# PHD STUDENTSHIP PROJECT PROPOSAL

## FUNDER DETAILS

**Studentship funded by:** The Institute of Cancer Research

## PROJECT DETAILS

**Project title:** Targeting RNA helicases to suppress aberrant androgen receptor expression and abrogate persistent androgen receptor signalling in lethal prostate cancer

## SUPERVISORY TEAM

**Primary Supervisor**
- Dr Adam Sharp

**Associate Supervisor(s)**
- Dr Paul Clarke, Dr Juan Jimenez Vacas, Dr Jon Welti

**Secondary Supervisor**
- Professor Johann de Bono

## DIVISIONAL AFFILIATION

**Primary Division**
- Clinical Studies

**Primary Team**
- Translational Therapeutics

**Site**
- Sutton

## ABSTRACT

**BACKGROUND:** Despite robust responses to abiraterone and enzalutamide which target full length androgen receptor (AR-FL) signalling, patients with advanced prostate cancer inevitably progress to lethal, treatment-resistant, prostate cancer with persistent AR signalling. Mechanisms driving resistance to these treatments include AR gene amplification, AR-FL activating mutations, and AR splice variant-7 (AR-V7) expression, none of which are impacted by currently available therapies. Therefore, novel therapeutic strategies blocking mechanisms driving persistent AR signalling are urgently needed. **HYPOTHESIS:** We hypothesise that specific RNA helicases play a critical role in AR RNA metabolism and provide a druggable therapeutic target to suppress AR-FL/V7 expression and abrogate persistent AR signalling in lethal prostate cancer. **AIMS:** (1) Determine the role of RNA helicases in AR RNA metabolism; (2) Validate RNA helicases as a novel therapeutic target to inhibit AR RNA metabolism and overcome persistent AR signalling in lethal prostate cancer; (3) Evaluate the clinical significance of RNA helicases expression in lethal prostate cancer. **IMPACT:** This innovative research proposal has the potential to develop a novel treatment strategy that could improve the outcome and quality of life for men suffering from lethal prostate cancer.
LITERATURE REFERENCES


CANDIDATE PROFILE

Note: the ICR’s standard minimum entry requirement is a relevant undergraduate Honours degree (First or 2:1).

Pre-requisite qualifications of applicants: Master’s or BSc in Biomedical Sciences (or a related subject)
| Intended learning outcomes: | • RNA analysis (RT-PCR, RNA-sequencing, RIP-sequencing)  
• Protein analysis (western blot, proteomics)  
• Molecular cloning (site directed mutagenesis)  
• Genomic manipulation (siRNA, shRNA, CRISPR)  
• Patient derived models (in vivo and in vitro)  
• Clinical biomarker validation, development and qualification (transcriptome and immunofluorescence)  
• Data analysis and Scientific writing |
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<td><strong>ADVERTISING DETAILS</strong></td>
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| Project suitable for a student with a background in: | ☒ Biological Sciences  
☐ Physics or Engineering  
☐ Chemistry  
☐ Maths, Statistics or Epidemiology |