingham.ac.uk**
To apply	Please apply online via **the University of Nottingham application page**