

Job description

Postdoctoral Training Fellow: Target and E3 Ligase Discovery, Biology, Centre for Protein Degradation

Candidate Information

October 2024

| Department / division: | Centre for Protein Degradation, Division of Cancer Therapeutics |
|--------------------------|--|
| Location: | Sutton, on site |
| Pay grade / staff group: | Postdoctoral Training Fellow: £41,600 – £48,200 per annum* * £35,844 until PhD award |
| Hours / duration: | Full time (35 hours per week), Monday to Friday. Fixed term contract for 3 years in the first instance. |
| Reports to: | Dr Agnieszka Konopacka, Group Leader, Induced Proximity Therapeutics, ICR Centre for Protein Degradation, Centre for Cancer Drug Discovery. |

Our mission is to make the discoveries that defeat cancer.

Context

The ICR Centre for Protein Degradation has been established to accelerate targeted protein degradation-based drug discovery — an innovative approach utilizing drug-induced degradation of harmful proteins *via* cell endogenous protein disposal system. Our aim is to discover novel molecular glue degraders and PROTACs for treatment of the most challenging cancers. Based at the ICR's Centre for Cancer Drug Discovery (CCDD) the CPD benefits from state-of-the-art drug discovery platforms — medicinal chemistry, biology, biophysics, structural biology, proteomics, computational modelling, as well as strong cancer biology and clinical expertise within the CCDD, the ICR and the Royal Marsden

Hospital. We also have established collaborations with biotech and pharma industry.

The Induced Proximity Therapeutics team within the Centre for Protein Degradation focuses on biology aspects of targeted protein degradation drug discovery and supports the CPD in the following areas of research: 1) drug screening, profiling and molecular mechanism of action, 2) target identification and validation, 3) characterisation of novel E3 ligases. This role will focus on discovery of novel targets and E3 ligases for induced proximity therapeutics (areas 2 & 3).

The postholder will be working in a multidisciplinary team in the Centre for Protein Degradation (CPD) on **discovery and validation of novel molecular glue and PROTAC targets and E3 ligases** for challenging oncology indications, contributing to our exploratory and drug discovery projects.

This position is suitable for a strong team player passionate about innovative solutions for cancer drug discovery. They should have a solid background in **cancer cell and molecular biology**, and hands-on experience in **cell biology** and *in vitro* genetic manipulation techniques applicable for target validation and interrogation of cell signalling pathways. Experience in targeted protein degradation, biochemical and pharmacology assays would be an additional advantage.

The position is offered on a **3-year fixed-term** contract in the first instance*. Starting salary is in the range of £41,600 – £48,200 per annum depending on experience † .

- * Postdoctoral Training Fellows can be employed for maximum 7 years as postdocs at ICR, providing total postdoctoral experience (including previous employment at this level elsewhere) does not exceed 10 years.
- † If the candidate has completed their viva but has not yet been awarded their PhD, the starting salary will be £35,844, pre-PhD level. Progression to the full PDTF scale will commence once confirmation of PhD award is received. Award must be provided within 6 months of start date.

Annual leave entitlement is **28 days per annum**. There is an additional entitlement to 8 bank/public holidays and 3 ICR-set privilege days.

Main purpose of the job

The primary focus of this role will be to discover and validate novel molecular glue and PROTAC targets and E3 ligases for challenging oncology applications.

Further information

You may contact Dr Agnieszka Konopacka for further information by emailing Agnieszka.Konopacka@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.

Key duties

Duties and responsibilities

Perform experiments to validate targets for novel molecular glue degraders (MGDs) and PROTACs, and characterise novel E3 ligases

Develop cell models for target validation and E3 ligase discovery (e.g. degron tagging, CRISPR KI/ KO, lentivirus transduction)

Design cell-based and *in vitro* assays to assess effects of target degradation and downstream signalling

Develop novel proximity technologies for biological characterisation of MGDs and PROTACs, novel targets and E3 ligases

Routinely use cell biology, genetic and pharmacological manipulation techniques to interrogate novel targets and E3 ligases

Prepare samples for proteomics, analyse and interpret data (in collaboration with the data science and proteomics groups)

Design and run experiments, analyse and interpret data

Maintain accurate electronic experimental records

Work effectively as part of a multidisciplinary team of disease and drug discovery scientists including biologists, biophysicists and chemists and with external collaborators

Keep up to date with relevant scientific literature

Prepare and present results at internal or external meetings

Prepare data for patent applications and publications

Contribute to publications, regularly present data internally and externally

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.

Person specification

Education and Knowledge

| PhD in biological/biochemical sciences | Essential |
|---|-----------|
| Knowledge of cancer cell biology | Essential |
| Expertise in molecular biology and <i>in vitro</i> genetic manipulation techniques | Essential |
| Excellent technical expertise (cell models, genetic manipulation, WB, IP, immunofluorescence imaging or flow cytometry) | Essential |
| Knowledge of targeted protein degradation and ubiquitination biology | Desirable |
| Knowledge pharmacology | Desirable |
| Knowledge of biochemistry | Desirable |

Skills

| Intellectual curiosity and strong motivation to learn novel technologies and achieve professional excellence | Essential |
|--|-----------|
| Excellent skills in cell and molecular biology techniques | Essential |
| Ability to adapt and develop technologies | Essential |
| Ability to plan, organise and prioritise work across multiple projects | Essential |
| Good oral and written communication skills | Essential |
| Great collaboration skills, including with interdisciplinary teams | Essential |
| Great computer skills (MS Office, computer software relevant to the role) | Essential |
| Great data analysis and documentation skills | |

Experience

| Experience working in cell and molecular biology lab | |
|--|--|
| Experience in molecular cloning and genetic manipulation techniques (CRISPR KO/KI, siRNA, lentivirus transduction, generation transgenic cell lines) | |
| Experience in broad range of cellular/molecular biology techniques (e.g. western blot, immunoprecipitation, immunofluorescence imaging, luminescence assays – HiBiT, ELISA, flow cytometry, nanoBRET, FRET, proximity labelling) | |
| Experience in working with cell cancer models and assays (e.g., viability, proliferation, apoptosis, migration) | |
| Experience in targeted protein degradation assays (e.g., degradation potency, ubiquitination, ternary complex) | |
| Experience in drug target validation | |
| Experience in pharmacological assays (e.g., protein degradation, binding, ternary complex) | |



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.

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

Centre for Cancer Drug Discovery at the ICR

Scientists in the Centre for Cancer Drug Discovery (CCDD) implement innovative drug discovery technologies, discover novel drug modalities

and develop these as rapidly as possible from the laboratory through to hypothesis-testing early clinical trials. We publish our work extensively and have a large network of collaborations with academia, biotechnology companies, and the pharmaceutical industry. Our drug discovery Biology teams are dedicated to translational and drug discovery research, applying molecular pharmacology and cancer biology approaches to explore the therapeutic potential of new targets, and implementing functional and mechanistic assays to support progression of new therapeutics.

Centre for Protein Degradation

Based at the ICR's Centre for Cancer Drug Discovery (CCDD) Centre for Protein Degradation (CPD) has been established to accelerate targeted protein degradation-based drug discovery - an innovative approach utilizing drug-induced degradation of harmful proteins via cell endogenous protein disposal system. The CPD benefits from state-of-the-art drug discovery platforms – medicinal chemistry, biophysics, structural biology, proteomics, computational modelling, as well as strong cancer biology and clinical expertise within the CCDD, the ICR and the Royal Marsden Hospital, as well as strong collaborations with biotech and pharma industry.

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."











Professor Kristian Helin Chief Executive