DPhil in Cancer Science

University of Oxford

GSK Studentships

2026 Intake Project Booklet

OXFORD CANCER

UNIVERSITY OF OXFORD

NHS
Oxford University Hospitals
NHS Foundation Trust

GO-PRECISE Studentship Project Booklet

Introduction

This handbook provides an overview for prospective students looking to apply for a GO-PRECISE DPhil as part of the GSK funded studentships.

Global biopharma company GSK is investing up to £50 million in a collaboration with Oxford to advance the understanding of how cancer develops, which could inform future development of vaccines to prevent cancer. The agreement establishes the GSK-Oxford Cancer Immuno-Prevention Programme, aimed at exploring the potential of cancer prevention through vaccination.

The programme leverages the complementary expertise of GSK and Oxford in the science of the immune system, vaccine development and cancer biology. It is hoped that the insights generated through the programme into how cancer develops could inform new approaches to vaccination for cancer prevention, offering fresh hope in the fight against the disease.

Students will receive a world-leading research training experience that integrates an education initiative spanning cancer patient care, tumour biology and research impact; on- and post-programme mentorship; and a specialised, fundamental, subject-specific training tailored to individual research needs. Students participating in the scheme will be offered:

- a choice of interdisciplinary cutting-edge cancer research projects.
- the ability to gain a working in-depth knowledge of the fundamentals of cancer biology and cancer patient care through advanced level seminars.
- a world-renowned research environment that encourages the student's originality and creativity in their research.
- opportunities to develop skills in making and testing hypotheses, in developing new theories, and in planning and conducting experiments.
- an environment in which to develop skills in written work, oral presentation and publishing the results of their research in high-profile scientific journals, through constructive feedback of written work and oral presentations.

At the end of their DPhil course, students should:

- have a thorough knowledge of the basic principles of cancer research including the relevant literature and a comprehensive understanding of scientific methods and techniques applicable to their research.
- be able to demonstrate originality in the application of knowledge, together with a practical understanding of how research and enquiry are used to create and interpret knowledge in their field.

- have developed the ability to critically evaluate current research and research techniques and methodologies.
- be able to act autonomously in the planning and implementation of research.
- have the grounding for becoming an influential cancer researcher of the future.

Selection Criteria & Eligibility

Successful applicants will enrol on a four-year programme with the first year consisting of two six-month rotations within the selected project labs. This provides students with a broad base of experience and the opportunity to explore different aspects of research. All students are admitted directly to work under the supervision of a Principle Investigator (PI).

Eligibility – Non-Clinical/Fundamental Scientist. Science graduates that hold (or be predicted to achieve) the equivalent of a first-class or strong upper second-class undergraduate degree with honours in biological, medical, or chemical science, as appropriate for the projects offered.

All applicants will be judged on the following:

- commitment and passion to a career in cancer research
- evidence of motivation for and understanding of the proposed area of study
- commitment to the subject, beyond the requirements of the degree course
- preliminary knowledge of relevant research techniques
- capacity for sustained and intense work
- reasoning ability and academic curiosity.

Funding

All offered places are fully funded at the home rate. This includes salary/stipend, University/College fees, and a research consumables budget.

Stipend provisions are summarised below:

- Four years of stipend at the flat rate of £ 22,113 per annum.

How to Apply

Prospective students must apply with a **prioritised list of three projects selected from the GSK booklet by midday Thursday 8th January.**

Apply through the University of Oxford Graduate Admissions website for the relevant track.

- Track 3 (Non-Clinical/Fundamental Scientist - Biological background)

On the application form, in the section headed **'Departmental Studentship Applications'**, you must indicate that you are applying for the GSK studentship and enter the reference code for this studentship **"GSK25"**

Shortlisted students will be invited to interview in January. If successful, students will then begin their first year with two lab rotations. It is strongly suggested that students contact supervisors of projects they are interested in applying for prior to application.

Projects

Clicking on a project title below will take you to the relevant project page. The 6-month rotational project can be found at the end of each project page.

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1. Building a clinical and genetic data resource of BRCA carriers to support the development of preventative cancer vaccines – Sarah Blagden

Primary Supervisor: Sarah Blagden
Additional Supervisors: James Chettle

Abstract of the project
Approximately 5-10% of breast cancers are due to an underlying inherited cancer predisposition. In the general population, germline pathogenic variants occur in approximately 1 in 380 individuals for BRCA1 and 1 in 270 individuals for BRCA2. Women who carry a BRCA1 or BRCA2 variant have a 40-85% and 20-50% lifetime risk of developing breast and ovarian cancer, respectively. Individuals may also be at increased risk of other cancers such as pancreatic cancer, prostate cancer, and melanomas. Current management options for women with a BRCA variant include risk-reducing mastectomy (removal of both breasts) and risk-reducing salpingo-oophorectomy (removal of ovaries and fallopian tubes) at 35-40 years of age.

