



Postdoctoral Training Fellow, Chromosomal Translocations & Intracellular Antibody Group

Candidate Information

April 2022

The Institute of Cancer Research

About our organisation

We are one of the world's most influential cancer research institutes with an outstanding record of achievement dating back more than 100 years. We are world leaders in identifying cancer genes, discovering cancer drugs and developing precision radiotherapy. Together with our hospital partner The Royal Marsden, we are rated in the top four centres for cancer research and treatment worldwide.

As well as being a world-class institute, we are a college of the University of London. We came top in the league table of university research quality compiled from the Research Excellence Framework (REF 2014).

We have charitable status and rely on support from partner organisations, charities, donors and the general public.

We have more than 1000 staff and postgraduate students across three sites – in Chelsea and Sutton.

Division of Cancer Therapeutics, Chromosomal Translocations Group

Professor Terry Rabbits' research is focused on with new strategies using intracellular antibodies and derivatives for therapy aimed at hard-to-drug chromosomal translocation gene products. The research of the group is multi-disciplinary, integrating molecular and cellular biology,

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intracellular antibody design, chemical biology, drug discovery and structural biology.

We are focussed on with new strategies for therapy aimed at chromosomal translocation gene products, like LMO2 and translocation protein fusions, and hard-to-drug proteins, like mutant RAS and MYC. The RAS family of oncogenic proteins is the most mutated in human cancer with the KRAS isoform being the most frequently mutated protein. We have used intracellular antibodies that bind preferentially to activated RAS in cancer to develop chemical surrogates of the antibody binding site in a technology termed Antibody derived compound technology (Abd). The Abd approach can be applied to hard-to-drug targets where the recombinant protein cannot easily be made but also to find protein-protein interaction inhibitors where the exact protein-protein interaction partner is not known. Applying this to RAS allowed us to develop chemical series that bind near the switch region and act as PPI inhibitors.

By implementing the Abd technology with a KRAS-selective intracellular antibody, we have recently identified a set of chemical hits that require characterization and enhancement. This aim of the project requires the further biophysical and biochemical assessment of the KRAS-specific chemical matter, followed by hit to lead development towards the goal of KRAS binding compounds for the treatment of KRAS-mutant cancer.

The long-term goal is to consolidate generic strategies for deploying intracellular antibodies as lead molecules for specific forms/family members or other variants, such as splice variants. This will lead to general methods for drug discovery in cancer treatment and in other diseases.

Our mission
is to make the
discoveries that
defeat cancer.

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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'.



Pursuing excellence

We aspire to excellence in everything we do, and aim to be leaders in our field.



Acting with Integrity

We promote an open and honest environment that gives credit and acknowledges mistakes, so that our actions stand up to scrutiny.



Valuing all our people

We value the contribution of all our people, help them reach their full potential, and treat everyone with kindness and respect.



Working together

We collaborate with colleagues and partners to bring together different skills, resources and perspectives.



Leading innovation

We do things differently in ways that no one else has done before, and share the expertise and learning we gain.



Making a difference

We all play our part, doing a little bit more, a little bit better, to help improve the lives of people with cancer.



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.”

Professor Kristian Helin
Chief Executive

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Job description

Department / division:	Division of Cancer Therapeutics
Pay grade / staff group:	Postdoctoral Training Fellow
Hours / duration:	Full time (35 hours per week), Monday to Friday. Fixed term contract until 31 August 2023
Reports to:	Professor Terry Rabbitts
Main purpose of the job:	Develop KRAS-specific compounds derived using intracellular antibodies

Duties and responsibilities:

Work with and improve new KRAS-binding compounds
Conduct structural analysis of binding of compounds to RAS protein
Perform in vitro biochemical and biophysical assays to determine the binding characteristics of the RAS-binding compounds
Perform cell-based assays to assess efficacy of RAS-binding compounds
Prepare reports of results for oral or written presentations at internal and external meetings and for publication in scientific journals or patents
Ensure that work conforms to the requirements of COSHH, Local Rules for Health and Safety, Home Office regulations and other Codes of Practice as required by the ICR Safety Policy
Work and communicate effectively with other members of the Team, and external collaborators

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

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 (or equivalent) in molecular/structural biology or chemical biology	E
Strong knowledge of chemical biology and biophysical methods	E
Strong knowledge of protein structure analysis	E
Strong knowledge of RAS biology in cancer	E
Deep knowledge of molecular immunology	D

Skills

Recombinant protein expression and purification	E
Structural biology analysis including X ray crystallography and NMR	E
Molecular biology techniques, including PCR, cloning, mutagenesis	E
Cell biology, such as western blotting, flow cytometry, immunofluorescence	E
RAS protein bioassays	E
Synthesis of organic compounds	D
Systemic delivery protocols in pre-clinical models	D

Experience

Experience with protein-ligand interaction methods, such as AlphaLISA, surface plasmon resonance	E
Experience with recombinant protein preparation and purification in E coli and mammalian cells	E
Experience with biophysical methods, such as fluorescence polarization, ITC, waterLOGSY	E
Experience with mammalian protein-protein interaction cell assays, such as BRET	E
Experience with X-ray crystallography structure determination	E
Use of computational software to study compound analogues and protein-ligand interaction, such as DOCKING or similar	E
Hands on experience with organic chemistry synthesis	D
HO Personal Licence	D
Proven publication record in high impact peer-reviewed journals	D

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Benefits

We offer a fantastic working environment, great opportunities for career development and the chance to make a real difference to defeat cancer. We aim to recruit and develop the best – the most outstanding scientists and clinicians, and the most talented professional and administrative staff.

The annual leave entitlement for full time employees is 28 days per annum on joining. This will increase by a further day after 2 years' and 5 years' service.

Staff membership to the Universities Superannuation Scheme (USS) is available. The USS is a defined benefit scheme and provides a highly competitive pension scheme with robust benefits. The rate of contributions is determined by USS and details of the costs and benefits of this scheme can be found on their website. If staff are transferring from the NHS, they can opt to remain members of the NHS Pension Scheme.

We offer a range of family friendly benefits such as flexible working, a parents' group, and a maternity mentoring scheme. Other great benefits include interest free loans for discounted season tickets for travel and bicycle purchases, access to the NHS discounts website, a free and confidential Employee Assistance Programme which offers a range of well-being, financial and legal advice services, two staff restaurants, and access to a gym and sporting facilities at our Sutton site.

Further information

You may contact Prof. Terry Rabbits for further information by emailing terry.rabbits@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.