ICR The Institute of Cancer Research

Job description

Postdoctoral Training Fellow: Molecular Mechanisms of Cell Cycle Regulation

Candidate Information

July 2024

Department / division:	**Molecular Mechanisms of Cell Cycle Regulation Group, Structural Biology Division**
Pay grade / staff group:	Postdoctoral Training Fellow
Hours / duration:	Full time (35 hours per week), fixed term for 3 years
Reports to:	Dr Claudio Alfieri, Group Leader

Context

This Wellcome Trust-funded Postdoctoral Training Fellow position is based in the *Molecular Mechanisms of Cell Cycle Regulation Group* at the Chester Beatty Laboratories, Fulham Road in London.

This project aims to investigate the molecular mechanisms of cell cycle regulation by macromolecular complexes involved in cell proliferation decisions, by combining genome engineering, proteomics and in situ structural biology.

Molecular Mechanisms of Cell Cycle Regulation Group

The cell cycle is the fundamental biological process where the cell coordinates chromosome replication and segregation with cell growth and division.

This interdisciplinary project which combines structural and cell biology, focuses on dissecting the molecular mechanisms of cell cycle regulation mediated by macromolecular complexes.

The Alfieri lab is specialised in studying these complexes [1-5] by using a combination of protein complex reconstitution, biochemical analysis,

wellcome

Our mission is to make the discoveries that defeat cancer.

structural characterization by cryo-EM and functional analysis in cell lines.

References:

[1] ALFIERI, C., CHANG, L. & BARFORD, D. 2018. Mechanism for remodelling of the cell cycle checkpoint protein MAD2 by the ATPase TRIP13. *Nature,* 559**,** 274-278.
[2] ALFIERI, C., CHANG, L., ZHANG, Z., YANG, J., MASLEN, S., SKEHEL, M. & BARFORD, D. 2016. Molecular basis of APC/C regulation by the spindle assembly checkpoint. *Nature,* 536**,** 431-436.
[3] ALFIERI, C., TISCHER, T. & BARFORD, D. 2020. A unique binding mode of Nek2A to the APC/C allows its ubiquitination during prometaphase. *EMBO Rep,* 21**,** e49831.
[4] KOLIOPOULOS, M. G., MUHAMMAD, R., ROUMELIOTIS, T. I., BEURON, F., CHOUDHARY, J. S. & ALFIERI, C. 2022. Structure of a nucleosome-bound MuvB transcription factor complex reveals DNA remodelling. Nat Commun, 13, 5075.
[5] WAN, M. S. M., MUHAMMAD, R., KOLIOPOULOS, M. G., ROUMELIOTIS, T. I., CHOUDHARY, J. S., ALFIERI, C. (2023) Mechanism of assembly, activation and lysine selection by the SIN3B histone deacetylase complex. Nat Commun 2023, 14 (1), 2556.

This position is offered on a fixed term contract for 3 years initially. Starting salary is in the range of £35,844* to £42,372 per annum inclusive based on previous postdoctoral experience. In addition to annual performance related pay awards, the salary scales are reviewed annually to consider cost of living increases. The position is based at the ICR site in Chelsea. Annual leave entitlement is 28 days per annum. There is an additional entitlement to 8 bank/public holidays and 3 ICR-set privilege day.

(*£35,844 for thesis submitted, awaiting PhD award)

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Main purpose of the job

We are seeking a motivated and ambitious candidate for a Postdoctoral Training Fellow position to study the mechanisms of cell cycle regulation by macromolecular complexes which function as cell proliferation switches. Synchronised expression of cell cycle genes requires the action of specific transcriptional regulators which recognise cell cycle genes promoters and drive their cell cycle dependant transcription.

A key regulator of cell cycle dependant transcription that we study in my lab is the evolutionary conserved five-subunit (i.e. RbBP4, LIN9, LIN37, LIN52 and LIN54) protein complex named MuvB and its associated factors.

MuvB is a remarkably interesting transcriptional regulator because of its peculiar dual function as a transcriptional activator and repressor. This “yingyiang” activity of MuvB is crucial for both cell cycle exit and cell proliferation. MuvB represses around 1000 genes during a cell cycle arrest and by changing associated factors and post-translational modifications, it switches from a transcriptional repressor to an activator during the G2/M cell cycle phase transition in proliferating cells.

The key goal of our research program is to understand how the transcriptional regulator MuvB switches from repressor to activator and how this impacts cellular proliferation decisions within the cell cycle and in cancer.

Within this project the candidate will work in a multi-disciplinary project involving (i) native purifications of MuvB complexes from human RPE1-hTERT cells, and mass spectrometry analysis of their interactions with associated factors and complexes with enzymatic activity, and post-translational modifications (PTMs) that accompany the MuvB switch (ii) cell biology to investigate cellular localisation changes in different cell cycle stages through live cell imaging, super-resolution microscopy and in situ structural biology, Correlative Light and Electron Microscopy (CLEM).

