Job Title: Research Associate in Biochemistry

Department/Division/Faculty: Institute of Clinical Sciences

Campus location: Hammersmith

Job Family/Level: Academic and Research, Level B

Salary Range: £37,904 to £42,065 per annum

Responsible to: Christian Speck

Key Working Relationships (internal): Members of the DNA Replication group

Contract type: Fixed term to 4 July 2020

Research Programme
The DNA replication group, Imperial College London, is looking to recruit a motivated and highly creative Research Associate interested in investigating the role of DNA replication factors in initiation of DNA replication using biochemical and approaches.

Purpose of the Post
One of the most fundamental properties of all living things is the ability to replicate their DNA, which allows cells to pass on their genetic material from parent to progeny. During DNA replication the replicative helicase is loaded onto DNA through an ATP-hydrolysis driven process, which involves several helicase loading factors. In S-phase the loaded helicase becomes activated by a large number replication factors that assemble into the replication fork, which synthesizes the DNA. Crucially, the loading of the replicative helicase is tightly controlled, with too much or too little helicase loading resulting in genomic instability, tumorgenesis and aging. During the last 10 years’ a biochemical system employing purified proteins from budding yeast has been used by the Speck lab to generate fundamental insights into DNA replication (Evrin et al PNAS 2009; Fernandez-Cid et al Mol Cell 2013; Sun et al Nature Structure & Mol. Biology 2013; Sun et al Genes & Dev 2014; Samel et al Genes & Dev 2015; Herrera et al NAR 2015 and Fu et al eLife 2015; Noguchi PNAS 2017). Recent structural insights into helicase loading has provided key insights into the process (Yuan et al NSMB 2017). Based on this knowledge we will investigate how the helicase ring is opened and closed around DNA.

The successful candidate will use biochemical assays to discover how Cdt1 functions in MCM2-7 ring opening and closing and how this protein regulates ATP hydrolysis. He/She will work together with lab members to obtain high resolution cryo-EM structures of several reaction intermediates. The candidate will be able to take advantage of well-developed protocols and methods. However, there is plenty of scope to develop novel creative biochemical assays, to set-up new procedures or apply biophysical approaches such as single molecule FRET. In vitro results will be confirmed using yeast genetics and chromatin binding assays.

This project will take into account the background and interests of the candidate and will offer significant training opportunities. Prof. Speck will be mentoring the candidate in the writing of grants and publications, and will be actively support the career development. During the course of the project the applicant will enjoy a stimulating research environment and will develop deep insights into DNA replication, genome stability and epigenetics.

We offer:
• The possibility to work on a cutting-edge project using state-of-the-art technology in a highly motivated research team
• A stimulating, diverse and international research environment
• Advanced training opportunities.
Job Description

References:
Cryo-EM structure of Mcm2-7 double hexamer on DNA suggests a lagging strand DNA extrusion model
PNAS, Nov 7;114(45):E9529-E9538
*Shared first authorship #Corresponding author

From structure to mechanism – understanding initiation of DNA replication
Genes & Development, Jun 1;31(11):1073-1088

Speck C# and Li H# (2017)
Structural basis of MCM2-7 replicative helicase loading by ORC-Cdc6 and Cdt1
Nature Structure & Molecular Biology, Mar;24(3):316-324 – IF 13.3
*Shared first authorship #Corresponding author

# Corresponding author


* Shared first authorship # Corresponding author

# Corresponding author


* Shared first authorship # Corresponding author

*Shared first authorship # Corresponding author

*Shared first authorship # Corresponding author

Key Responsibilities

Research Duties
- To take initiatives in the planning of research
- To direct the work of small research teams
- To identify and develop suitable techniques, and apparatus, for the collection and analysis of data
- To conduct data analysis
- To generate reagents for the project
- To design and carry out scientific experiments in accordance with the project
- To maintain highly organised and accurate records of experimental work
- To prepare material for presentation in oral and poster formats and present findings to colleagues and at conferences
- To contribute to writing bids for research grants
Job Description

