Primary supervisor: Richard Lee **Institution:** ICR

Project title:
Lung cancer early detection: novel liquid biopsy technologies with a metabolomics focus

Project summary:
Lung cancer is the commonest cause of cancer deaths in the UK and worldwide, largely due to late stage diagnosis. 'Targeted Lung Health Checks' identify early stage lung cancers by screening people with high-risk smoking history, with 20-26% reduction in lung cancer mortality (NLST/NELSON trials). NHS England has initiated a £100M+ Targeted Lung Health Check Program that will scan in early phases in excess of 100,000 patients with Low Dose CT nationally (Co-Led by Dr Lee), highlighting the growing importance of this area, also under review by the National Screening Committee for consideration of full national roll-out in 55-74 year olds. RM Partners is one of the lung health check sites with blood specimens for biomarker development already collected in over 800 participants as part of the LHC Biomarker Study (REC 19/LO/1887 CI Lee).

A key problem is that detection of small, indeterminate tumours called nodules on these scans is common and results in considerable resource burden and psychological harm. In the NELSON study, 27,053 CT scans identified 2,503 indeterminate findings – 243 (10%) were diagnosed with lung cancer at a subsequent scan. Existing literature reports that 3-11% of lung nodules are malignant. Evolving 'Liquid biopsies' can reveal tumour material secreted into the blood to genotype or phenotype cancer traits for more personalised diagnostic and treatment approaches. Whilst interest has advanced in ctDNA and methylation technologies, it is recognised that other biomarker technologies are needed to address the limitations of these assays.

Malignant tumours often have their specific metabolic hallmarks, however, these metabolites secreted by tumours undergo enormous systemic dilution, making their detection in blood or urine extremely challenging. We will pursue a different strategy, focusing on the isolation of tumour-derived extracellular vesicles and using them as a diagnostic proxy for the early detection and subtyping of lung cancer.

Through an existing collaboration between the Convergence Sciences Centre, NHLI, and Phenome Centre at Imperial College, the candidate will combine novel genomics and metabolomics biomarker technologies to improve false positive/negative rates in those with indeterminate findings e.g. lung nodules.

Supervisory team:
Richard Lee (ICR), Miriam Moffatt (Imperial), William Cookson (Imperial)

Clinical specialties:
Respiratory Medicine, Medical Oncology, Clinical Oncology, Radiology