



**Industrial CASE Studentship Advertisement – 2021-22**

**Supervisor(s) names:** Professor Fiona Powrie<sup>1</sup>  
Dr Nicholas Ilott (he/him)<sup>1</sup>  
Dr Petar Scepanovic<sup>2</sup>

**Department(s)/ Organisations:** <sup>1</sup>Kennedy Institute of Rheumatology, University of Oxford  
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**Project Title:** Physiological cross-talk between the liver and gut in healthy aging

**Brief description of project:**

The liver and the intestine interact in a complex manner to maintain mutually beneficial homeostatic functions. This cross-talk involves the modification of liver-derived factors such as bile acids and conjugated bilirubin by the small and large intestinal microbiota, enabling modulation of intestinal functions. Breakdown in such homeostatic functions can lead to diseases of the liver and intestine including Primary Sclerosing Cholangitis.

In this project we aim to better understand the liver-microbiome-gut axis in health using an interdisciplinary systems physiology approach.

The approaches undertaken will involve the analysis of high-throughput RNA-sequencing data from both publicly available human samples (GTEx project (<https://www.gtexportal.org/home/>)) as well as mouse models. The project will involve analysing data derived from the liver and the intestine in order to characterise correlated functions between these two organs. During this part of the project you will be supervised by Dr Nicholas Ilott (Kennedy Institute of Rheumatology) to develop skills in the development and application of bioinformatics pipelines as well as developing an R package for the analysis of cross-tissue gene expression networks. These tools will further be applied to answer the question of how liver-gut interactions change over the course of the lifespan through the comparison of liver-gut co-expression networks across ages in mouse models.

Metabolic output from the gut microbiota plays a role in mediating liver-gut interactions. As such, you will work with Petar Scepanovic (Roche, Basel, Switzerland) over the course of 6 months to 1 year where you will integrate within BEDA (Bioinformatics Exploratory Data Analysis) team - a group of computational biologist and biostatisticians within pRED. There you will develop computational models that predict metabolic output from complex metagenomic data. You will integrate these models with additional data from in vitro experimental models of bacterial consortia to determine metabolic outputs that contribute to liver-gut cross-talk. Indeed, you will utilise a model consortium of 12 bacterial strains in order to 1) computationally predict their ability to metabolise liver-derived factors and 2) experimentally validate this ability using bacterial culture techniques. Together with experienced laboratory staff at the Oxford Centre for Microbiome Studies (OCMS), you will gain training in anaerobic and aerobic bacterial culturing



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techniques and the application of such techniques to explore context-dependent metabolite profiles.

Finally, we aim to investigate how liver-microbiome-gut interactions break down in disease. You will therefore leverage the expertise in mouse models and gnotobiotics at the OCMS in order to determine the effects of different microbial consortia on liver and gut dysfunction and the potential of bacterial therapies in cholestatic disease.

#### **Attributes of suitable applicants:**

Applicants should have a 1st or 2:1 Honours degree or MSc in biology or related discipline.

#### **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 £15,285 per year, which will be supplemented by the industrial partner with an additional £6,000 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](http://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.*