Course Information Sheet for entry in 2022-23: DPhil in Paediatrics

About the course

The DPhil in Paediatrics provides opportunities for study in a broad range of basic, translational and clinical science related to child health including major strengths in developmental immunology and haematology, infectious disease, vaccines, paediatric imaging and neuromuscular biology, mucosal immunology and gastroenterology. You will become part of a vibrant research community both within the department and in the wider University.

You will develop generic research skills by making use of a range of research training and skills development offered by the medical sciences division, alongside direction by your supervisor in specific research methods in relation to your project. You are encouraged to develop a literature review in your first year and to attend courses in manuscript and thesis writing and in presentation skills. At the heart of the skills provision are regular group meetings and the annual departmental Research Day where you will present and develop your research ideas and proposals with the benefit of feedback and support from your peers.

Research themes and areas

Philip Goulder

It is becoming increasingly clear that immune sex differences have a substantial impact on outcome from infectious disease and vaccines. The group's own studies of children who became infected with HIV in utero show that these immune sex differences start before birth and have substantial impact before birth. Female fetuses born to mothers who themselves become infected with HIV during pregnancy are 2-3x more susceptible to infection than male fetuses. The reason, the group believes, is that the female fetus shares with her mother a strong dependence on the innate immune response, and specifically type I interferon (IFN-I) production in response to viruses such as HIV, to protect against infection. Thus, the virus that evades this defence in the mother is highly IFN-I-resistant, and this same highly IFN-I-resistant virus evades the same innate response in the female fetus, but not male fetuses, who are more susceptible to IFN-I-sensitive viruses with high replicative capacity (Adland et al Nature Communications, 2020).

The Goulder Group Research theme focuses on two related goals: the first being to define the mechanisms and impact of immune sex differences in early life; and the second being to define the immune responses in early life that maximise the potential for achieve cure in HIV-infected children. HIV provides an ideal tool to help understand the immune sex differences that are present in early life and their impact. A cohort of 250 HIV-infected mother child pairs in KwaZulu-Natal, South Africa, followed from the infant's birth, form the focus of much of this work in the Peter Medawar Building in Oxford. The exposure of sex-discordant twins to other infections (CMV) and to vaccines provide an additional unique means of evaluating early-life immune sex differences.

Caroline Hartley

One in 13 babies are born prematurely; understanding and mitigating the long-term impact of premature birth is important to improve the lives of these children. Apnoea - the cessation of breathing - is a common pathology associated with prematurity. These potentially life-threatening events can result in reduced cerebral oxygenation and frequent apnoeas have been associated with long-term effects including reduced childhood cognitive ability. The focus of the research group is to understand the interaction between apnoea and brain development in premature infants, and to investigate how physiology is altered by pharmacological and non-pharmacological interventions. The group is part of a multidisciplinary team of clinicians, nurses, mathematicians, engineers and scientists. The group's work focuses on the collection and use of EEG (electroencephalography) and vital signs (heart rate, respiratory rate etc) data, and the group develops signal processing techniques and uses machine learning to derive tools with the aim to ultimately improve outcomes for prematurely-born children.

Georg Hollander

The thymus is the anatomical site where T cells are generated and instructed to provide protective immunity against pathogens whilst ignoring the individual's own tissues. Thymic epithelial cells (TEC), an essential component of the organ's 3-dimensional scaffold, attract T cell precursor from the peripheral blood, foster their differentiation in a bespoke micro-environment, and help to select developing T cells based on their antigen specificities. Based on their distinct structural, phenotypic, and transcriptomic features, TEC are differentiated into distinct subtypes. Defects in TEC differentiation and function are incompatible with a normal generation of naive T cells and therefore frequently associated with severe combined immunodeficiencies or a loss of immunological tolerance. The research of the laboratory seeks to detail the genetic and epigenetic control of TEC development and function combining multi-parameter flow cytometry, advanced histological and molecular methods, proteomics, mathematical modelling and transcriptomic analyses at both population level and single cell resolution.

Teresa Lambe: Emerging and Outbreak pathogens

Despite therapeutic advances, the continued emergence and re-emergence of novel infectious pathogens can have devastating healthcare impacts. Increased global interdependence and the ease of human, animal and trade movements facilitate transmission and present multiple opportunities for pathogen spread.

