**Project Title**  
“Illuminating the hypoxic tumour microenvironment in situ”

**Group Leader**  
Robert Bristow

**Research Group**  
Translational Oncogenomics

This 4-year PhD studentship offered in Professor Rob Bristow’s research group is based at the Cancer Research UK Manchester Institute, Manchester Cancer Research Centre, Oglesby Cancer Research Building, Manchester

A central challenge in prostate cancer research is to understand how localized primary tumours progress to become metastatic and lethal. There is growing evidence to support the idea that features of the tumour microenvironment such as hypoxia can drive the evolution of tumour sub-clones with aggressive phenotypes. Our lab previously reported that the co-presence of tumour hypoxia (based on mRNA signatures or needle electrode measurements) and genomic instability synergistically portend rapid relapse after primary treatment for prostate cancer - supporting the concept that a hostile tumour microenvironment may drive selection of a distinctive genomic profile and rapid failure due to occult metastases.

This project aims to characterise the hypoxic microenvironment in prostate cancers by capitalizing on samples collected as part of the PROXIES trial. Patients participating in PROXIES receive a dose of the hypoxia tracer molecule Pimonidazole prior to undergoing surgery to remove the diseased prostate. The successful applicant will utilize these clinical samples, analysing pimonidazole-labelled (ie hypoxic) sub-regions using cutting-edge in-situ techniques. Intra prostatic heterogeneity will be assessed in hypoxic and non-hypoxic areas for aggressive tumour clones using bulk spatial and single cell techniques to assess differential transcriptomics, proteomics and metabolomics. Positive findings will be functionally assessed using Tert-immortalised human prostate cells for resulting phenotypes. This project will reveal novel insights into the biology of hypoxic tumours and the likelihood of progression to metastasis.

**University of Manchester entry: September 2022**