3.5 Year PhD Studentship available for September 2018

Department: Molecular and Cellular Biology

Supervisors: Professor Mark Carr mdc12@leicester.ac.uk
Dr Gareth Hall gh126@leicester.ac.uk

Eligibility: UK /EU applicants only

Project Title: Pioneering of antibody-assisted structure-based drug discovery for cancer targets

Project Description:

The Ph.D project will focus on pioneering the application of innovative antibody-assisted approaches to structure-based drug discovery and design for a selection of proteins shown to be key drivers of major human cancers. This will involve the generation of diverse panels of high affinity antibodies against several fully validated cancer drug targets to allow the identification, characterisation and exploitation of new opportunities for drug discovery.

Structures obtained for a selected portfolio of antibodies bound to target proteins will provide an essential foundation for both structure-based design and fragment-based screening approaches to obtain small molecule modulators of activity that mimic the interactions seen with antibodies, providing a novel, potentially more effective route to new small molecule therapeutics.

Project Aims and Description

The project will aim to: i) generate a diverse portfolio of VHH antibodies against a number of proteins identified as attractive cancer therapeutic targets, ii) to identify function modulating antibodies for further investigation through appropriate functional assays, iii) to use a range of biophysical approaches to characterise selected antibody-target protein complexes and iv) to obtain high resolution structures for a number of protein therapeutic targets with function modulating antibodies bound.

The project will be carried out in collaboration with LifeArc and is expected to identify new opportunities for cancer drug discovery, which could be progressed to produce new candidate therapeutics. The planned work will include a number of diverse types of cancer targets, with several immune modulating proteins, kinases and E3 ligases attractive and tractable targets for the proposed project. The project will also provide a thorough research training in many aspects of protein science, structural biology and functional assays, together with the opportunity for the Ph.D student to spend an extended period of time (4-6 months) working in LifeArc’s Centre for Therapeutics Discovery in Stevenage.
Prof. Carr’s group have very extensive experience in the expression and purification of a very diverse range of therapeutic target proteins using both bacterial and eukaryotic expression systems. We also have a significant number of current projects focussed on the determination of structures for either potential therapeutic antibodies or small molecule inhibitors bound to target proteins using both X-ray crystallography and NMR Spectroscopy.

In recent work we have used the antibody-assisted approach to identify new allosteric regulatory sites and have obtained high resolution crystal structures for complexes formed with a number of selected antibodies to determine the molecular basis of the modulation of activity. This work will now inform new opportunities for drug discovery and together with recent published work from our group on IL-16 and from others on K-ras validates the potential of this innovative approach.

References:


Funding details:

This studentship is fully funded for 3.5 years by the University of Leicester and LifeArc, with an enhanced tax-free stipend of £17,500, research costs and tuition fees at the UK/EU rate.

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:

You should submit your application using our [online application system](#).

**Apply for Molecular and Cell Biology Research / September 2018**

In the funding section of the application please indicate you wish to be considered for A College of Life Sciences Studentship

In the proposal section please provide the name of the supervisor and project title. Include a personal statement explaining why you want to be considered for this project.

Project / Funding Enquiries:
Professor Mark Carr ([mdc12@leicester.ac.uk](mailto:mdc12@leicester.ac.uk))

Dr Gareth Hall ([gh126@leicester.ac.uk](mailto:gh126@leicester.ac.uk))

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