UNIVERSITY OF LEEDS

CANDIDATE BRIEF

Research Fellow in Biochemistry and Biophysics of Chaperone Function, Faculty of Biological Sciences

Salary: Grade 7 (£37,099 - £44,263 p.a.)

Reference: FBSAS1073

Available on a fixed-term, full-time basis for 39 months, with a latest start date of 1st April 2024 and latest end date of 1st July 2027 (external funding).

This role will be based on the university campus. We are open to discussing flexible working arrangements.

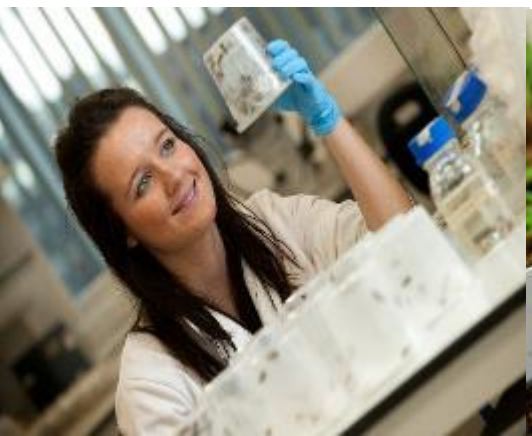
Research Fellow in Biochemistry and Biophysics of Chaperone Function,
School of Molecular and Cellular Biology, Astbury Centre for Structural Molecular Biology

Are you an ambitious researcher looking for your next challenge? Do you have an established background in protein structure and function analysis? Do you want to further your career in one of the UKs leading research intensive Universities?

Antibiotic resistance is projected to cause 10 million deaths per year by 2050, with gram-negative (diderm) pathogens comprising 9 of the 12 bacteria that pose the greatest threat to human health (World Health Organisation). These pathogens have a unique outer membrane (OM) that acts as a first line of defence against an assault from potentially harmful molecules to the bacteria, such as antibiotics. Finding ways to prevent correct assembly of the OM may therefore produce new routes to kill gram-negative bacteria, or make them more susceptible to existing antibiotics. Recently, we have been studying the mechanism by which beta-barrel outer membrane proteins (OMPs) reach the OM, how chaperones facilitate OMP delivery across the periplasm, and how the β-barrel assembly machinery (BAM) folds/inserts its clients into the OM, yielding new insights into the mechanism of OM assembly (e.g. Schiffrin et al, Commun Biol, 2022; White et al., Nat Commun, 2021; Calabrese et al, Nat Commun, 2020).

In this project we aim to gain new information about a key player in OMP assembly, the periplasmic chaperone SurA. This work builds on our previous studies, in which we have identified two key hotspot regions on SurA that are critical for OMP recognition and we are looking for a new team member to help us address the following important questions, using biochemical and biophysical tools:

- What are the sequence determinants for OMP recognition at the hotspot regions we have already identified?
- How does SurA modulate the conformational ensemble of its different OMP clients and remodel them to ensure they remain folding-competent and ready for delivery to BAM?
- How do mutations in key hotspots alter the range of OMPs found in the OM and are different hotspots on SurA responsible for binding different OMPs?



- Can we target the OMP binding hotspots on SurA as a route to new antibacterials?

Given that deletion of SurA results in OM defects, including impaired virulence factor assembly, reduced pathogenicity, induction of cell envelope stress responses, and loss of OM integrity (heightened sensitivity to antibiotics), SurA could be a good target for the development of new antimicrobial agents. However, this is hampered by a lack of mechanistic knowledge about SurA function. This project aims to address this gap in our understanding, by combining cutting edge biophysical, structural, and biochemical approaches to target this fascinating chaperone machinery.

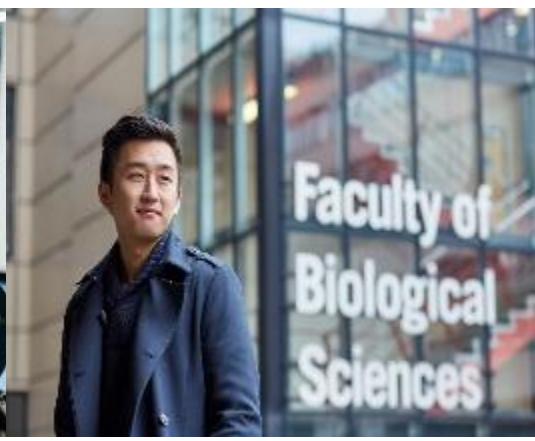
You will be based in the laboratories of Dr Antonio Calabrese, Prof Sheena Radford and Dr Anastasia Zhurvaleva, and work closely with collaborators within the Astbury Centre at Leeds. In order to answer these vital questions we will apply integrative structural biology methods, giving you an opportunity to enhance you skills and to learn different methods to study biological mechanisms in our collaborative and supportive team. You should have a PhD (or be close to completion) in Chemistry, Biochemistry, Biophysics or a related discipline. You should have significant experience in protein structure/function analysis and training in any techniques that you lack experience in will be provided.