- To analyse, manage and communicate data, ensuring the validity and reliability of the data at all times
- To draft publications and prepare them for submission to refereed journals
- To submit publications to refereed journals
- To actively contribute to the smooth running of the laboratory in co-ordination with other members of the group
- To form a good working relationship with other members of the group and actively participate in team work
- To promote the reputation of the group, Centre, the Department and the College
- To develop contacts and research collaborations within the Centre, the College and the wider community
- To submit publications to refereed journals
- To provide guidance to staff and students
- To attend relevant workshops and conferences as necessary
- To develop contacts and research collaborations within the College and the wider community
- To promote the reputation of the Group, the Department and the College
- To provide guidance to PhD Students
- To publish in high quality journals and to present data at national and international meetings.
- To collaborate with other allied scientists within Imperial College and elsewhere in London and abroad, as appropriate.
- Assist in the supervision of undergraduate and postgraduate research students and research assistants as required.
- To comply with the College, Division, and Unit safety practices and to attend courses on safety when appropriate.
- Any other duties as may be deemed reasonable by Head of group as well as Head of Division/Department/Section.

Other Duties

- To undertake appropriate administration tasks
- To attend relevant meetings
- To undertake any necessary training and/or development
- Any other duties commensurate with the grade of the post as directed by line manager / supervisor

Person Specification

Requirements
Candidates/post holders will be expected to demonstrate the following:

<table>
<thead>
<tr>
<th>Essential (E)</th>
<th>Desirable (D)</th>
</tr>
</thead>
</table>

**Education**

- PhD in Biochemistry, Molecular Biology or a closely related discipline, or equivalent research, industrial or commercial experience  
  E
- Strong Academic Record  
  E

**Knowledge & Experience**

- At least one first-author publication in an internationally recognised peer-reviewed journal (published or submitted)  
  E
- The candidate should be highly ambitious and will aim to develop and publish major research projects.  
  E
- Strong background in Biochemistry  
  E
- Strong experience in protein expression, purification  
  E
## Job Description

- Solid knowledge in working with purified proteins
- Background in the areas of molecular machines, the chromatin field, structure determination & modelling, DNA replication, cell cycle, DNA repair, or the broader area of genome stability
- Background in yeast genetics and/or bioinformatics
- Previous experience in supervising and training other researchers (e.g. students)

### Skills & Abilities
- Ability to conduct a detailed review of recent literature
- Ability to develop and apply new concepts
- Creative approach to problem-solving
- Excellent verbal communication skills and the ability to deal with a wide range of people
- Excellent written communication skills and the ability to write clearly and succinctly for publication
- Ability to direct the work of a small research team and motivate others to produce a high standard of work
- Ability to organise own work with minimal supervision
- Ability to prioritise own work in response to deadlines
- Advanced computer skills, including word-processing, spreadsheets and the Internet

### Personal Attributes
- Willingness to work as part of a team and to be open-minded and cooperative
- Flexible attitude towards work
- Discipline and regard for confidentiality and security at all times
- Willingness to work out of normal working hours (including weekends) if the requirements of the project demand
- Willingness to undertake any necessary training for the role
- Willingness to travel both within the United Kingdom and abroad to conduct research and attend conferences

Please note that job descriptions cannot be exhaustive and the post-holder may be required to undertake other duties, which are broadly in line with the above key responsibilities.

Imperial College is committed to equality of opportunity and to eliminating discrimination. All employees are expected to follow the 7 Imperial Expectations detailed below:

1) Champion a positive approach to change and opportunity
2) Communicate regularly and effectively within and across teams
3) Consider the thoughts and expectations of others
4) Deliver positive outcomes
5) Encourage inclusive participation and eliminate discrimination
6) Support and develop staff to optimise talent
7) Work in a planned and managed way

Employees are also required to comply with all College policies and regulations paying special attention to:

- Confidentiality
- Conflict of Interest
- Data Protection
- Equal Opportunities
- Financial Regulations
- Health and Safety
- Information Technology
- Smoking
- Private Engagements and Register of Interests
They must also undertake specific training and assume responsibility for safety relevant to specific roles, as set out on the College Website Health and Safety Structure and Responsibilities page.