**University of Leicester**

**Future 50 PhD Scholarship**

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| **Project Reference** | RI IPH Shaw |

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| **First Supervisor** | Prof Jacqui A Shaw | | |
| **School/Department** | Genetics and Genome Biology | | |
| **Email** | Js39@le.ac.uk | **Telephone Ext** | 3148 |

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| **Second Supervisor** | Ricky Joshi | | |
| **School/Department** | GGB | | |
| **Email** | Rsj17@le.ac.uk | **Telephone Ext** |  |

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| **Additional Supervisor** | Dr Bookie (Ayodele) Olubukola, Consultant Medical Oncologist UHL (Olubukola.ayodele@uhl-tr.nhs.uk) |

**Section 2 – *Project Information***

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| **Project Title** | Circulating RNA as a liquid biopsy for cancer detection and tissue-of-origin prediction | |
| **Project Highlights:** | 1. | Comparison of RNA profiles in plasma of patients with breast cancer with circulating tumour DNA (ctDNA) in the same patients and samples - does the combined use of ctDNA and circulating RNA expand the opportunities for precision treatment, and monitoring treatment response? |
| 2. | Comparison of plasma RNA profiles with RNA profiles of circulating tumour cells (CTCs) in the same patient blood samples – determining which RNA source is more useful. |
| 3. | Use of Oxford Nanopore technology (ONT) sequencing workflows for full transcript sequence analysis and tissue of origin prediction |
| **Project Summary** | | |
| This project seeks to investigate circulating RNA as a liquid biopsy (LB) of breast cancer, and compare this to detection of circulating tumour derived DNA termed (ctDNA). The majority of liquid biopsy studies in breast cancer to date have focused on analysis of plasma ctDNA and circulating tumour cells (CTCs). Work by our group has shown that additional information can be derived from combined analysis of ctDNA and CTCs from the same blood sample, highlighting clinically-actionable gene changes that are acquired with disease progression.  The hypothesis to be tested in this studentship is that analysis of the RNA cargo of blood plasma is needed to robustly define the full repertoire of LB analyses. A recent study reported the first transcriptome-wide characterization of circulating free RNA (cfRNA) in cancer including 46 patients with stage 3 breast cancer. Results suggest the potential for both cancer detection and tissue-of-origin prediction. Since plasma ctDNA and RNA may originate from different cell populations within the tumour, we propose that the combined use of ctDNA and RNA will expand the opportunities for treatment stratification, monitoring response, emergence of resistance and potentially early detection of cancer.  The student will determine the optimum workflow for maximum recovery of plasma RNA for subsequent transcriptomic analyses and apply this to plasma samples from 50 patients with breast cancer. In collaboration, we are developing simple workflows on the ThermoFisher Kingfisher platform to maximise recovery of cfRNA from plasma for transcriptomic profiling and to separately isolate CTCs for CTC transcriptomics. The student will profile RNA from plasma and/or CTCs and compare this to paired plasma ctDNA. In an exciting development, the Oxford Nanopore Technologies Promethion platform will be used to generate full length transcript data and plasma ctDNA data, and raw reads will be processed using standard algorithms available at the ONT github repository (<https://github.com/nanoporetech>).  Results will be used to compare the sensitivity and specificity of RNA and ctDNA detection in the same patients and samples.  The supervisory team will support wet lab aspects in the Shaw lab, informatics in the Joshi group and patient recruitment with samples collected to the local cancer biobank through Dr Ayodele’s clinics. | | |