There are a number of novel and dangerous pathogens with recognised pandemic potential, including but not limited to, SARS-CoV-2, Ebola, Marburg, Lassa Fever, Nipah, and Crimean Congo haemorrhagic fever. My team are currently focusing on the development and testing of the Oxford/AstraZeneca (ChAdOx1 nCoV-19/AZD1222) vaccine against SARS-CoV-2 working closely with Oxford Vaccine Group and global teams.

It is widely recognised that the health of humans and animals are interdependent and a number of emerging infectious diseases have a robust animal reservoir. The group are therefore delineating protective immune responses following natural infection in both human and animals to inform therapeutic development and vaccine design.

Using this information, the group are developing vaccines for a number of emerging pathogens with careful consideration of implications for veterinary cross-over and working closely with collaborators at the Pirbright Institute and NIH. Some of the works are at the pre-clinical stage while others have progressed to clinical trials.

This DPhil represents an exciting opportunity to build on the current and innovative program of vaccine development for emerging and outbreak pathogens while working in close collaboration with the Wellcome Trust major overseas research programme in Kilifi, Kenya and other key players for vaccine development against Emerging Pathogens.

Both specialised subject training and generic research capabilities will be developed, including but not limited to:

- Vaccine design (Molecular cloning & vaccine generation)
- Immunogenicity assessment of human samples
- Cellular immune assays (ELISpot, FACS & Intracellular Cytokine Staining (ICS))
- Humoral immune assays (ELISA, FACS & Cultured ELISpot)
- Development of translational assays (Pseudotyped virus assay)

All students will be expected to analyse, interpret and present their data internally and at appropriate conferences. This project will provide a broad range of transferable skills with a unique insight into translational research.

Martin Maiden: The application of the evolutionary and population approaches to the genomic analysis of bacterial pathogens for translation into public health interventions, especially immunisation.

Specific organism interests include the pathogenic Neisseria and Campylobacter. Highly interdisciplinary work across the Medical and MPLS Divisions. See, for example: MacLennan JM, Rodrigues CMC, Bratcher HB, Lekshmi A, Finn A, Oliver J, et al. Meningococcal carriage in periods of high and low invasive meningococcal disease incidence in the UK: comparison of UKMenCar1-4 cross-sectional survey results (Reference: Lancet Infect Dis. 2021;21:677-87. Epub 2021/01/23. doi: 10.1016/S1473-3099(20)30842-2. PMID: 33482143)

Daniel O'Connor: Utilising the "-omics" toolkit to elucidate the mechanisms underlying immune responses to vaccines and infections.

This theme of work explores multi-omics data across a spectrum of immune perturbation — vaccination through to infection. Research includes elucidating the genetic determinants of vaccine responses, describing novel immune correlates of protection, and developing rapid and accurate diagnostics.

Carlo Rinaldi

The overall purpose of the group's research is to reduce the global burden of hereditary neurological disease. This goal is pursued through three strategic aims:

1. identification of genes associated with neurological diseases,
2. advancement of the current understanding of the molecular mechanisms of pathogenesis in these diseases, and
3. development of effective treatments for hereditary neurological diseases.

This work has recently led to the development of an innovative gene therapy approach for a genetic condition named spinal and bulbar muscular atrophy, relying on viral delivery of an isoform of the disease gene Androgen Receptor and suitable for translation into the clinic (see reference: doi.org 10.1126/sciadv.abi6896) and the identification of genetic variants in the ATP6V0A1 gene as a cause of severe neurodevelopmental conditions (see reference: doi.org 10.1101/2021.06.01.21257500).

In particular, the group are interested in understanding the mechanisms underlying the diversification of the human transcriptomic (RNA editing), the ways those contribute to the functioning of the motor unit in health and disease, and how this knowledge can be harvested to enable targeted correction of mutations in coding sequences of RNA for treatment.

The group employs a combination of transcriptomic analyses, advanced microscopy, cellular and biochemical studies in human iPSC-derived neurons, disease models in mice, and translational studies in human subjects. The group's expectation is that these studies will ultimately reveal central disease mechanisms of neuromuscular diseases and serve as a foundation for the development of effective disease-modifying therapies.

