Medicines & Healthcare products Regulatory Agency

NIBSC

UNIVERSITY OF OXFORD

PhD studentship – Division of Bacteriology

Position: PhD Student
Division: Bacteriology, NIBSC
Location: South Mimms, Potters Bar, Hertfordshire
Reference number: SCI03X
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 and characterisation of a novel vaccine for *Bordetella pertussis* (whooping cough).

A 3-year full-time **DPhil studentship** is available at the National Institute for Biological Standards and Control, Division of Bacteriology, in collaboration with the Oxford Vaccine Group (OVG), University of Oxford. The studentship is expected to start on 1st October 2018.

Purpose of the studentship

Whooping cough is caused by the bacterium *Bordetella pertussis*. Despite the fact that it is a vaccine-preventable disease, whooping cough remains endemic worldwide and pertussis is still an important public health problem. There has been a resurgence of reported pertussis cases in many regions of the world, even where infant vaccination rates are high. This resurgence of pertussis may be, in part, associated with the bacterium's ability to evade the host immune response owing to antigen variation and/or poor or short-lived adaptive immunity induced by the acellular pertussis vaccine (ACV) when compared to the whole cell pertussis vaccine (WCV) that they replaced. Protection against pertussis relies on both humoral and cellular (Th1 type) immune responses. Seemingly of critical importance are recent studies showing that while the WCV generated a strong antigen-specific Th1 response, ACV induced mixed Th1/Th2 responses in humans. Currently, ACV is administered with alum as the adjuvant which favours the induction of Th2 response and antibodies. However, they do not effectively stimulate Th1 responses necessary for induction of CD8+ cytotoxic T cell response which is critical for immunity to *B. pertussis*. The use of adjuvants that stimulate a Th2 response in a vaccine for a disease that requires a Th1 response for protection leads to a less effective vaccine. Given the increasing incidence of pertussis in vaccinated populations, strategies to improve the efficacy and longevity of the protection induced by vaccines are required.

Viral vectors have been developed for increased T-cell induction. These have been predominantly developed for viral infections, but the Oxford Vaccine Group have recently developed viral vector based vaccines to prevent other Gram negative extracellular bacterial pathogens. In collaboration with NIBSC, the Oxford Vaccine Group have already developed four viral vector based vaccines against *B. pertussis*. These viral vectors are based on replication-deficient adenovirus and Modified Vaccinia Ankara (MVA). Preliminary characterisation of the vaccine constructs have demonstrated that the adenovirus based vaccine induced an antibody response when administered by the intramuscular route.

One of the main problems associated with using viral vectors for expressing bacterial antigens is that they infect mammalian cells and the proteins against which the immune response is generated are produced by the mammalian cells. However, the post-translation modification systems in bacterial and eukaryotic cells are very different. In the latter glycosylation can occur that does not occur in prokaryotic cells. Also, in bacteria there are multiple steps for trafficking proteins which are not found in mammalian cells therefore it's not clear whether bacterial proteins expressed in mammalian cells (having been introduced by viral vectors) will be folded in such a way as to elicit an effective immune response against the pathogen. However, OVG and NIBSC have found that adenovirus based viral vectors against *B. pertussis* can elicit an antibody response in mice.

The aim of this project is to characterise the viral vector based pertussis vaccine candidates already constructed in terms of cellular and humoral responses, and investigate the expression of the bacterial protein in mammalian cells. The DPhil candidate will also investigate the use of other *B. pertussis* proteins as antigens with the intention of bringing the candidates to Phase I clinical trial.

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 your supervisors and interact appropriately and effectively with other staff.
- To fulfil the requirements of the University DPhil 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 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 University of Oxford

We aim to lead the world in research and education for the benefit of society both in the UK and globally. Oxford's researchers engage with academic, commercial and cultural partners across the world to stimulate high-quality research and enable innovation through a broad range of social, policy and economic impacts.

We believe our strengths lie both in empowering individuals and teams to address fundamental questions of global significance, and in providing all of our staff with a welcoming and inclusive workplace that supports everyone to develop and do their best work. Recognising that diversity is a great strength, and vital for innovation and creativity, we aspire to build a truly diverse community which values and respects every individual's unique contribution.

