Postdoctoral Research Associate in Structural Biology: Drug Discovery in Leishmaniasis

Department of Chemistry

Closing date: 6 March 2019
Interview date: to be confirmed
Vacancy reference: 7343
INTRODUCTION

The position is to work in the group of Professor Tony Wilkinson on the structural and functional characterisation of post-translational modification enzymes in Leishmania.

This MRC Global Challenges Research Fund position will study parasite enzymes including protein kinases and deubiquitinases that represent potential drug targets in Leishmaniasis. The goal of the proposed work is to contribute to the validation of new drug targets through the production and crystallisation of recombinant proteins and the determination of their three-dimensional structures to facilitate the understanding of their function and to define the binding sites for substrates and later for inhibitors. The first targets include the Otubain deubiquitinase and the aurora kinase from Leishmania donovani.

The successful candidate will work in a collaboration with the group of Jeremy Mottram in the Immunology and Infection Group in the Department of Biology at York and the group of Professor Nahid Ali at the CSIR – Indian Institute of Technology in Kolkata, India. The position offers the opportunity for cutting-edge structural and chemical biology in the field of structural parasitology in a world-renowned and friendly group.

The Department of Chemistry is one of the UK’s leading Chemistry departments and we are renowned internationally for our research. This is combined with a commitment to teaching and outstanding student satisfaction, and we have been recognised consistently for our family-friendly policies and are proud of our Athena SWAN Gold Award: http://www.york.ac.uk/chemistry/department/athenaswan/

As a Department we strive to provide a working environment which allows all staff and students to contribute fully, to flourish, and to excel. We aim to ensure that there is a supportive and egalitarian culture at all levels and across all staff groups. We promote good practice and a strong culture of equality in higher education. Further information can be found within this brief and on our website: www.york.ac.uk/chemistry/
JOB DESCRIPTION

Main purpose of the role

Conduct research on Leishmania Otubain and Aurora Kinase, under the supervision of senior colleagues

Express genes in E coli, purify and crystallise proteins, solve structures by X-ray crystallography

Study interactions using various biophysical methods

Prepare manuscripts for publication

Work in a large research group and contribute to its diverse functions

Assist in the identification and development of potential areas of research and the development of proposals for independent or collaborative research projects

Key responsibilities

To conduct individual and collaborative research projects, duties to include: analysis and interpretation of research data; use of appropriate research techniques and methods; writing up of research results and dissemination through publications, seminar and conference presentations and public engagement and outreach activities; contributing to the identification of possible new areas of research

To keep up to date with diverse literature related to the project and its techniques.

To contribute to the preparation of research proposals and applications to external bodies

To undertake appropriate organisational and administrative activities connected to the research project, including conference organisation, and the development of promotional or educational material including website maintenance and development

To develop and initiate collaborative working internally and externally, duties to include: the building of internal contacts and participation in internal networks; collaboration with colleagues on joint projects as required; participation in and identification of external networks in order to share information and identify potential opportunities for collaboration and possible sources of funding; attendance at and contribution to relevant meetings

To provide guidance to other staff and students, as required, as well as coordinating the work of small research teams

To assist with undergraduate teaching in own area of expertise; notably by the supervision of project students.

At a glance

<table>
<thead>
<tr>
<th>Salary</th>
<th>£32,236—£39,609 a year (University of York Grade 6)</th>
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<tbody>
<tr>
<td>Hours of work</td>
<td>Full-time (37 hours)</td>
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<tr>
<td>Contract type</td>
<td>Fixed-term (24 months)</td>
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<tr>
<td>Based at</td>
<td>Heslington Campus West</td>
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## PERSON SPECIFICATION

<table>
<thead>
<tr>
<th>Qualifications</th>
<th>Essential / Desirable</th>
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<tbody>
<tr>
<td>First degree in Biochemistry, Cell Biology, Chemistry or related disciplines</td>
<td>Essential</td>
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<tr>
<td>PhD in Enzymology, Cell Biology, Structural Biology, or equivalent experience</td>
<td>Essential</td>
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### Knowledge

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<tr>
<th>Knowledge</th>
<th>Essential / Desirable</th>
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<tbody>
<tr>
<td>Knowledge of post-translational modification systems</td>
<td>Essential</td>
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<tr>
<td>Knowledge of modern structural biology approaches</td>
<td>Essential</td>
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<tr>
<td>Knowledge of work in the Wilkinson group</td>
<td>Essential</td>
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<td>Knowledge of protein structure analysis</td>
<td>Essential</td>
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### Skills, abilities and competencies