Thomas Roberts: RNA medicine

Strategies for therapeutic manipulation of gene expression have matured to the point where there are now multiple FDA-approved drugs with diverse mechanisms of action including gene silencing (via RNase H-active gapmer oligonucleotides or RNA interference using siRNA) and direct antagonism of proteins (using aptamers), and exon skipping/inclusion using steric block oligonucleotides. Of particular interest are splice switching oligonucleotides that can rescue expression of proteins associated with Duchenne muscular dystrophy (DMD) and spinal muscular atrophy (SMA) – both paediatric muscle-wasting disorders which previously had very limited treatment options. Central to the development of these therapies is an understanding of disease nucleic acid biology (in terms of understanding the target mRNA splicing) and drug nucleic acid chemistry (the design, composition, and delivery of the therapeutic molecule). These exciting developments are paving the way for a plethora of new molecule medicines across a wide spectrum of disease indications. The group are interested in developing new modalities of therapeutic gene manipulation, including gene editing, RNA editing, and gene activation. Primarily, the group are focused on neuromuscular diseases (such as DMD and SMA) and infantile epileptic encephalopathies (such as Dravet syndrome).

Work in the group encompasses:

1. investigations of novel RNA-targeting or RNA-based therapeutic strategies;
2. gene expression profiling to better understand disease (especially in terms of spatial-restriction, sub-cellular localisation, and non-coding RNA); and
3. the development of biomarkers for monitoring responses to therapeutic intervention (with a particular focus on small RNA biomarkers).

Laurent Servais: STRONG (Specialised Translational Research Oxford Neuromuscular Group)

STRONG (Specialised Translational Research Oxford Neuromuscular Group) has a special interest for newborns screening of genetic condition, Angelman syndrome, innovative outcomes using magneto-inertial technology and wearable devices and natural history studies. The group are working with patients in order to design and conduct efficient clinical trials.

Rebeccah Slater: Paediatric Neuroimaging Group

The Paediatric Neuroimaging Group can offer a range of DPhil projects related to early life neurodevelopment and clinical research translation. The group's work is focussed on better understanding the development and treatment of infant pain. The groups places great importance on translating mechanistic insights from research into clinical practice and can offer DPhil students opportunities to focus on mechanistic research, clinical trials, methodology development (MRI, EEG and analytical approaches) and provide opportunities to work with industry, academia and regulators to optimise the acceleration of innovations into practice.

Rinn Song/Else Bijker: Novel Diagnostics for Paediatric Tuberculosis

Tuberculosis (TB) remains a significant cause of morbidity and mortality in children, particularly in low- and middle-income countries, with an estimated incidence of one million cases per year. Diagnosis of TB is complex, especially in young children, because their symptoms are non-specific, they cannot expectorate sputum and often have paucibacillary disease. Despite significant advances in TB diagnostics made in the last decade, they barely impacted on paediatric TB. As a result, under-diagnosis of those with TB is common. Improving paediatric TB diagnosis is very important, not only for individual patients, but also for the assessment of the true burden of paediatric TB and the development of new treatments and vaccines which is hindered by the lack of a reliable reference standard.

New approaches for diagnosis of paediatric TB are urgently needed, especially in three areas that the group is working on:

1. tests that can be used at the point of care level;
2. non-sputum-based tests; and
3. tests that can accurately identify the children with TB currently classified as microbiologically negative.

The group works together in a strong consortium of world-leading scientists and collaborators from around the world, including Uganda, Peru, the United States of America, Switzerland and Canada: the Feasibility of Novel Diagnostics for TB in Endemic Countries (FEND for TB) Consortium, funded by the U.S. National Institutes of Health for five years. The previous NIH-funded consortium led to the development of the GeneXpert Assay. The objective of the FEND for TB Consortium is to support the evaluation of early-stage tuberculosis diagnostic assays and strategies in the context of existing clinical algorithms in tuberculosis endemic countries. FEND for TB conducts early-stage diagnostic accuracy and feasibility studies and then feeds back to assay developers to facilitate the efficiency of the iterative assay evaluation-assay revision process. The consortium also involves a group of highly-recognised experts in modelling to evaluate impact, cost-effectiveness and other key factors to consider for the possible implementation of promising novel TB tests.

This project would offer a variety of exciting opportunities, including in-country study implementation and supervision, biostatistical and analytical work, modelling research, and through close collaboration with the Foundation for Innovative New Diagnostics (FIND) insight and contributions to the process of working with the WHO in their regulatory approval process of new diagnostic tests for TB. For further information, please see the grant information for FEND for FB and the grant information for Novel and Optimized Diagnostics for Pediatric TB (both external links).

