Project Title

A multidisciplinary approach to target MYC-driven childhood cancers

About This PhD Project

Institute of Cancer Research

Supervised by Prof. Pantelis Ed Tate, Prof. Louis Chelser and Prof. Andrea Sottoriva

The student will be registered at Imperial College, leading to the award of a PhD from Imperial College, London

Project Description

Aberrant expression, mutation or amplification of the key transcription factor and oncogene MYC, and its neural homologue MYCN, defines 20% of poor-outcome adult and childhood cancers, making MYC an important, but undrugged cancer target. Aberrant MYC activity is a known driver of poor clinical outcome and resistance to chemotherapy in significant subsets of children with brain and solid tumours (glioblastoma, medulloblastoma, rhabdomyosarcoma and neuroblastoma). These tumours remain a treatment challenge and collectively account for a majority of annual deaths from cancer in children. Paediatric cancer is a highest-priority area for Cancer Research UK support under the CRUK Kids & Teens strategy, linking leading paediatric cancer scientists with investigators expert in drug discovery and development.

Our labs have made the exciting discovery that oncogenic expression of MYC/MYCN exposes a novel druggable vulnerability which can be targeted with potent and selective inhibitors of specific protein posttranslational modification (PTM) pathways. Furthermore, the Tate lab has developed a platform of chemical probe technology uniquely capable of unlocking novel mechanisms of action in protein PTM pathways, along with extremely potent and selective inhibitors of these pathways, whilst the Chesler lab has established the in vitro and in vivo models required to unpick the complex biology underlying MYCN-dependency.

As the student on this project you will be at the centre of a multidisciplinary collaboration to understand the mode of action of inhibitors targeting PTM pathways in MYCN-driven childhood cancers, with additional broad applications in a range of MYC-driven cancers. You will apply chemical proteomic tools and novel drugs currently in preclinical development to drive validation of drug targets in these pathways. Your research work will be based between the lead supervisors' labs at the state-of-the-art Molecular Sciences Research Hub at Imperial's White City campus, the Francis Crick Institute, and Centre for Paediatric Experimental Medicine at the Institute of Cancer Research. You will also interact with scientists at Myricx Pharma, a drug discovery spinout from Imperial College and the Francis Crick Institute focused on preclinical development of PTM pathway inhibitors in cancer. You will receive training in all relevant aspects of chemical biology, proteomics, cancer cell biology and in vivo models. You will also benefit from membership of the joint ICR/Imperial Cancer Research UK Convergence Science Centre.

Keywords /Subject Areas

Childhood cancers
Novel therapies
Synthetic lethality
Chemical proteomics
Post-translational modification
Chemical biology

Candidate profile

This project would ideally suit candidates with a Masters level qualification in cancer biology, chemical biology, medicinal chemistry, biochemistry or a closer related subject, with research experience in a multidisciplinary team, and a strong interest in drug target validation and novel methods in the context of cancer.

How to apply

Full details about these studentship projects, and the online application form, are available on our website, at: www.icr.ac.uk/phds Applications for all projects should be made online https://apply.icr.ac.uk/ . Please ensure that you read and follow the application instructions carefully.