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<tr>
<th>Skills, abilities and competencies</th>
<th>Essential / Desirable</th>
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<tbody>
<tr>
<td>Skill in the expression of genes</td>
<td>Essential</td>
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<td>Skill in mapping protein-ligand interactions</td>
<td>Essential</td>
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<tr>
<td>Skill in analysing enzymes, including 3D structure determination by X-ray crystallography</td>
<td>Essential</td>
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<tr>
<td>Highly developed communication skills to engage effectively with a wide ranging audience, both orally and in writing in the English language, using a range of media</td>
<td>Essential</td>
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<tr>
<td>Ability and passion to write up research work for publication in high profile journals and engage in public dissemination.</td>
<td>Essential</td>
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<tr>
<td>Ability to develop research objectives, projects and proposals for own and joint research, with the assistance of a mentor if required</td>
<td>Essential</td>
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<tr>
<td>Competency to conduct individual and collaborative research projects</td>
<td>Essential</td>
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<tr>
<td>Ability to identify sources of funding and contribute to the process of securing funds, with collaborators if required</td>
<td>Essential</td>
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<td>Competency to make presentations at conferences or exhibit work in other appropriate events</td>
<td>Essential</td>
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## PERSON SPECIFICATION

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<tr>
<th>Experience</th>
<th>Essential / Desirable</th>
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<tr>
<td>Experience of carrying out both independent and collaborative research</td>
<td>Essential</td>
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<tr>
<td>Quantifiable experience of writing up research work for publication</td>
<td>Essential</td>
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<tr>
<td>Ability to work as part of a team and also to work independently using own initiative</td>
<td>Essential</td>
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<tr>
<td>Experience in gene expression and protein purification</td>
<td>Essential</td>
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## Personal attributes

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<th>Essential / Desirable</th>
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<tr>
<td>Avid commitment to reading the scientific literature, in a pro-active manner</td>
<td>Essential</td>
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<tr>
<td>Interest in and enthusiasm for enzymology, 3-D structure, chemical biology and the project</td>
<td>Essential</td>
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<tr>
<td>Collaborative ethos, and ability to contribute to a happy and stimulating working atmosphere</td>
<td>Essential</td>
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<tr>
<td>Positive attitude to colleagues and students</td>
<td>Essential</td>
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<tr>
<td>Willingness to work proactively with colleagues in other work areas/institutions</td>
<td>Essential</td>
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<tr>
<td>Ability to plan and prioritise own work in order to meet deadlines, including using personal initiative to plan research programmes</td>
<td>Essential</td>
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<tr>
<td>Commitment to personal development and updating of knowledge and skills</td>
<td>Essential</td>
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Tony Wilkinson is in the York Structural Biology Laboratory. He has had a career-long interest in the relationship between structure, function and specificity in proteins. His group has worked on the role of phosphorylation in bacterial development. In recent years, his research has embraced parasite proteins with extended studies of parasite N-myristoyltransferases as drug targets in leishmaniasis and malaria and where the group generated proteins for high-throughput inhibitor screening and solved numerous crystal structures to guide our medicinal chemistry collaborators in increasing the potency of the resulting hits. This interest has broadened to post-translational modification systems in Leishmania through collaboration with Jeremy Mottram whose group is defining the essentiality of PTM genes in these species and defining the associated cellular functions with a view to targeting in drug discovery.

Applicants called for interview are strongly advised to have a good knowledge, and understanding, of the work in this research group and its recent publications.

The York Structural Biology Laboratory currently comprises around 70 staff and PhD students, including thirteen academic staff and one professor emerita. The laboratory’s research can be categorised broadly under three main headings:

- **Structural Biology**: The determination of the structure(s) of proteins and their complexes with other proteins, nucleic acids and ligands. Increasing use of high throughput technologies means that many hundreds of different proteins are under study at any one time, with the targets selected on the basis of their biochemical or biological function. In addition, there is great expertise in York in protein chemistry and crystallisation for tackling challenging proteins, such as multi-molecular complexes or membrane proteins. When integrated with exploration of the cell and molecular biology of the targets, the structural work is providing major insights into the molecular mechanisms underlying biological function. The laboratory has recently invested in CryoEM which will come on-stream in 2018.

- **Chemical Biology and Biological Chemistry**: The group has considerable strength in probing the chemistry of biological processes in areas such as structural enzymology, reaction mechanisms and fundamental studies of molecular interactions. There is also growing interest in biocatalysis: the discovery, optimisation and exploitation of enzymes for chemical synthesis. In addition, the group is using structure based methods to design ligands to act as chemical tools to disrupt and probe the biology of specific proteins and pathways.
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- Crystallographic Methods: York is world renowned for the development of the experimental and in particular computational methods used by crystallographers worldwide. This includes new approaches in molecular replacement and refinement (MOLREP, REFMAC) as well as increased streamlining model building into electron density (QUANTA and COOT). York is also a major centre for the UK collaborative effort in crystallographic computing, CCP4.