Like all cancers, BRCA-associated cancers progress through a pre-cancerous stage. There is growing interest in identifying and targeting these early lesions to prevent cancer from developing. Ongoing research is focused on characterising pre-malignant abnormalities at the molecular level and utilising these characteristics to inform new preventative approaches, including preventative vaccines.

Importantly, not all individuals carrying a pathogenic BRCA1 or BRCA2 variant have the same risk of developing cancer. The concepts of variable expressivity and incomplete penetrance are key to understanding the heterogeneity seen in BRCA-related cancers. An individual's cancer risk is shaped by a complex interplay of genetic and non-genetic factors, including variant-specific effects, family history, lifestyle, and polygenic modifiers. For example, the BRCA2 variant c.9976A>T (p.Lys3326Ter) has been shown to confer a significantly lower risk of breast and ovarian cancer compared to other truncating BRCA2 variants, highlighting the importance of variant-level risk stratification in clinical management.

Project Aim
The overarching aim of this research project is to develop a robust clinical and genetic data resource of individuals with a BRCA1/2 variant. This resource will support improved understanding of cancer risk variability and facilitate the development of a neoepitope-based vaccine. Ultimately, the project seeks to lay the groundwork for a preventative cancer vaccine clinical trial for BRCA1/2 carriers.

Research Objectives and Proposed Outcomes

Work Package 1: Direct-to-Patient Database Development

Objective: To establish "MyBRCA" a comprehensive clinical and genetic data resource of BRCA1/2 carriers to support future research into cancer risk, treatment, and prevention.
This work package involves the design and development of a database aimed at collecting detailed genetic, clinical, and lifestyle data from individuals with BRCA1 or BRCA2 variants.

Key activities will include:

- Obtaining informed consent from participants

- Collecting and biobanking biological samples (e.g., blood, saliva)
- Performing genetic testing
- Recording longitudinal clinical outcomes and lifestyle factors that may modify risk

Work Package 2: Vaccine Design and Development

Objective: To utilise the data resource to inform the design and pre-clinical development of a preventative vaccine for BRCA1/2 carriers.
This work package supports and complements ongoing efforts to identify tumour-specific, non-canonical antigens seen in BRCA-related cancers.
The goal is to design a vaccine capable of priming the immune system against pre-malignant or early tumour cells in BRCA carriers, thereby reducing the likelihood of cancer progression.

Work Package 3: Facilitate Preventative Cancer Vaccine Clinical Trial Development

Objective: To develop a clinical trial protocol for a preventative cancer vaccine targeted at individuals with a BRCA1/2 variant.

In this work package, insights from the data resource will be used for development of the clinical trial protocol. This includes:

- Stratifying patients by variant type, family history, and personal risk profile to identify optimal trial candidates
- Informing eligibility criteria and trial endpoints
- Using the data resource for potential participant recruitment and follow-up

Translational Potential
Breast cancer affects approximately 1 in 7 women during their lifetime, and ovarian cancer remains the sixth most common cancer among women in the UK. Despite advances in treatment, prevention and early detection remain the most effective strategies for reducing cancer-related morbidity and mortality.

This project will improve our understanding of the clinical and genetic basis of BRCA1/2 and lay the groundwork for vaccine development and subsequent vaccine clinical trials for this patient cohort. While this proposal focuses on BRCA-related cancers, the insights gained may also inform prevention strategies for other malignancies.

Training Opportunities
This interdisciplinary project provides a range of training opportunities including:

- Biological sample collection and biobanking
- Handling and analysis of clinical and genetic datasets
- Use of bioinformatic tools
- Exposure to translational immunology and vaccine design
- Clinical trial protocol development

2. Characterising and tracking vaccine specific T Cells in the periphery and in tumour sites, following the administration of novel cancer vaccines in humans – Ellie Barnes

Primary Supervisor: Ellie Barnes
Additional Supervisors: Tim Elliott, Felipe Galvez-Cancino

Abstract of the project
We have used state of the art approaches to characterise the magnitude, phenotype and function of vaccine generated T cells in the blood, after vaccination with ChAdOx1 and mRNA vaccine platforms. These approaches used stimulation of peripheral blood cells with vaccine antigen [1], and more recently cells sorting (using Flow Cytometry) of activated T cells after antigen stimulation (using the AIM assays) for T cell quantification, followed by sc-RNA sequencing of AIM+ T cells for in depth characterisation of T cell phenotype, cell interactions, and TCR repertoire characterisation [manuscripts in preparation/submission]. In this DPhil project you will; (i) apply similar sc-RNA seq approaches to assess in vivo human T cell responses to novel cancer vaccines, (ii) additionally track TCR clonotypes detected in the periphery in response to vaccination, to tissue sites of cancer/pre-cancer and iii) characterise in detail, the immune landscape in patients at high risk of cancer, using multiparametric flow cytometry and correlate this with subsequent vaccine responsiveness (e.g. heavy smokers/lung cancer patients vs healthy controls receiving lung cancer vaccines). This is an exciting opportunity to apply state of the art immune technologies to the development of novel cancer vaccines in humans.

