Post-doctoral Scientist in Cancer Immunology

Job Description

Job Title	**Post-doctoral Scientist**
Group	Liver Regeneration & Tissue Engineering, & Liver Immunology
Reporting to	Dr Luca Urbani (PI) and Prof Shilpa Chokshi (PI and Acting Director)
Duration	2 years initially
Salary	£38,816 - £41,468 per annum (salary point depending on experience and skills)
Annual leave	27 days per annum
Starting date	June 2024

CLOSING DATE FOR APPLICATIONS: 4PM Thursday 7th March 2024

The Role

The Foundation for Liver Research (FLR) is seeking an enthusiastic and dynamic new member of staff to join the Liver Regeneration and Tissue Engineering group and the Liver Immunology group, at either postdoctoral level or as Research Assistant (Masters graduate). The post holder will have responsibility for the day-to-day management and coordination of a project looking at the immunomodulatory properties of the extracellular matrix (ECM) in hepatocellular carcinoma and other liver cancers, in particular the cross-talk between immune cells and specific ECM-associated proteins.

He/she/they will provide technical support by helping with lab organisation, conducting research experiments, collecting and analysing data, reviewing the literature, writing reports and manuscripts for publication, and presenting their research at internal and external scientific meetings/conferences. The post holder will be a point of contact for staff and students regarding experimental procedures and techniques for the research area. The post holder will also act as a mentor and supervisor to junior members of the research team and visiting students.

Foundation for Liver Research & Roger Williams Institute of Hepatology

The Foundation for Liver Research was established in 1974 to develop and extend research into diseases of the human liver. For over 30 years the Foundation has supported ground-breaking

research programmes into liver disease including much of the early pioneering work at King's College Hospital into liver transplantation and acute liver failure, under the direction of Professor Roger Williams. Since 2016 research has taken place within the purpose-built Institute of Hepatology, recently renamed the Roger Williams Institute of Hepatology (RW-IoH) which provides laboratory space for up to 65 research staff. Major areas of research during the past 5yrs have included viral hepatitis, hepatocellular carcinoma, liver tissue engineering, complications of cirrhosis, liver-gut axis, chronic and acute liver disease and liver immunology. The Foundation is involved in a number of international research programmes and scientific meetings. Further information on the Foundation can be obtained at: http://www.liver-research.org.uk

The RW-IoH operates as an independent research organisation in partnership with King's College London, and there are close research links with King's College Hospital and access to clinical material. Research in the RW-IoH is organised around major research projects within the common overall theme of Liver Cell Injury and Repair.

Background

The aim of the project is to study the crosstalk between immune cells and the extracellular matrix (ECM) in primary (HCC) and secondary (colon cancer metastasis) liver cancer using patient-derived cells and ECM extracts. The final goal is to understand how the extracellular compartment of the tumour microenvironment can modulate immune cell activity and phenotypes.

The interaction of tumour microenvironment with cancer cells is closely involved with tumour development, progression and drug resistance. The TME is a complex network composed of multiple non-malignant cells including cancer associated fibroblasts (CAFs), endothelial cells, immune and inflammatory cells and the extracellular matrix (ECM). The ECM is a dynamic web of molecules that provides structural support and biochemical cues, and is fundamental in different tissue processes.

It is well established that liver cancer is associated with profound remodelling of the liver ECM, which becomes stiffer and modulates cell behaviour, tumour progression, metastatic dissemination and immune cell evasion and function. While it is known that the ECM has immunomodulatory properties, the impact of tumour-specific ECM proteins on anti-tumour immune responses is unknown.

Immunotherapy and in particular checkpoint receptor inhibition (CRI) is a promising therapeutic avenue in liver cancer to rescue exhausted and dysfunctional immune cells and restore anti-tumour immunity. However, in HCC response rate is only 20% and many patients are resistant to CRI or become refractory after an initial response. The role of the ECM in response or resistance to CRI in liver cancers in unknown.

Our team has been addressing these issues by combining the expertise of Prof Chokshi's group in studies of liver immunology and checkpoint receptors, and the knowledge and technologies in matrix biology of Dr Urbani's group.

With this project, we aim to determine the immunomodulatory properties of specific cancer ECM proteins in HCC and other liver cancers and their potential role in orchestrating tumour-specific immunity and response to immunotherapy. The project will include isolation and culture of circulating and tissue infiltrating human immune cells and co-culture with different ECM-extracts

obtained with decellularisation of tissue samples. Pathways identified will be further investigated in co-culture experiments of immune cells with in vitro hepatic stellate cells- or CAF-derived matrix obtained in vitro with established protocols, to better understand mechanisms of interaction of immune cells with the remodelled tumour ECM.