The Department of Chemistry

The Department of Chemistry: [http://www.york.ac.uk/chemistry](http://www.york.ac.uk/chemistry) is one of the largest and most successful academic departments at York. The Department was placed in the top ten UK universities for Research Power by the 2014 Research Excellence Framework exercise (REF). Amongst our academic staff we have five Fellows of the Royal Society and many national and international prize winners, contributing to a dynamic and thriving department. The excellence of Chemistry at York was recognised by the outstanding 3rd place in both the 2019 Guardian and Times University League Table guides and 6th place in the 2019 Complete University Guide.

The Department has nearly 60 academic staff (including teaching-only staff), more than 600 undergraduate students, approximately 160 graduate students (mainly studying for PhDs) and over 80 research associates and fellows. The Department has a group of coherent laboratories, recently extended and modernised, which provide an excellent environment for both teaching and research; £35M has been spent on new buildings and equipment in the last seven years.

Staff in the Department of Chemistry undertake research in a wide range of fields and there are particular strengths in analytical and archaeological science, atmospheric chemistry, chemical and structural biology, green chemistry, materials chemistry, metalloproteins, organometallic and catalytic chemistry, synthetic organic chemistry and time-resolved spectroscopy.

We have nearly 30 administrative staff (including those funded externally), as well as over 50 technical staff who provide assistance in the teaching and research laboratories and maintain the workshops (mechanical, glass and electronics) supporting these activities.

The undergraduate programmes, which typically attract over 1200 applications for the ca 180 places, have a flexible, modular structure with opportunities for specialisation in environmental, industrial and medicinal chemistry. There are three-year (BSc) and four-year (MChem) courses with opportunities for students to spend a year at one of a number of overseas universities or in industry. Students rated the
THE DEPARTMENT

Department with an overall satisfaction rating of 97% in the National Student Survey 2018.

The Gold Award from Athena SWAN: https://www.york.ac.uk/chemistry/ed/ for promoting women in science was won by the Department of Chemistry in 2007 and renewed in 2010 and 2015. This was the first Gold award made in this scheme. The Athena SWAN Charter recognises and celebrates good employment practice for women working in science, engineering and technology (SET) in higher education and research.

The case studies on our Equality and Diversity website: https://www.york.ac.uk/chemistry/ed/fam-friendly-work/ illustrate the variety of working arrangements of staff which are supported by the Department.

The Department of Chemistry operates a set of family-friendly practices. Staff working patterns are flexible and a formal Flexitime system is also in operation. The Department has developed a maternity and paternity leave procedure to help provide support for staff and the University has a nursery http://www.york.ac.uk/univ/nrsry/.

The Department provides support for all categories of staff in their applications for promotion, role reviews, awards, prizes and rewarding excellence nominations. Staff are encouraged to attend training events and take up opportunities for professional development including those offered by the award-winning University Learning and Development Team: http://www.york.ac.uk/admin/hr/training/. The Department strives to address diversity inequalities to ensure that there is a culture that supports equality and encourages better representation throughout the Department. Support for all staff at all stages of their career is recognised as being extremely important; individuals will be allocated a specific mentor to help support them in future career development. Social events are also held regularly for members of staff.

Opportunities for employment for partners exist across the University, Science City York or within the City of York. The Department recognises that employment for partners can be an issue for new employees and will be understanding if you raise this and will do its best to help.

The Department is committed to establishing a culture of environmental good practice and all staff are asked to go about their duties in a resource efficient way and minimise impacts to the environment wherever possible.

The University has recently invested heavily in Chemistry. The Dorothy Hodgkin Building was completed in two phases. The first, housing Analytical Science and Synthetic Chemistry, opened in 2005, while the second phase housing catalytic, materials and synthetic chemistry was completed in 2012. The department is exceptionally well equipped for NMR spectroscopy and departmental instruments are housed in a purpose-built building opened in 2006, while the Wellcome-Wolfson-funded Centre for Hyperpolarisation in Magnetic Resonance (CHyM) was completed in October 2012. The Wolfson Atmospheric Chemistry Laboratories were opened in 2013 and have recently been extended (2018 and a two-storey building housing new teaching and research laboratories (to house Green Chemistry) and offices was completed in March 2014. The department has recently secured funding from the Wellcome Trust, the Wolfson Foundation, a generous alumnus and the university to acquire a 200 kV cryo-electron microscope and a building in which to house it. Construction and installation are expected in 2019.
A place where we can ALL be ourselves #EqualityatYork

THE UNIVERSITY

Founded on principles of excellence, equality and opportunity for all, the University of York opened in 1963 with just 230 students. In 2018 it is the home of more than 17,000 students across more than 30 academic departments and research centres. Since opening over fifty years ago, we have become one of the world's leading universities and a member of the prestigious Russell Group.

