Applications are invited for a 3 year PhD Studentship focused on Targeting BAP1 mutated mesothelioma via synthetic lethal disruption of DNA double-strand repair based at the University of Leicester, joining the Mesothelioma Research Programme.

Available to UK/EU applicants only

Project Description

There is currently a lack of effective treatment for patients with mesothelioma upon disease progression following initial chemotherapy. Individualising therapy through the use of predictive biomarkers has revolutionised the treatment of several cancers (notably breast, lung, and melanoma), yet for mesothelioma, molecularly stratified therapies are still lacking. Accordingly the NIHR-commissioned James Lind Alliance has identified this approach as a top research priority for the UK.

Loss of expression of BRCA1 is frequent in mesothelioma, however the cause and consequence of this, with respect to DNA repair, is unknown. The objective of these studies will be to determine the functional interaction between BAP1/BRCA1 and DNA repair in mesothelioma, to establish whether BRCA1 is causally associated with the BAP1 subtype of mesotheliomas.

This PhD project will test the hypothesis that inactivation of the BAP1/BRCA1 tumour suppressor axis leads to disruption homologous DNA repair in mesothelioma, exposing vulnerability can be therapeutically exploited via inhibition of poly-ADP ribose polymerase (PARP), to induce synthetic lethality in vitro and in vivo. The goal will parallel development of a phase IIa proof of concept clinical trial to evaluate PARP inhibition in DNA damage sensitive mesotheliomas, with the aim of modelling determinants of sensitivity and resistance in order to optimise effective therapy in a setting of unmet need.

This project is translationally focused and will provide excellent training in laboratory skills including cell culture, gene manipulations, cloning, mutagenesis, Crispr-Cas9 knockout, in vitro and in vivo pharmacology, and immunohistochemistry. The student will be supported by two supervisors (Fennell/Brown) with extensive PhD training experience. The research student will be supported in the laboratory by a senior (Grade 8) post-doctoral scientist, and weekly meetings will be convened to review progress in detail. Formal progress reviews at 3 months and 1 year are a mandatory component of PhD training in the University. Opportunities will be available for international presentation of research, and 1st authorship of good impact publication will be expected by the time of submission.

The College of Medicine, Biological Sciences and Psychology offers an exciting and dynamic environment for graduate education. Our PGR population currently numbers 654 and is the home for several doctoral training schemes (MRC-DTP; IMPACT, BBSRC-MIBTP the third largest in the country, MRC pathology node, collaboration on NERC-CENTA and MD) and a large number of independently funded programmes. A College Research Degrees Committee oversees and supports all research postgraduate provision; it works with the Research Committee to place postgraduate studentships within active research groups, and with the College Academic Committee and University Graduate School to ensure that training and supervision match the guidelines set out in
the University Code of Practice. Post Graduate training begins with a formal assessment of need with a supervisor followed by training need selection. Training is organised into the 4 ‘vitae domains’ and is provided by our Research and Enterprise Division or individual service units and supervisors within College Departments and Themes. Students have access to state of the art centralised biotechnology facilities and a purpose built animal facility; addressing the vulnerable skills agenda. Students are encouraged to become involved in the wider application and use of their skills set with training and practical experience of enterprise and engagement in internships. The college is the home for GENIE where many of our students gain experience in communicating research to the wider community. We have excellent facilities/programmed activities to engage PGR interaction away from the bench in the form of the general PGR Café Research, and an annual festival of post-graduate research. Our philosophy matches that of vitae to Empower researchers to make an impact in their careers and their research and to strive for excellence. Postgraduate training is firmly embedded as an integral part of College research and education strategy. In the 2016 QAA review university of Leicester was commended for ‘the continuing effective oversight of the postgraduate research student experience (QAA code: B11)’.

How to apply
Please submit a formal application using our online application system at: http://www2.le.ac.uk/research-degrees/phd/applyphd - including a CV, degree certificate/transcript, cover letter/statement of interest and names of two academic referees. On the application system use Programme of Study – Cancer Studies Research. Please make sure you include the project title and supervisor’s name with your statement of interest on the application form.

The deadline for applications is the 17th July 2017. Shortlisting and interviews (either by Skype or in person) will take place shortly after.

Funding Notes
This funded position covers £16,000 pa stipend, PhD fees at UK/EU rates for 3 years and a contribution to travel and consumables.

The Successful Candidate
The successful candidate will be jointly supervised by Professor Dean A. Fennell and Professor Karen Brown, University of Leicester and University Hospitals of Leicester NHS Trust.

Ideal candidates will have a strong background in cancer biology, pharmacology/therapeutics with a clear understanding of DNA repair deficiencies in neoplasia. Eligible candidates will have recently received an MSc and/or a First or high 2:1 BSc in a relevant subject. Due to restrictions on the funding this studentship is open to UK/EEU national students only.

Email Now
Informal enquiries may be addressed to: Dr Dean A. Fennell PhD FRCP (df132@le.ac.uk) or Dr Sara Busacca PhD (sb580@leicester.ac.uk).

For application queries, please contact Amy King (amy.king@uhl-tr.nhs.uk).

Deadline: 17th July 2017
Interviews will take place by Skype or in person shortly after the deadline.