

Course Information Sheet for entry in 2023-24: 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.

Expand each supervisor's name below to read more about the research themes and areas.

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).

Daniela Ferreira

Despite available vaccines, pneumonia is still a major killer affecting particularly vulnerable populations, such as children and the elderly. Pneumococcal infections are most common in the winter with secondary pneumococcal pneumonia being the major cause of mortality following seasonal and pandemic influenza infection. Our group uses Human Infection Challenge models in which participants are deliberately infected with live respiratory viruses and bacteria to study host-pathogen interactions, immune responses, pathogen transmission and to accelerate development of vaccines. Our group offers exciting DPhil projects in the following areas:

- Host and pathogen gene expression associate with pneumococcal shedding
- Systemic and mucosal correlates of protection to respiratory infection and vaccination
- Susceptibility to respiratory disease: chronic inflammation, comorbidities and immuneeaging
- Interaction of viral and bacterial co-infections and immune response modulation
- Use of nanoparticle platforms to develop treatments for virus and bacterial respiratory infections
- Computational biology and machine learning

Each project can be tailored to give the student exposure to their methods of interest including B and T cell ELISPOTs, ELISAs, Lumindex, multicolour flow cytometry and cell sorting, transcriptomic analysis at population and single cell level, and extensive data analysis (including R) and computational biology (machine learning).

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. This group's work is focused on the South African HIV epidemic. Although the group is based in Oxford, they have over the past 20 years developed strong collaborations in Durban and Kimberley, South Africa.

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.

Caroline develops approaches to analyse infant brain activity and physiological data, such as heart rate and oxygen saturation, to address clinically relevant questions in the field of neonatal neuroscience. Caroline's research focuses on understanding the impact of apnoea on premature infant brain development, and providing measures to improve the assessment and treatment of pain in infants.

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 episodes of apnoea have been associated with long-term effects including reduced childhood cognitive ability. 1 in every 10 babies are born prematurely; understanding and mitigating the long-term impact of premature birth is important to improve the lives of these 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 is 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.

Andrew Pollard

Oxford Vaccine Group

At the Oxford vaccine group our mission is the design, development, clinical evaluation and laboratory testing of vaccines to improve human health. We aim to achieve our mission with major programmes on:

- pneumococcal infection and vaccines (Daniela Ferreira);
- viral outbreak pathogens (Teresa Lambe);
- typhoid, paratyphoid, *Coxiella*, meningococcus and plague (Andrew Pollard);
- non-typhoidal salmonella (Maheshi Ramasamy);
- TB (Rinn Song);
- use of “omics” to interrogate vaccine responses (O'Connor); and
- social sciences of vaccines (Samantha Vanderslott).

Further details can be found under names of individual investigators. These major programmes above are in addition to a broad programme of work on COVID19 and the use of human challenge models and other experimental medicine studies. Our work includes opportunities for PhD training for potential students from both clinical and scientific backgrounds.

Maheshi Ramasamy

Enteric infections and mucosal immune responses

Infections caused by Gram negative bacteria are a major cause of childhood morbidity and mortality in low and middle income countries. Disease control ultimately requires access to good sanitation, but the current lack of sensitive diagnostic tests and increasing resistance to commonly used antibiotics make vaccines against these pathogens a cost-effective medium-term solution.

This theme investigates immunity against enteric pathogens with a focus on non-typhoidal Salmonella disease. Projects can range from assessing vaccines in healthy volunteer clinical trials to developing laboratory techniques to measure systemic and mucosal immune responses.

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).
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Anindita Roy

The developmental stage-specific cellular and molecular characteristics of fetal and postnatal progenitors are likely to determine the biology of ALL at different ages. We are particularly interested in high-risk childhood ALL, such as infant ALL and Down syndrome associated ALL. We have recently developed a novel MLL-AF4+ infant ALL model using primary human haematopoietic stem and progenitor cells. The overarching aim of research in our lab is to improve the outcomes of children with high-risk ALL.

The current DPhil projects are in these areas:

1. Developing faithful models of high-risk childhood ALL to better understand leukaemia initiation and maintenance at different ages;
 2. Mechanistic studies to understand key drivers of childhood ALL;
 3. Target discovery and translation of findings from (1) and (2) into preclinical studies; and
 4. Projects using multi-omics to understand how cell intrinsic and/or microenvironmental characteristics of the developmental stage at which a leukaemia originates, drives the biology of leukaemia at different ages.
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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.

Rebecca 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 group 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.

Samantha Vanderslott

Vaccines, Health and Society (VHAS) Unit

The Vaccines, Health and Society (VHAS) Unit is a multidisciplinary research centre that seeks to improve understanding of the roles played by different individuals and groups and their interaction with healthcare practice and medical research. The unit aims to produce theoretical and empirical research in social sciences and create a bridge to public health issues through policy advice, interventions, and public engagement. We draw on a variety of disciplines from sociology, history, behavioural science, health economics, and public policy to combine a wide set of tools and literatures. Further, being based within the Oxford Vaccine Group, benefits from the unique opportunity to interact with vaccinologists, epidemiologists, immunologists, and clinicians. A particular focus lies on studying actors' attitudes and behaviour towards vaccination in society, policy,

and media, across time and geographies. More broadly, our interests are also in a wide range of public health topics, including issue prioritisation, disease history, and social mobilisation. Our research unit runs regular research seminars, has ongoing collaborative writing groups on a wide range of topics, and frequently hosts visiting researchers, providing a lively environment for DPhil candidates. We can support a range of DPhil projects on the social aspects of vaccination and health, including co-supervision with other groups within the Department of Paediatrics (and in exceptional cases outside of the department).

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. During your program of study you would be expected to meet with your supervisor at least three times a term.

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. It is highly recommended that individuals speak to and consider a supervisor before they make a formal application.

Assessment

Formal assessment of progress will be made at three points during the course: transfer of status from Probationary Research Student (PRS) status to DPhil Status; this occurs in the 4th term. This is followed by confirmation of status which traditionally takes place either at the departmental annual research day held in late April or at the end of the ninth term. Then the final thesis and oral examination (*viva voce*) before the twelfth term ends.

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 2023-24

Fee status	Annual Course fees
Home	£8,960
Overseas	£29,700

Information about course fees

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 2023-24 is £572, 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 2023-24 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 for one month

	Lower range	Upper range
Food	£300	£470
Accommodation	£715	£860
Personal items	£180	£305
Social activities	£40	£90
Study costs	£35	£80
Other	£20	£35
Total	£1,290	£1,840

Likely living costs for nine months

	Lower range	Upper range
Food	£2,700	£4,230
Accommodation	£6,435	£7,740
Personal items	£1,620	£2,745
Social activities	£360	£810
Study costs	£315	£720
Other	£180	£315
Total	£11,610	£16,560

Likely living costs for twelve months

	Lower range	Upper range
Food	£3,600	£5,640
Accommodation	£8,580	£10,320
Personal items	£2,160	£3,660
Social activities	£480	£1,080
Study costs	£420	£960
Other	£240	£420
Total	£15,480	£22,080

When planning your finances for any future years of study at Oxford beyond 2023-24, it is suggested that you allow for potential increases in living expenses of 5% or more each year – although this rate may vary significantly depending on how the national economic situation develops.

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>).