What does the role entail?

As a Research Fellow your main duties will include:

- Designing, planning and conducting a programme of investigation, in consultation with Dr Antonio Calabrese, Prof Sheena Radford and Dr Anastasia Zhurvaleva;
- Generating independent and original research ideas and methods to study outer membrane protein biogenesis and chaperone function with an aim to extend our research portfolio;
- Studying SurA chaperone – client OMP interactions in vitro and in vivo using mutagenesis, folding experiments and other biochemical assays.
- Applying integrative structural biology techniques to study chaperone function, including using state-of-the-art structural proteomics methods, e.g. crosslinking, hydrogen-deuterium exchange, native mass spectrometry, quantitative proteomics, NMR spectroscopy and smFRET;
- Bring skills and expertise in one of the key technologies listed above, and





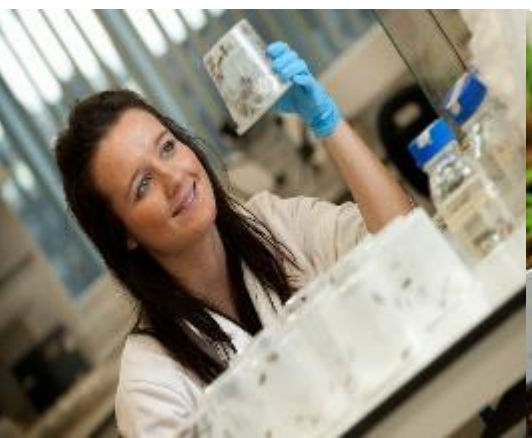
- Making a significant contribution to the dissemination of research results by publication in leading peer-reviewed journals, and by presentation at national and international meetings;
- Working independently and as part of a larger team of researchers, both internally and externally, to develop new research links and collaborations and engage in knowledge transfer activities where appropriate;
- Keeping up to date with recent advances in fields of research associated with the project;
- Contributing to the supervision of junior researchers and PhD students and acting as a mentor to less experienced colleagues;
- Evaluating methods and techniques used and results obtained by other researchers and relating such evaluations to your own research;
- To contribute to, and to encourage, a safe working environment.

These duties provide a framework for the role and should not be regarded as a definitive list. Other reasonable duties may be required consistent with the grade of the post.

What will you bring to the role?

As a Research Fellow you will have:

- A PhD (or close to completion) in Biochemistry, Chemistry, Physics, Biophysics or a closely allied discipline;
- Experience in molecular biology and recombinant protein expression.
- Substantial experience in using biophysical techniques to study protein structure and function.
- Experience in one or more of:
    - State-of-the-art mass spectrometry technologies to study protein structure/function (e.g. chemical crosslinking, native mass spectrometry, hydrogen-deuterium exchange);
    - Single-molecule FRET, NMR spectroscopy or other methods to analyse protein conformations and dynamics.
- Experience of successful collaborations and team working;
- Good data management, analytical and computer skills;
- The ability to design, execute and write up experimental work independently as well as a proven ability to work effectively and responsibly without close supervision;



- A developing track record of peer reviewed publications in international journals;
- Excellent communication skills, both written and verbal, and the ability to communicate your research at national and international conferences;
- Good time management and planning skills, with the ability to meet tight deadlines;
- A proven ability to work well both independently and as part of a team;
- Ability to work accurately and carefully;
- A strong commitment to your own continuous professional development.

You may also have:

- Experience in structural modelling, docking and molecular dynamics.
- Experience in any of the following: CD, fluorescence, SPR, ITC, X-ray crystallography, cryo-EM.

How to apply

You can apply for this role online; more guidance can be found on our How to Apply information page. Applications should be submitted by **23.59** (UK time) on the advertised closing date.

Your application should include:

- A supporting statement providing evidence to support each requirement listed on the 'What will you bring to the role' section of the Candidate Brief (no more than two sides of A4, minimum font size 11);
- An academic curriculum vitae, including a list of your publications.