We are consistently recognised as one of the leading Higher Education Institutes and are ranked 16th in the Times & Sunday Times league table (2017). The University of York has won six Times Higher Education (THE) Awards and five Queen’s Anniversary Prizes.

The University is proud of its association with Athena SWAN, holding 12 awards in support of gender equality, representation and success for all, with gold awards for Chemistry and Biology and a University-wide bronze award.

Of 154 universities that took part in the Research Excellence Framework (REF) in 2014, The University of York ranked 14th overall and 10th for the impact of our research. The University is consistently in the top ten UK research universities and attracts over £60m a year of funding from research alone.

Our vision is to make the University of York a world leader in the creation of knowledge through fundamental and applied research, the sharing of knowledge by teaching students from varied backgrounds and the application of knowledge for the health, prosperity and well-being of people and society.
Attractive workplace

Centred around the picturesque village of Heslington on the edge of the city of York, our colleges are set in an attractive landscaped campus. York enjoys a safe, friendly atmosphere with facilities including bars, shops, theatres and concert halls all within easy walking distance.

The University has undergone an unprecedented period of expansion and renewal since 2000. We have invested in twenty new buildings on the original campus and have completed the first and second phases of a £750m campus expansion. Our investment in new colleges, teaching and learning spaces, laboratories, research facilities and a new sports village mean there has never been a better time to join us.

During this period of change we’ve worked hard to retain our friendly, informal and collegiate atmosphere, which is important to our core values of inclusivity and interdisciplinarity.

We have a thriving international community and are committed to providing staff moving to York with as much support as possible through our Relocation Package and Welcome Officers.

The University is committed to promoting a diverse and inclusive community - a place where we can all be ourselves and succeed on merit. We offer a range of family friendly, inclusive employment policies, flexible working arrangements, staff engagement forums, campus facilities and services to support staff from different backgrounds.

For further information please visit our employee benefit pages.
The City of York

Internationally acclaimed for its rich heritage and historic architecture, York’s bustling streets are filled with visitors from all over the world. Within its medieval walls you will find the iconic gothic Minster, Clifford’s Tower and the Shambles - just a few of the many attractions.

But York isn’t just a great place to visit - it’s also a great place to live and work. While nourishing a vibrant cosmopolitan atmosphere, York still maintains the friendly sense of community unique to a small city.

Visit www.visityork.org for more information on the city of York

Shopping, culture and entertainment

York boasts specialist and unique boutiques but also all the high street stores on its busy shopping streets. Alongside them you will find cinemas, theatres, an opera house, art galleries, a vast range of restaurants, live music venues and clubs. York is particularly renowned for its multitude of pubs and bars, from the modern to the medieval.

Housing and schools

Whether you choose to live close to the city, in one of the surrounding villages or further afield, you will find a wide range of housing within comfortable distance of York and the University. For families, the area has a range of excellent schools both in the state and independent sector.

Great location

York is one of Britain’s best-connected cities. Halfway between London and Edinburgh on the East Coast mainline, on intercity trains you can reach London King’s Cross in less than two hours and Edinburgh in two and a half hours. York is also well served by road links, and it is easily accessible from the A1, M1 and the M62.

For those travelling from overseas, Manchester Airport is two hours away and Heathrow Airport just three and a half. Flights from nearby Leeds Bradford Airport provide easy access to mainland Europe. By Eurostar from London St Pancras, Paris is just over six hours away.

Yorkshire

The Lonely Planet guide recently declared Yorkshire the third best region in the world to visit. There is something to cater to every taste, whether it be the rugged landscapes of the Moors or the Dales, the picturesque seaside towns of Scarborough and Robin Hoods Bay, the gothic architecture of Whitby or the vibrancy of cosmopolitan Leeds.
Apply online

- Go to https://jobs.york.ac.uk
- Find this job using reference 7343
- Complete the online application form

You will need to submit your completed application by midnight (local UK time) on 6 March 2019

What will I need?

You will need to upload:

- your CV
- a letter describing how you meet the requirements of the job

You will also need details of 2 referees.

Help and assistance

Direct any informal queries to Prof Tony Wilkinson (tony.wilkinson@york.ac.uk)

If you have any questions about your application, contact the HR Services team:

recruitment@york.ac.uk
+44 (0)1904 324835