Different techniques will be used to characterise the immune cell response to the different patient derived ECMs and then correlate the findings with in vivo/clinical data. Techniques will include: FACS, Luminex, T cell proliferation assay, proteomics, spatial transcriptomics and proteomics, etc.

In conclusion, we aim to show how individual components of the remodelled ECM in liver cancer can impede anti-tumour immunity and, by identifying therapeutic targets, how these effects might be mitigated. This project could provide a precious body of knowledge about how the ECM shields the tumour from the immune system and may control local response to CRI and could open new therapeutic avenues in treating liver cancer.

Post Specification
The post holder will be responsible for the following:

1. *Design and perform immune cell-ECM co-culture experiments*
2. *To study the phenotype and function of immune cells when exposed to the ECM extracts*
3. *To study the dynamic interaction of specific ECM proteins and immune cells in the tumour microenvironment*

Specific tasks include:

- Immune cell isolation, culture and characterisation;
- Decellularized ECM preparation and characterisation;
- Human blood and tissue collection and processing
- Work with human tissue and coordination of relationship with surgical and histopathology teams
- Optimisation of co-culture protocols
- Analysis of cellular phenotypes and ECM composition
- Planning, conducting and reporting statistical analyses
- Liaising with other researchers working on related data
- Coordination and reporting of research project
- Co-ordinating production of final report and associated outputs
- Presenting findings of the research at meetings
- Contributing to writing up results for publication
- Coordinate master students and research technicians

The post offers an excellent career development opportunity for a laboratory scientist with experience in molecular immunology or cancer immunology. Training will be available and there will be opportunity for the post holder to develop his/her/their own interests within the scope of the project.

The following skills and attributes are required for the post-doctoral position:

Essential skills:-

- PhD in immunology, cancer immunology or cancer matrix biology (for post doc candidates only)
- Experience in solid cancer microenvironment studies
- Experience with isolation and culture of human immune cells
- Hands-on experience with cell-culture and molecular biology techniques
- Hand-on experience with molecular immunology techniques
- Laboratory-based research experience in DNA, RNA and protein assays (ELISA)
- In depth experience in Flow Cytometry, preferably using a Fortessa
- Laboratory-based experience in fluorescence microscopy and immunofluorescence protocols
- Excellent organisation skills and the ability to work independently
- Good publication record in Cancer Immunology in leading peer-reviewed journals
- The ability to prepare data for publication including statistical analysis
- Experience of cross-discipline collaboration
- Proven ability to work with colleagues and initiate multi-disciplinary projects
- Ability to present research findings at internal, national and international meetings
- Good interpersonal skills that demonstrate the ability to establish and maintain effective working relationships with students, staff, peers and management
- Commitment to Health and Safety
- Excellent written communication skills in English

Desirable skills:-

- Experience of working with ECM, Biomaterials and/or decellularisation techniques
- Previous experience and success in writing research grants proposals

The appointee will be expected:-

- To design, set-up and run experiments in relation to the project after consultation with the Principal Investigators to effectively record, analyse, acquire and write-up results
- To perform laboratory-based assays on cells and tissues obtained from human samples
- Contribute to internal meetings and external national and international hepatology meetings
- Contribute to the preparation and drafting of research bids and proposals
- Provide training, support and advice to undergraduates and PhD students and research technicians
- Participate in collaborative research projects
- Undertake GCP and HTA training to facilitate appropriate interaction with hospital staff and patient participants from who research samples are derived
- Publish research findings in peer-reviewed international journals
- Contribute to overall activities of the Institute
- Any other duties commensurate with the grading of the post as required by the Principal Investigator, Chief Scientific Officer and Director
- 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.

The post is offered for a period of 2 years with possibility of extension. As part of the appointment with the Foundation for Liver Research, the appointee will be put forward for an honorary appointment with King's College London.

To apply: send a 1-page covering letter explaining your background and suitability for our team, together with a detailed CV describing your research experience to date and including names and contact details of two referees, one of whom is the current/most recent employer, to:

James Poynton, Chief Operating Officer, Foundation for Liver Research:
j.poynton@researchinliver.org.uk

Please name documents you send as follows:

<surname, first name, RS62, *{CV}**or**{covering letter}*> **Quote Job Ref: RS62**

For informal enquiries contact Dr Luca Urbani, Principal Investigator:
luca.urbani@researchinliver.org.uk

In the event that you are invited for interview we will contact you by email confirming the arrangements.

The Roger Williams Institute of Hepatology and the Foundation for Liver Research are committed to fostering a safe and welcoming working environment where everyone feels valued.