Supervision

The allocation of graduate supervision for this course is the responsibility of the Department of Paediatrics and it is not always possible to accommodate the preferences of incoming graduate students to work with a particular member of staff. Under exceptional circumstances a supervisor may be found outside the Department of Paediatrics.

You will join one of the department's research groups with primary supervision provided by faculty members in one of the department's laboratory or clinical research facilities.

Assessment

Formal assessment of progress will be made at three points during the course: transfer of status, confirmation of status which traditionally takes place at the departmental annual research day held each summer and then final thesis examination.

Changes to courses

The University will seek to deliver this course in accordance with the description set out above. However, there may be situations in which it is desirable or necessary for the University to make changes in course provision, either before or after registration. These may include significant changes made necessary by a pandemic (including Covid-19), epidemic or local health emergency. For further information, please see the University's Terms and Conditions (http://www.graduate.ox.ac.uk/terms) and our page on changes to courses (http://www.graduate.ox.ac.uk/coursechanges).

Expected length of course

	Full Time Only
Expected length	3 to 4 years

Costs

Annual fees for entry in 2022-23

Fee status	Annual Course fees
Home	£8,620
Overseas	£28,560

Further details about fee status eligibility can be found on the fee status webpage (http://www.graduate.ox.ac.uk/feestatus).

Course fees are payable each year, for the duration of your fee liability (your fee liability is the length of time for which you are required to pay course fees). For courses lasting longer than one year, please be aware that fees will usually increase annually. Information about how much fees and other costs may increase is set out in the University's Terms and Conditions (http://www.graduate.ox.ac.uk/terms).

Course fees cover your teaching as well as other academic services and facilities provided to support your studies. Unless specified in the additional cost information (below), course fees do not cover your accommodation, residential costs or other living costs. They also don’t cover any additional costs and charges that are outlined in the additional cost information.

Graduate students who have reached the end of their standard period of fee liability may be required to pay a termly University and/or a college continuation charge.

The University continuation charge, per term for entry in 2022-23 is £548, please be aware that this will increase annually. For part-time students, the termly charge will be half of the termly rate payable by full-time students.

If a college continuation charge applies (not applicable for non-matriculated courses) it is likely to be in the region of £100 to £600 per term. Please contact your college for more details.

Additional cost information

There are no compulsory elements of this course that entail additional costs beyond fees (or, after fee liability ends, continuation charges) and living costs. However, please note that, depending on your choice of research topic and the research required to complete it, you may incur additional expenses, such as travel expenses, research expenses, and field trips. You will need to meet these additional costs, although you may be able to apply for small grants from your department and/or college to help you cover some of these expenses.

Living costs

In addition to your course fees, you will need to ensure that you have adequate funds to support your living costs for the duration of your course.

The likely living costs for 2022-23 are published below. These costs are based on a single, full-time graduate student, with no dependants, living in Oxford. We provide the cost per month so you can multiply up by the number of months you expect to live in Oxford.

Likely living costs

	Likely living costs for 1 month		Likely living costs for 9 months		Likely living costs for 12 months	
	Lower range	**Upper range**	**Lower range**	**Upper range**	**Lower range**	**Upper range**
Food	£290	£410	£2,610	£3,690	£3,480	£4,920
Accommodation	£680	£810	£6,120	£7,290	£8,160	£9,720
Personal items	£135	£260	£1,215	£2,340	£1,620	£3,120
Social activities	£45	£120	£405	£1,080	£540	£1,440
Study costs	£45	£100	£405	£900	£540	£1,200
Other	£20	£55	£180	£495	£240	£660
Total	£1,215	£1,755	£10,935	£15,795	£14,580	£21,060

When planning your finances for any future years of study at Oxford beyond 2022-23, you should allow for an estimated increase in living expenses of 3% each year.

More information about how these figures have been calculated is available at www.graduate.ox.ac.uk/livingcosts.

Document accessibility

If you require an accessible version of the document please contact Graduate Admissions and Recruitment by email (graduate.admissions@admin.ox.ac.uk) or via the online form (http://www.graduate.ox.ac.uk/ask).