ICR The Institute of Cancer Research

Postdoctoral Training Fellow:

In situ structural biology

Candidate Information

February 2025

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 second in the league table of university research quality compiled from the Research Excellence Framework (REF 2021). 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.

Academic Services

At the ICR we aim to defeat cancer through scientific excellence, innovation and partnership. These principles also underpin our approach to scientific infrastructure, which is among the very best of any research centre in the UK. ICR benefits from our continual investment in world-leading scientific services that combine cutting-edge equipment with a highly skilled workforce.

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Structural Biology of Cell Signalling Team, Divisions of Structural Biology and Cancer Biology

Work in the Structural Biology of Cell Signalling Team, led by Professor Sebastian Guettler, in the ICR Divisions of Structural Biology and Cancer Biology centres on the molecular mechanisms of Wnt/β-catenin signalling and telomere maintenance, both of which play key roles in stem cells and a wide range of cancers. A core interest of the team is to understand how ADP-ribosylation, a complex and extremely versatile post-translational modification, controls both of these systems, and how ADP-ribosyltransferases are themselves regulated.

We seek a **Postdoctoral Training Fellow** to investigate the structure of macromolecular assemblies *in situ*, using cryogenic fluorescence microscopy and cryo-electron tomography (**cryo-ET**), with a particular focus on the mechanisms of the ADP-ribosyltransferase tankyrase. The Team Member will be supported by ICR's Light and Electron Microscopy Facilities and benefit from recent investments into *in situ* structural biology at the ICR. These include a Leica EM GP2 plunge freezer, an EM ICE high-pressure freezer, an Ultracut ultramicrotome with an FC7 cryo-chamber, a STELLARIS 5 cryo-confocal microscope, and a Thermo Fisher Scientific Selectris energy filter for ICR's Glacios TEM. We further have access to a 300-keV Titan Krios TEM, based at the Francis Crick Institute, as members of the London Consortium for Cryo-EM (LonCEM), as well as FIB-SEM and Titan Krios Instruments at the Electron Bio-Imaging Centre (eBIC) at the Diamond Light Source through a Block Allocation Group with regular experimental slots. An initiative to establish FIB-SEM at the ICR is under way.

For more information on our work, please refer to the publications below and visit our lab website https:/sguettlerlab.org. General information on Postdocs at the ICR can be found here: https://www.icr.ac.uk/study-and-careers/careers-at-the-icr/postdocs.

Pillay, N., Mariotti, L., Zaleska, M., Inian, O., Jessop, M., Hibbs, S., Desfosses, A., Hopkins, P.C.R., Templeton, C.M., Beuron, F., Morris, E.P., and Guettler, S. (2022). Structural basis of tankyrase activation by polymerization. Nature 612(7938), 162-169.

Ranes, M., Zaleska, M., Sakalas, S., Knight, R., and Guettler, S. (2021). Reconstitution of the destruction complex defines roles of AXIN polymers and APC in β-catenin capture, phosphorylation, and ubiquitylation. Molecular Cell 81, 3246–3261.e11.

Pollock, K., Liu, M., Zaleska, M., Pfuhl, M., Collins, I., Guettler, S. (2019). Fragment-based screening identifies molecules targeting the substrate-binding ankyrin repeat domains of tankyrase. Sci Rep 9, 19130.

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:	Structural Biology and Cancer Biology
Pay grade / staff group:	Postdoctoral Training Fellow
Hours / duration:	Full time (35 hours per week), Fixed term contract for three years with possibility of extension
Reports to:	Sebastian Guettler
Main purpose of the job:	*In situ* structural characterisation of signalling assemblies by cryo-CLEM and cryo-ET

Duties and responsibilities:

Together with team members and collaborators, to shape and conduct a multidisciplinary, innovative research programme both through intellectual and experimental contributions, and to lead *in situ* structural biology initiatives in the laboratory
To generate mammalian cell lines with endogenous fluorescent tags for *in situ* imaging
To prepare samples for imaging by cryo-fluorescence microscopy and cryo-ET, including cell culture, vitrification, cryo-ultramicrotomy and FIB-SEM, and image these by cryo-ET
Together with colleagues in ICR's Light Microscopy and Electron Microscopy Facilities, to develop and optimise workflows for the structural characterisation of macromolecular complexes *in situ* using cryo-fluorescence microscopy, cryo-EM and cryo-ET
To work with colleagues at the Electron Bio-Imaging Centre (eBIC) at the Diamond Light Source, the Francis Crick Institute and the ICR to prepare samples by FIB-SEM for imaging by cryo-ET
To acquire and process cryo-EM and cryo-ET data
To interpret experimental findings, generate and test hypotheses of molecular mechanisms informed by structural studies, and to plan future experiments
To work both independently and collaboratively, and to consult when appropriate
To familiarise yourself with the use and maintenance of specialised laboratory equipment
To work in a flexible but organised manner to meet objectives and deadlines
To maintain accurate records of experiments and data, in accordance with ICR regulations
To further develop a knowledge of the literature in the subject areas studied by the laboratory
To present your work in seminars and participate in journal clubs
To draft and co-write research publications resulting from the project
To attend scientific conferences and courses, as agreed with the Group Leader
To contribute to the academic life and positive research culture of the laboratory, and by extension that of the ICR

To interact with the Group Leader and other Team and Division Members, fostering a positive working environment
To contribute to the supervision and training of junior staff
Any general laboratory duties that will be shared with other Members of the team

General

All Staff must ensure 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.

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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Person specification

Education and Knowledge

PhD in a biological science or any other area relevant to the laboratory's research	Essential
Evidence of contributing to research publications	Essential

Skills

Demonstrable ability to design and conduct experiments	Essential
Demonstrable skills in cryo-EM (sample preparation, data collection, data processing, model building) and a strong desire to learn *in situ* structural biology approaches (cryo-fluorescence microscopy, cryo-ET)	Essential
Demonstrable skills in mammalian cell culture	Desirable
Demonstrable skills in cryo-CLEM and cryo-ET	Desirable
Demonstrable skills in recombinant DNA techniques (cloning)	Desirable
Competent at laboratory techniques, including protocol development and optimisation, problem solving, and troubleshooting	Essential
Ability to work effectively and efficiently, both independently and as part of a team	Essential
Good observation skills, attention to detail and ability to keep appropriate records	Essential
Proficient IT skills, including those required for specialist structural biology applications	Essential
Excellent oral and written communication skills	Essential
Excellent organisational skills.	Essential
Excellent interpersonal skills with the ability to establish effective working relationships	Essential
Independent scientific thinking and readiness to acquire a solid knowledge of the literature relevant to the project	Essential
Enthusiasm to actively develop and shape an innovative research project	Essential
Committed to learning new techniques/approaches required for the project	Essential

Experience

Solid experience in cryo-EM, including data collection, data processing and model building	Essential
Experience in *in situ* structural biology (cryo-fluorescence microscopy, cryo-ET)	Desirable

Benefits

as a minimum requirement candidates must have submitted their thesis by the start date of their employment and awarded their PhD within the six month probationary period.

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 Sebastian Guettler for further information by emailing sebastian.guettler@icr.ac.uk. This job description reflects the current position and is subject to review and alteration in detail and emphasis in the light of future changes or development.