OXFORD INTERDISCIPLINARY BIOSCIENCE
Doctoral Training Partnership

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Industrial CASE Studentship Advertisement – for 2020 entry

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Project Title: Development of Raman Spectroscopy for Analysis of Single Cell Metabolism

Brief description of project*:

Metabolism is a highly dynamic process whose regulation is fundamental to biology. Traditional methodologies to study metabolism are incapable of measuring flux through pathways with temporal and spatial resolution at the single cell level. Single-cell Raman spectra (SCRS), which are label-free and molecular vibrational profiles of single cells, offer a unique cellular phenotype. SCRS can be coupled with stable isotope probing (Raman-SIP) to measure specific functions of cell metabolism by exploiting the shifts in selected Raman bands when cells incorporate stable isotopes (e.g. 13C, 15N, 2H). For example, Raman spectroscopy has been used to image glucose turnover in individual glycogen granules alongside mitochondria, nuclei, lipid membranes and droplets in single cells. Due to the non-destructive nature of Raman spectroscopy individual cells displaying particular metabolic changes can be selected for downstream analysis using Raman activated cell sorting techniques such as Raman-activated microfluidic sorting (RAMS).

This studentship aims to expand the Raman spectroscopy toolkit for assessing metabolic flux in mammalian cells at the single cell level and to develop the RAMS method to isolate cell populations with altered metabolic flux. This technology development will be applied to previously intractable research questions such as the transfer of metabolites between cells and the effects of drugs on an

*References:

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individual cell basis with spatial resolution. Cell populations with divergent metabolism isolated by RAMS will be linked to downstream single cell cultivation and single cell -omics to enable, at last, a link between RNA expression of metabolic pathways and the metabolism itself. This will be a major improvement in technology to understand metabolic networks.

This multidisciplinary project will be carried out between the Departments of Engineering, Oncology and the Novo Nordisk Research Centre Oxford under the supervision of Professor Huang, Professor Harris, and Dr Ruby, respectively. Prospective students will develop specialized technical expertise in Raman spectroscopy and Raman activated cell sorting, including AI approaches to data analysis, in Professor Huang's Synthetic Biology & Single Cell Biotechnology group. Additionally by working with Professor Harris and Dr Ruby they will gain hands-on experience working with cancer cell lines and primary cells, as well as single cell RNA sequencing, and knowledge of the role of metabolic flux (e.g. glycogenolysis, lipogenesis, lipolysis) in cancer and cardiometabolic disease.

Attributes of suitable applicants:

Ideal candidates for this PhD studentship will have strong academic background (1st or 2.1 BSc) in a relevant scientific subject with requisite computational skills. Organisational skills, personal drive and ability to work well with others are essential in a suitable candidate. Genuine fascination in metabolism and curiosity to develop novel metrics of metabolic flux is greatly appreciated.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council BBSRC. BBSRC eligibility criteria apply (https://www.ukri.org/files/legacy/publications/rcuk-training-grant-guide-pdf/ Annexe 1). EU nationals who do not meet BBSRC residence criteria are encouraged to contact the programme administrator to check their eligibility for BBSRC funding before submitting a formal application. Successful students will receive a stipend of no less than the standard RCUK stipend rate, currently set at £15,285 per year, which will usually be supplemented by the industrial partner.

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 be able to take full advantage of the training and networking opportunities available through the DTP. For further, details please visit www.biodtp.ox.ac.uk.