



PhD studentship – Division of Bacteriology

Position: PhD Student

Division: Bacteriology, NIBSC

Location: South Mimms, Potters Bar, Hertfordshire

Reference number: SCI03Y

Grade and salary range: PhD Student - £18,500 annual stipend

Contract Type: 3-year Fixed Term Contract

Closing Date: 12 noon UK time (midday) on Friday 09 March 2018

Title: Development of a novel glyco-conjugate vaccine against Group A *Streptococcus*.

A 3-year full-time studentship is available at the National Institute for Biological Standards and Control (NIBSC), Division of Bacteriology, in collaboration with the Department of Pathogen and Molecular Biology, London School of Hygiene and Tropical Medicine (LSHTM). The studentship is expected to start on 1st October 2018.

Purpose of the studentship

Group A *Streptococcus* (GAS) infection can cause mild symptoms, like pharyngitis, or develop to serious invasive diseases such as toxic shock syndrome and necrotising fasciitis, with further immunological disorders including rheumatic heart disease (RHD). Increases in scarlet fever in the UK and the worldwide impact of RHD especially in some of the poorest regions of the world render this organism of particular interest, especially in consideration of a cost effective global vaccine. There is currently no commercially available vaccine against GAS infections, but a large number of virulence factors have been identified, such as M-protein, the major virulence factor. A vaccine covering 30 M-protein serotypes has reached Phase II clinical trials, however, its long-term use and worldwide efficacy is questionable due to disparate distribution of serotypes between developed and developing countries. Other antigens have been investigated but it is likely that a multi-component vaccine will be necessary for broad coverage against GAS as many of these vaccine candidates, including the M protein, are limited by strain variability.

The cell wall polysaccharide (PS) of GAS is conserved between all strains and is composed of a poly-rhamnose backbone with alternating N-acetyl glucosamine (GlcNAc) side chains. The presence of antibodies against the GAS PS has been suggested to be a correlate of protection against throat carriage in a study of children in Mexico. The GlcNAc residues have been shown to stimulate cross-reactive antibodies with human cardiac myosin, hypothesised to be linked to the development of RHD. The poly-rhamnose backbone however does not induce cross-reactive antibodies and is protective in animal models of infection, though not to the same extent as the M protein. Employed in isolation, PS is a poor immunogen for inducing memory responses.

Glyco-conjugate vaccines are of interest as they provide a longer lasting humoral immune response than PS antigens alone. The conserved nature of the GAS PS makes its use in a glyco-conjugate vaccine using GAS protective protein antigens as a carrier of great interest as it would induce an immune response to both antigens. Conjugation of PS to protein carriers is classically undertaken chemically; however, this method is costly and difficult to control. Biological conjugation can be conducted with the *Campylobacter jejuni* glycosyltransferase PglB, which has been successfully used to produce recombinant glyco-conjugate vaccine candidates for a number of pathogens by means of multi-plasmid expression in *E. coli*.

We hypothesise that immunisation with a conjugate made from GAS protein(s) and the GAS PS poly-rhamnose backbone should induce an effective antibody response to the PS and the carrierprotein(s), providing wide serotype coverage. The research will also question whether this conjugation can be undertaken biologically using recombinant technology.

The student will investigate the following key areas: evaluation of the chemical conjugation of GAS PS to GAS protein antigens with physico-chemical techniques; immunogenicity and efficacy of the vaccine candidates; the use of the biological conjugation with PglB recombinant vaccine technology.

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.

About NIBSC

NIBSC is a centre of the Medicines and Healthcare products Regulatory Agency (MHRA) which enhances and improves the health of millions of people every day through the effective regulation of medicines and medical devices, underpinned by science and research.

NIBSC is a global leader in the characterisation, standardisation and control of biological medicines and has a major role in protecting and improving public health globally. 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. Our 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.

About the London School of Hygiene & Tropical Medicine

The London School of Hygiene & Tropical Medicine (LSHTM) is a world-leading centre for research and postgraduate education in public and global health. The mission is to improve health and health equity worldwide; working in partnership to achieve excellence in public and global health research, education and translation of knowledge into policy and practice.

Staff, students and alumni work in more than 150 countries in government, academia, international agencies and health services. The School's multidisciplinary expertise includes clinicians, epidemiologists, statisticians, social scientists, molecular biologists and immunologists, and we work with partners worldwide to support the development of teaching and research capacity. The LSHTM was named University of the Year 2016 by Times Higher Education, in recognition of our response to the Ebola epidemic. The LSHTM Department of Pathogen and Molecular Biology is part of the Faculty of Infectious and Tropical Diseases.

The project will be supervised by Drs. Alexandra Shaw and Fatme Mawas (NIBSC) and Prof Brendan Wren (LSHTM). The student will be based primarily at NIBSC with the opportunity for attendance at the University for additional training.

Person Requirements

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

- an academic background in biochemistry or relevant life sciences
- a demonstrated aptitude in a laboratory setting and motivation to undertake research
- a demonstrated ability to work accurately and precisely
- excellent, demonstrated oral and written communication
- a demonstrated interest in the field of study
- some previous experience in biochemical, molecular and cellular biology techniques
- some knowledge of bacteriology and vaccines

Qualification requirements for LSHTM, Faculty of Infectious and Tropical Diseases

A first-class degree, or minimum an upper second-class Honours degree from a UK university, or an overseas qualification of an equivalent standard, or an appropriate Master's degree, in an appropriate area of study.

Funding

Tuition fees and consumables are covered and there is an £18,500 annual stipend. Please note funding is available for UK and European Economic Area (EEA) nationals only.

English language requirements

Applicants whose first language is not English are normally expected to meet the minimum University requirements (e.g. 7.0 IELTS). For further information click [here](#)

How to apply

Please submit:

- (i) a 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 by **12 noon UK time (midday) on Friday 09 March 2018.**

Please ensure the studentship reference number is included in the subject line of the email and your personal statement.

We are an equal opportunities employer and welcome applications from suitably qualified people regardless of age, gender, sexual orientation, marital status, race, religion, politics or disability. The Medicines and Healthcare products Regulatory Agency commits itself to the Guaranteed Interview Scheme (GIS). This means that it guarantees to interview all disabled candidates (as defined by the Disability Discrimination Act 1995), who satisfy the minimum essential criteria for the advertised post. If a candidate wishes to apply for consideration under this scheme, please include this in your covering letter.

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.