



## Post-doctoral Scientist in Mitochondrial Medicine

### Job Description

<b><u>Job Title</u></b>	<b>Post-doctoral Scientist</b>
<b><u>Group</u></b>	Mitochondrial Medicine for Liver Disease
<b><u>Reporting to</u></b>	Dr Elena Palma (PI)
<b><u>Duration</u></b>	2 years initially
<b><u>Salary</u></b>	£38,816 - £41,468 per annum (salary point depending on experience and skills)
<b><u>Annual leave</u></b>	27 days per annum
<b><u>Starting date</u></b>	July 2024

**CLOSING DATE FOR APPLICATIONS: 22<sup>nd</sup> June 2024**

Applications are invited for a Post-doctoral Scientist position to join the Mitochondrial Medicine for Liver Disease group, as part of the Roger Williams Institute of Hepatology. Funded by the Foundation for Liver Research, the post-holder will investigate the role of mitochondria and the potential to apply mitochondria-targeted interventions (including mitochondrial transplantation) to reduce the burden of liver disease.

The overall goal of the MitoMed group is to develop novel therapies for Alcohol-related Liver Disease (ALD) and primary liver cancers, employing strategies targeting mitochondria and multipronged approaches (i.e. cyclophilin inhibitors or combinatorial immunotherapies).

The research programme revolves around the following objectives:

- Elucidating the mitochondrial involvement in the progression of liver disease, the impact of ALD on mitochondrial dynamics and the significance of the clinical manifestation of hepatic megamitochondria.
- Applying mitochondrial transplantation to tackle liver disease, including for the rescue of marginal grafts to address the shortage of transplantable livers, and to advance experimental models of liver disease.
- Investigating pre-clinically the effects of multitargeted therapies for liver disease: on processes relevant for patient prognosis such as fibrosis, inflammation, liver regeneration (in ALD); and on the immune and stromal compartments in the tumour microenvironment (in hepatocellular and cholangiocarcinoma).
- Innovating translational patient-derived 3D models for the clinically relevant testing of therapeutic approaches, including efficacy and toxicity.

### **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 in close collaboration with King's College Hospital.

### **Post Specification**

The appointed Post-doctoral Scientist will be focussing on the mitochondria-related projects running in the lab (mitochondrial transplantation and/or mitochondrial dynamics in ALD, see more details below) according to their expertise and interest.

The post-holder will be expected to work collaboratively and effectively with internal/external collaborators involved in the project and other group members. 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 and act as a mentor and supervisor to junior members of the research team and students.

The post will suit an ambitious and highly motivated postdoctoral scientist, or a scientist who have recently been awarded a PhD, who enjoys working as a member of a newly formed team. Furthermore, the post will suit a scientist who wishes to develop their own career and pursue opportunities for independent fellowships in the next few years.

### **The appointee will be expected to:**

- Carry out high quality translational research using patient-derived models and clinical samples.
- Perform mitochondrial studies, including morphometric and functional assays and any other relevant mitochondrial analyses and set up related protocols at RW-IoH.
- Drive intellectually and technically their project and experimental design and contribute to the other projects in the lab.
- Engage willingly and effectively in collaborative work with other group members and collaborators.
- Prepare findings for publication and external presentation at national and international conferences.
- Maintain knowledge of the relevant scientific literature and advancements in the field.
- Contribute to the writing of grant applications, research bids for the FLR and assist with management of research budget.
- Actively participate to the effective running of the lab contributing to storage records, stocks and orders.
- Keep accurate, trustworthy records of all experimental work, operating procedures and results (including raw data) and databases detailing sample acquisition and clinical information.
- Take a creative and professional approach to analysing, discussing and presenting data and hypotheses in internal/external meetings.
- Demonstrate a commitment to training and supervising other group members, including staff and undergraduate/PhD students working in the laboratory and at RW-IoH.
- Carry out other duties within the scope, spirit and purpose of the job as requested by the Principal Investigator, Chief Scientific Officer and Director.
- Participate in and support engagement activities within the RW-IoH and societies of interest (i.e EASL, European Association for the Study of the Liver; ESBRA, European Society for Biomedical Research on Alcoholism; WMS, World Mitochondria Society).
- Undertake mandatory training as required by the FLR, including GCP and HTA training to facilitate appropriate interaction with hospital staff for specimen procurement.
- Strictly comply to Health & Safety regulations and practices.
- Actively follow FLR policies including Equality, Diversity and Inclusion principles.

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 nature of scientific work means it may be necessary to work outside of normal working hours in order to complete an experiment, or to process clinical specimens. An exact breakdown of percentage time spent in different duties is impossible to provide in a scientific job as the exact nature of day-to-day duties will evolve with the project.