Within this role the candidate will collaborate with other labs within the institute (Jyoti Choudhary, Alex Radzisheuskaya and Jörg Mansfeld) and will have the opportunity to supervise other group members.

Prior experience with cellular biochemistry is essential, experience with *in situ* structural biology is desirable.

The candidate will work in the *Molecular Mechanisms of Cell Cycle Regulation Group* within the ICR Division of Structural Biology headed by Prof. Laurence Pearl and Prof. Sebastian Guettler. The division has state-of-the-art facilities for protein expression and biophysics/x-ray crystallography, in particular the Electron Microscopy Facility is equipped with a Glacios 200kV with Falcon 4i detector with Selectris energy filter and the ICR has access to Krios microscopes via eBIC and the LonCEM consortium. The candidate will collaborate with labs within the ICR Division of Cancer Biology and with the ICR Light Microscopy Facility. The candidate will also collaborate with the state-of-the-art Proteomics Core Facility headed by Jyoti Choudhary.

Further information

You may contact Dr Claudio Alfieri for further information by emailing claudio.alfieri@icr.ac.uk. This job description is a reflection of the current position and is subject to review and alteration in detail and emphasis in the light of future changes or development.

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Duties and responsibilities

Key duties

Apply state-of-the-art cell biological, biochemical and structural methods to develop and deliver own research projects in collaboration with other members of the Molecular Mechanism of Cell Cycle Regulation Group.
Analyse, interpret, and communicate experimental results through both written reports and effective data visualisation
Analysis of relevant literature to establish new methods and to contribute developing experimentally testable hypotheses
Maintain effective and scientifically rigorous processes and procedures to support research
Present research findings in lab meetings and internal/external conferences and meetings
Work in a flexible but organised manner
To work in a flexible but organised manner
To meet objectives within pre-determined timescales
Familiarise yourself with the ICR's approach towards risk management including its policies and procedures, which require all staff to play an active part in identifying and managing risk
Any other duties, which may be required, which are consistent with the nature and grade of the post

Workforce Agreement for Postdoctoral Training Fellows

The ICR has a workforce agreement stating that Postdoctoral Training Fellows can only be employed for up to 7 years as PDTF at the ICR, providing total postdoctoral experience (including previous employment at this level elsewhere) does not exceed 10 years.

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General

All staff must ensure that they familiarise themselves with and adhere to any ICR policies that are relevant to their work and that all personal and sensitive personal data is treated with the utmost confidentiality and in line with the General Data Protection Regulations.
Any other duties that are consistent with the nature and grade of the post that may be required.
To work in accordance with the ICR's Values.
To promote a safe, healthy and fair environment for people to work, where bullying and harassment will not be tolerated.

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Person specification

Education and Knowledge

PhD in biochemistry, cell biology, molecular biology or similar	Essential
Broad knowledge in the fields of genome stability and cancer biology	Essential
Demonstrate an interest in the relevant scientific literature	Essential

Skills

Demonstrable laboratory techniques and trouble-shooting skills	Essential
Proven organisational skills and record keeping	Essential
Strong analytical skills and attention to detail	Essential
Excellent computer literacy and ability to analyse images using tools such as ImageJ or CellProfiler	Essential
Scripting skills using a language such as Python, MATLAB, or Mathematica	Desirable
Sequence analyses with publicly available databases (e.g., NCBI/TCGA)	Essential
Excellent communication skills, written (including scientific writing) and oral	Essential
Ability to work as part of a team	Essential
Willingness to learn new skills	Essential

Experience

Proven experience in working with human cells (sterile human tissue cell culture technique)	Essential
Proven experience in state-of-the-art molecular biological techniques	Essential
Experience in light microscopy and flow cytometry	Essential
Experience Immunostaining and Immunoblotting analyses	Essential
Experience in CRISPR/Cas9-mediated genome engineering or knock-out	Essential
Experience in standard biochemical techniques	Essential
Experience with *in situ* structural biology	Desirable

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About our organisation

The Institute of Cancer Research, London, is one of the world's most influential cancer research institutions with an outstanding track record of achievement dating back more than 100 years. Our mission is to make the discoveries that defeat cancer.

As well as being one of the UK's leading higher education institutions in research quality and impact, the ICR is consistently ranked as one of the world's most successful for industry collaboration. As a member institution of the University of London, we also provide postgraduate higher education of international distinction.

We are also a charity and rely on the support of partner organisations, funders, donors and the general public.

Read more to find out about our history, culture, and achievements, and how our funders, supporters and partnerships help drive our work.

Our values

The ICR has a highly skilled and committed workforce, with a wide variety of roles, each requiring different skills. But whether you work as a researcher, or work as part of our corporate team, your work and behaviour is underpinned by these six values. They are what bring us together as one team - as 'One ICR'.

> ***Our values set out how each of us at the ICR, works together to meet our mission – to make the discoveries that defeat cancer.*** *They summarise our desired behaviours, attitudes and culture – how we value one another and how we take pride in the work we do, to deliver impact for people with cancer and their loved ones."*
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> **Professor Kristian Helin**
> **Chief Executive**