MRC-funded IMPACT (Integrated Midlands Partnership for Biomedical Training) Doctoral Training Partnership 3.5 Year PhD Studentship available for September 2019

Department:  Department of Molecular and Cell Biology, University of Leicester
Leicester Cancer Research Centre, University of Leicester

Supervisors:  Professor Andrew Fry and Professor Karen Brown

Eligibility:  UK/EU applicants only

Project Title:  The role of Rho family GTPases in EML4-ALK driven cancer cell migration

Project Description:

Lung cancer is the leading cause of cancer-related mortality worldwide. Approximately 5% of patients express the EML4-ALK oncogenic fusion that joins the EML4 microtubule-associated protein to the tyrosine kinase domain of ALK. The majority of EML4-ALK lung cancer patients respond remarkably well to catalytic inhibitors of ALK. However, mutations in the catalytic site confer resistance and not all EML4-ALK patients respond with similar efficacy. Hence, new treatments are required.

Interestingly, alternative breakpoints create different EML4-ALK variants that have markedly different clinical outcomes and therapeutic responses. In a major recent discovery, we found that those EML4-ALK variants that bind microtubules (e.g. v3) induce a dramatic change in cell morphology and increase cell migration. Excitingly, this is consistent with EML4-ALK v3 conferring accelerated metastatic spread and worse overall patient survival.

This project will use cutting-edge molecular and cell biology techniques to test the hypothesis that members of the Rho GTPase family coordinate altered dynamics in the microtubule and actin cytoskeleton and that these underlies the observed changes in cell morphology and migration. The outcomes of this project will be a new mechanistic understanding of how EML4-ALK v3 alters cell polarity and migration, and identification of new therapeutic options for lung cancer patients.
References:


Bayliss et al. (2016) Molecular mechanisms that underpin EML4-ALK driven cancers and their response to targeted drugs. *Cell and Molecular Life Sciences* 73, 1209-1224.


Interviews will be held in the week commencing the 11th February 2019.

**Funding details:** MRC IMPACT DTP

**Entry requirements:**

Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject. The University of Leicester [English language](#) requirements apply where applicable.

**How to apply:**

Please apply via: [https://more.bham.ac.uk/mrc-impact/phd-opportunities/](https://more.bham.ac.uk/mrc-impact/phd-opportunities/)

**Project / Funding Enquiries:**

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Closing date for applications 20th January 2019