The following skills and attributes are required for the post-doctoral position and will be assessed at application and interview stage:

<b>Person specification Criteria</b>	<b>Essential or Desirable</b>
<b>Qualifications, experience and knowledge</b>	
PhD degree in Biology/ Biochemistry/Biomedical Sciences or related subject	E
Significant experience of working in a research laboratory	E
Background in mitochondrial pathophysiology	E
Significant experience in mitochondrial function and dynamics and related techniques, including confocal/multiphoton microscopy and Seahorse	E
Evidence of significant scientific contribution, including publications and/or presentation at national/international conferences	E
Knowledge of liver disease or organ transplantation	D
Practical experience with human and 3D models	D
<b>Skills and abilities</b>	
Proven ability and commitment to carry out high quality original research, leading to publication in peer-reviewed journals	E
Ability to design experimental studies and to optimise robust Standard Operating Procedure	E
Ability to prepare data for publication including statistical analysis	E
Excellent written and oral communication skills, including accurate and complete record keeping of experimental findings	E
Excellent organisational skills and ability to work independently	E
Experience in analysis and visualisation of large datasets (transcriptomic, proteomic) or spatial biology	D
Evidence of good time management and ability of working effectively to tight deadlines	D
Evidence of being able to generate original ideas by building on exciting concepts and advancements in the field	D
Previous experience and success in writing research grants proposals	D
<b>Personal attributes</b>	
Ability to work both independently and as part of a team, and collaborate/communicate effectively with clinical/basic researchers	E
Ability to work to the highest H&S, ethical and professional standards	E
Ability to prioritise workload and to operate safely and effectively with varied degrees of supervision and at a fast changing pace	E
Willingness to work outside normal working hours at short notice (e.g. clinical specimens)	E
Good interpersonal skills that demonstrate the ability to establish and maintain effective working relationships with students, staff, peers and management and patiently train other group members	E
Willingness and ability to exchange information with others	E

**Projects background:** Liver disease is currently one of the major causes of mortality and morbidity, as it accounts for the death of more than 2 million people globally every year (Devarbhavi H et al., 2023). Increased alcohol consumption, together with the progressive aging of the general population and the prevalence of metabolic factors, means that mortality is predicted to increase in the future.

A substantial body of literature describes the several direct and indirect effects of alcohol and Alcohol-related Liver Disease on mitochondria (Abdallah & Singal, 2020; García-Ruiz et al., 2013; Nassir & Ibdah, 2014). This mitochondrial dysfunction compromises the survival, function and regenerative capacity of the hepatocytes, with consequent repercussions on liver function as a whole. In addition, we and others have demonstrated that hepatic mitochondria can promptly undergo morphological adjustments in response to ethanol exposure, inducing adaptation or 'maladaptation' to this toxic agent as a result, and that mitochondrial dynamics, shape and mitochondria shaping proteins are affected in ALD (Das et al., 2012; D. Han et al., 2012; Palma et al., 2020; Palma, Ma, et al., 2019). Interestingly, the presence of disproportionately enlarged organelles, namely megamitochondria, in liver biopsies of ALD patients has been known since a long time (Chedid et al., 1986). Different clinical studies support the hypothesis that megamitochondria development is a beneficial adaptive response to alcohol and have shown that megamitochondria detection in liver biopsies is one of four clinical and histological parameters associated with a better outcome in terms of survival at 90 or 180 days in patients with alcohol-related hepatitis (Altamirano et al., 2014). Furthermore, investigations in experimental models have demonstrated both beneficial and detrimental effects of megamitochondria in ALD (Ma et al., 2023; Palma, Ma, et al., 2019). As such, a consensus has not been reached and further studies are required to elucidate better mitochondrial dynamics in the context of ALD and investigate the possibility to develop mitochondria-related therapeutic interventions to tackle this disease.

Furthermore, due to the silent nature of liver disease, the diagnosis is usually late and liver transplantation (LT) is still the only curative therapy available for patients with end-stage liver disease. LT has demonstrated remarkable efficacy, offering a near-normal quality of life to patients otherwise deemed for rapid death. Importantly, all newer indications and the success rate of LT have resulted in an unprecedented global demand for liver grafts and the consequent issue of a shortage of transplantable organs raising mortality rates among patients on the waiting list. Many groups have considered the use of previously discarded marginal or extended criteria donor (ECD) livers to overcome the limited availability of organs for transplantation. However, these grafts are at risk of poor function after implantation. In recent years, there has been a growing recognition of the critical importance of mitochondrial function in liver preservation and transplantation (Shi S et al., 2023; Saeb-Parsy K et al., 2021). Mitochondrial transplantation has been proved successful in in-vitro and in-vivo models to treat mitochondrial dysfunction in various tissues, including liver (Shi X et al., 2018; Fu A et al., 2017) and recently a promising study has reported that in an ex-vivo porcine model of renal transplantation, mitochondrial transplantation reduced damage (Rossi et al., 2023). In the current project we would like to apply mitochondrial transplantation for the rescue of marginal or ECD grafts to ultimately tackle the shortage of transplantable livers.

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](mailto:j.poynton@researchinliver.org.uk)

Please name documents you send as follows:

<surname, first name, RS65, {CV}**or**{covering letter}>

**Quote Job Ref: RS65**

For informal enquiries contact Dr Elena Palma, Principal Investigator:

[e.palma@researchinliver.org.uk](mailto:e.palma@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.**