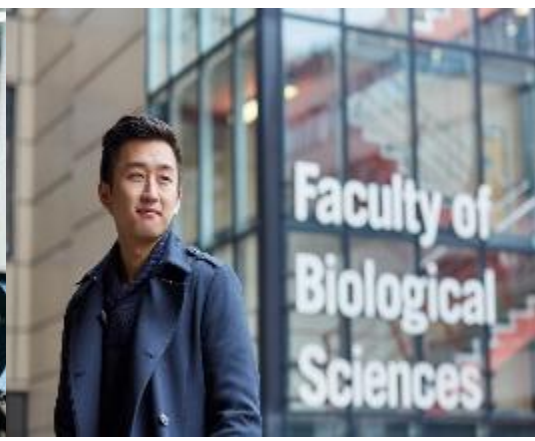
Contact information

To explore the post further or for any queries you may have, please contact:

Dr Antonio Calabrese, Sir Henry Dale Fellow and University Academic Fellow
Email: a.calabrese@leeds.ac.uk

Prof Sheena Radford, Astbury Professor of Biophysics
Email: s.e.radford@leeds.ac.uk





Dr Anastasia Zhurvaleva, Lecturer in Biological NMR Spectroscopy
Email: a.zhuravleva@leeds.ac.uk

Please note: If you are not a British or Irish citizen, from 1 January 2021 you will require permission to work in the UK. This will normally be in the form of a visa but, if you are an EEA/Swiss citizen and resident in the UK before 31 December 2020, this may be your passport or status under the EU Settlement Scheme.

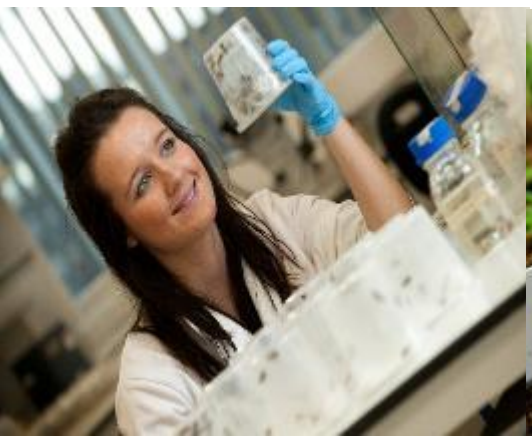
Additional information

Find out more about the Astbury Centre for Structural Molecular Biology, the Faculty of Biological Sciences and the School of Molecular and Cellular Biology. More information about the Calabrese and Radford Labs can be found at https://www.calabreselab.com. and http://sheena-radford-lab.uk/. Find out more about the research and facilities at the Astbury Centre.

At the University of Leeds, we are committed to providing a culture of inclusion, respect and equity of opportunity that attracts, supports, and retains the best students and staff from all backgrounds and from across the world. Whatever role we recruit for we are always striving to increase the diversity of our community, which each individual helps enrich and cultivate. We particularly encourage applications from, but not limited to Black, Asian, people who belong to a minority ethnic community; people who identify as LGBT+; and disabled people. Candidates will always be selected based on merit and ability.

Working at Leeds
We are a campus-based community and regular interaction with campus is an expectation of all roles in line with academic and service needs and the requirements of the role. We are also open to discussing flexible working arrangements. To find out more about the benefits of working at the University and what it is like to live and work in the Leeds area visit our Working at Leeds information page.

The University of Leeds and the Faculty of Biological Sciences are committed to providing equal opportunities for all and offer a range of family friendly policies. The University is a charter member of Athena SWAN (the national body that promotes gender equality in higher education), and the Faculty of Biological Sciences was awarded a Silver award in 2020. We are proud to be an inclusive Faculty that values all staff, and are happy to consider job share applications and requests for flexible



working arrangements from our employees. Our Athena SWAN webpage provides more information.

Candidates with disabilities
Information for candidates with disabilities, impairments or health conditions, including requesting alternative formats, can be found on our Accessibility information page or by getting in touch with us at disclosure@leeds.ac.uk.

Criminal record information

Rehabilitation of Offenders Act 1974
A criminal record check is not required for this position. However, all applicants will be required to declare if they have any 'unspent' criminal offences, including those pending.

Any offer of appointment will be in accordance with our Criminal Records policy. You can find out more about required checks and declarations in our Criminal Records information page.