While we have long traditions of scholarship, we are also forward-looking, creative and cutting-edge. Oxford is one of Europe's most entrepreneurial universities. Income from external research contracts in 2014/15 exceeded £522.9m and ranked first in the UK for university spin-outs, with more than 130 spin-off companies created to date. We are also recognised as leaders in support for social enterprise.

Join us and you will find a unique, democratic and international community, a great range of staff benefits and access to a vibrant array of cultural activities in the beautiful city of Oxford.

For more information please visit www.ox.ac.uk/about/organisation

Oxford Vaccine Group

The Oxford Vaccine Group (OVG) is led by Andrew J Pollard, Professor of Paediatric Infection and Immunity. Staff re based within a purpose built centre on the Churchill Hospital site and form part of the

Centre for Clinical Vaccinology and Tropical Medicine (CCVTM). The aim of OVG is to co-ordinate expertise in the study of microbial diseases and the immune response to microbes, in order to facilitate

research on the development and implementation of vaccines. This may include new, improved or combined vaccines for the adult and paediatric population.

Core group members include two Consultants in Vaccinology, a Director of Clinical Trials, a Senior Clinical Trials Manager, adult and paediatric clinical research fellows, adult and paediatric research nurses, project managers, QA manager, IT manager, and an administration team. The Infection and Immunity Laboratory includes post doctorate scientists, research assistants and DPhil students. Wider group members include professionals from a range of specialities including immunologists, microbiologists, statisticians, a community paediatrician, the local Health Protection team and a bioethicist.

Recent studies carried out by the group include:

- Pneumococcal conjugate vaccine studies in the elderly
- Polysaccharide and conjugate quadrivalent meningococcal vaccine studies in adults
- H1N1 vaccine studies in children
- Pneumococcal nasopharyngeal carriage epidemiology
- Meningococcal B vaccine development
- Development of a typhoid challenge model

More information about OVG may be found at the website: http://www.ovg.ox.ac.uk

Department of Paediatrics

The Department of Paediatrics was established in 1972 and is a part of the Medical Sciences Division. The Department has a major interest in infectious diseases on infancy and childhood and comprises clinical, teaching and research facilities within the Children's Hospital, the Women's Centre, the Institute of Molecular Medicine, the Peter Medawar Building, the Wellcome Trust Centre for Human Genetics (WTCHG) and the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM). We currently employ around 120 clinical practitioners, research scientists and administrative staff and have an annual non-research turnover in excess of £4 million, with more than 65 research grants.

For more information please visit: http://www.paediatrics.ox.ac.uk/

The University of Oxford is a member of the Athena SWAN Charter and holds an institutional Bronze Athena SWAN award. The Department of Paediatrics holds a departmental silver Athena SWAN award in recognition of its efforts to introduce organisational and cultural practices that promote gender equality and create a better working environment for both men and women.

Medical Sciences Division

We are an internationally recognized centre of excellence for biomedical and clinical research and teaching, and the largest academic division in the University of Oxford.
World-leading programmes, housed in state-of-the-art facilities, cover the full range of scientific endeavour from the molecule to the population. With our NHS partners we also foster the highest possible standards in patient care.

For more information please visit: http://www.medsci.ox.ac.uk/

The project will be supervised by Drs. Kevin Markey and Barbara Bolgiano (NIBSC) and Dr. Christine Rollier (OVG). 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 the 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
- a previous experience in molecular and cellular biology techniques
- some knowledge in virology

Qualification requirements for OVG, University of Oxford.
Applicants are normally expected to be predicted or have achieved a first-class or strong upper second-class undergraduate degree with honors (or equivalent international qualifications), as a minimum, in a subject relevant to the research project being applied for.

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 usually required to provide evidence of proficiency in English at the standard level required by the university. 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
(iii) apply for the DPhil course at University of Oxford (https://www.ox.ac.uk/admissions/graduate/courses/dphil-paediatrics?wssl=1) 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.