

## **PhD studentship (Ref: PhD\_BIO-21\_NIBSC)**

A 3-year full-time PhD studentship is available at the Division of Biotherapeutics, National Institute for Biological Standards and Control (NIBSC), in collaboration with the University of East London. The studentship is anticipated to commence on 1 October 2021.

### **Title**

In vitro immunoregulatory potency of Mesenchymal Stromal Cells-derived Extracellular Vesicles as cell-free therapeutics.

### **Project description**

Over the last 20 years Mesenchymal Stromal Cells (MSC) have emerged, after hemopoietic stem cells, as the second most investigated and applied somatic stem cell entity. MSC have been proven to mediate immunosuppressive as well as pro-regenerative activities. Against initial assumption, it is now believed that MSC primarily exert their therapeutic function in a paracrine, rather than cellular manner, namely via their secretome components. Extracellular Vesicles (EV) such as exosomes or microvesicles are sub-micron bilayer membrane structures enriched with proteins, nucleic acids and other active molecules that are part of the cells' secretome and are important mediators of cellular communication implicated in many physiological and pathological processes. Recently, evidence suggests EVs derived from MSC (MSC-EV) contribute towards modulation of the immune responses and they have been suggested as cell-free alternatives to stem cell therapies. The exact mechanism of MSC-EV immune regulatory action is still not well understood and the studies reporting their effect on T, B, NK and dendritic cells are controversial. Additionally, with the rapid development of the EV field over the last decade, it has become clear that there are difficulties in working with a heterogeneous population of nanoscale EVs, where standardised methods of isolation and characterisation have not been established, presenting a unique set of challenges when translating the technologies into viable and regulated therapies. It is known that differences in EV purification methodology can affect the molecular cargo of EV and therefore it is stipulated that this also can affect the function of EV as therapeutics or drug-delivery systems. There are currently over 20 clinical trials investigating the use of MSC-EV to treat inflammatory and degenerative conditions and MSC-EV have been successfully used in patients via emergency/compassionate regulatory approval. As MSC-EV transition into clinical applications becomes reality, the discrepancies and controversies about the biology, functions, characteristics and potency of MSC-EV and how to address them becomes urgent. These are likely to have arisen due to several factors: the diversity of MSC and their preparation, various methods of EV production and purification, a lack of standardised quality controlled assays and limited reproducibility of in vitro and in vivo functional assays.

The core objective of this PhD project is to identify the precise immunological targets of MSC-EV, and the effects of MSC-EV uptake by these targets. The project will also look at the effects of applied EV-isolation methods on MSC-EV function in vitro. This information will directly inform the development of reliable, standardised in vitro potency assays and potential reference materials for evaluation of MSC-EV immune regulatory potential.

The successful candidate will conduct a study to test the hypothesis that MSC-EV derived from various allogeneic sources and isolated using different methods can alter the immune regulatory effect they exert on immune cells in vitro. The student will receive broad technical training in in vitro cell-based assays and EV-biology, standardised flow cytometry and cell and electron imaging.

### **Key responsibilities**

- To undertake the research projects in line with the project aims
- To communicate effectively, orally and through written media, undertake presentations at scientific meetings and maintain excellent records
- To interact regularly and effectively with the supervisors and interact appropriately and effectively with other staff

- To fulfil the requirements of the University PhD programme and to undertake specific training as required by the host institutions

In addition to meeting all the academic, security and residency requirements, you will have:

- an academic background in molecular and cellular or stem cell biology, immunology or relevant life sciences
- a demonstrated aptitude in a laboratory setting and motivation to undertake research
- a demonstrated interest in the field of study and ability to work accurately and precisely
- a demonstrated excellent oral and written communication, and IT skills
- a previous experience in one or more of the key interest areas as an advantage
- some theoretical knowledge of MSC, EV and MSC-EV biology

NIBSC, the Centre of the Medicines and Healthcare products Regulatory Agency (MHRA), is a global leader in the characterisation, standardisation and control of biological medicines and has a major role in protecting and improving public health worldwide. NIBSC is the leading WHO International Laboratory for Biological Standardisation and is responsible for producing and distributing over 90% of all WHO International Standards introduced for the quality assurance of biological medicines. NIBSC scientists also test products, carry out valuable research and provide advice on a routine basis and in response to emergencies. The importance of the Institute's work is well recognised nationally and internationally.

The Division of Biotherapeutics has a broad remit covering all biological products with a therapeutic potential in humans, excluding vaccines. Our core functions of standardisation and product control testing are underpinned by a programme of applied research.

The student will be registered with the School of Health, Sports and Biosciences at the University of East London.

The student will be supervised by Drs Anna Nowocin and Melanie Moore (NIBSC), Lesley Smyth (University of East London). The student will be based primarily at NIBSC with the opportunity for attendance at the University for additional training and work when required.

### **Qualification requirements for University of East London**

Minimum entry requirements are 2:1 (or international equivalent) in a relevant subject; or a 2.2 (or international equivalent) and a masters' degree, both in a relevant subject.

### **Funding**

Tuition fees are covered; there is provision for laboratory consumables and travel to conferences and the University; there is a student stipend of £18,500 p.a.

### **English language requirements**

Applicants whose first language is not English (and whose undergraduate degree was not taught in English) must fulfil the minimum requirements of an IELTS score of 6.5 with no less than 6.0 in any element.

### **Visas and immigration**

Applicants will be subject to UK immigration requirements with demonstration of the right to reside and study in the UK.

### **To apply**

Send (i) your CV including the name and contact details of two academic referees and (ii) a personal statement of no more than 1000 words explaining your interest in this project and aspirations for undertaking a PhD to [studentship@nibsc.org](mailto:studentship@nibsc.org) by 5 pm (UK time) on Wednesday, 17 February 2021.

Please ensure the studentship reference number PhD\_BIO-21\_NIBSC is included in the subject line of the email and your personal statement.

If you have a disability defined by the Equality Act 2010 (<https://www.gov.uk/definition-of-disability-under-equality-act-2010>) you may apply under the UK Civil Service Guaranteed Interview Scheme provided that you meet all of the qualifications, skills, requirements and experience defined as essential for the studentship. You must submit the Guaranteed Interview Scheme Declaration form with your application: this can be found at <https://www.gov.uk/government/publications/guaranteed-interview-scheme> At interview all applicants will be assessed solely on merit.

Any offer of a studentship is conditional upon successful background screening which includes, but is not limited to, checks on identity, qualifications and right to study in the UK.