Research objectives and proposed outcomes
Recent advances in cancer vaccines, such as mRNA neoantigen platforms demonstrate the capacity to induce durable, functional CD8+ T cell responses that correlate with prolonged recurrence-free survival in malignancies like pancreatic ductal adenocarcinoma. However, challenges persist in understanding the spatial distribution, clonal persistence, and tissue-specific adaptation of vaccine-induced T cells. Current methodologies combine antigen-specific T cell enrichment (e.g., AIM assays), single-cell RNA sequencing (scRNA-seq) for phenotypic profiling, and TCR clonotype tracking (e.g., CloneTrack) to decode differentiation states and longevity. Despite progress, gaps remain in linking peripheral immunity to intratumoural activity and identifying pre-vaccination immune landscapes that predict clinical efficacy. This project will bridge these gaps using cutting-edge multimodal technologies.

Work Package 1: High-resolution profiling of vaccine-induced T cell responses

Objective: Systematically map the phenotype, transcriptional programs, and clonal dynamics of vaccine-specific T cells in blood using longitudinal scRNA-seq with paired TCR analysis.
Methodology: Enrich antigen-specific CD8+ T cells via AIM assays and flow cytometry; Perform scRNA-seq with integrated TCR sequencing (10x Genomics) to resolve clonotype-specific differentiation trajectories; Apply PhenoTrack

Work Package 2: Spatial mapping of vaccine-specific T cell clonotypes

To link peripheral clonal persistence to intratumoural activity, revealing mechanisms of immune escape or clonal pruning.
Objective: Track peripheral TCR clones to pre-malignant/tumour sites and assess their functional impact on tumour evolution.

Methodology: Cross-reference blood TCR clonotypes with TCR sequences from tumour biopsies using single-cell or spatial transcriptomics; Deploy multiplex immunohistochemistry to spatially resolve clonally **expanded** T cells in tissue microenvironments; Analyse tumour phylogenetics to evaluate selective pressure on immunogenic neoantigens.

Work Package 3: Immune landscape stratification in high-risk cohorts

Objective: To establish immune stratification frameworks to personalize vaccine timing and combinatorial therapies by defining pre-vaccination immune signatures predictive of response in high-risk populations (e.g., smokers at risk for lung cancer).
Methodology: Use high-parameter flow cytometry (30+ markers to encompass include exhaustion markers, memory subsets, and innate lymphoid populations) to profile baseline immune states in peripheral blood and tissues. Integrate with scRNA-seq datasets from Work Package 1 to identify predictive biomarkers of vaccine responsiveness; Validate findings against reference T cell atlases

Training opportunities
This project will provide training in transcriptomics, spatial biology, and immune monitoring to advance mechanistic understanding and clinical translation of next-generation cancer vaccines.

References
[1] https://www.nature.com/articles/s41591-023-02414-4

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3. Impact of different LNP formulations on T cell immunodominance – Tim Elliott

Primary Supervisor: Tim Elliott
Additional Supervisors: Maria Aggelakopoulou

Abstract of the project
This research proposal aims to investigate the impact of mRNA and lipid nanoparticle (LNP) formulations on T cell immunodominance. Recent studies have shown that LNP-based mRNA vaccines can elicit potent T cell responses and enhance humoral immunity (1). However, the specific effects of different LNP compositions and mRNA modifications on T cell immunodominance patterns remain unclear. We hypothesize that altering LNP components, such as ionizable lipids and fusogenic helper lipids, as well as mRNA modifications, will influence antigen presentation and subsequent T cell activation, potentially shifting immunodominance hierarchies (2). By systematically evaluating various LNP-mRNA formulations in both *in vitro* and *in vivo* models, we aim to identify optimal combinations that can selectively enhance desired T cell responses against specific epitopes. This research will provide valuable insights for the rational design of more effective mRNA vaccines and could have significant implications for improving vaccine efficacy against infectious diseases and cancer.

Research objectives and proposed outcomes
Emerging evidence highlights lipid nanoparticles (LNPs) as critical platforms for mRNA vaccine delivery, with composition-dependent effects on immune activation. Recent studies demonstrate that LNP formulations containing ionizable lipids (e.g., C12-200, cKK-E12), β-sitosterol, and fusogenic helper lipids like DOPE enhance antigen presentation in dendritic cells (DCs) and drive robust T cell proliferation and cytokine production (IFN-γ, TNF-α, IL-2). Concurrently, mRNA modifications such as N4-acetylcytidine (ac4C) by NAT10 and m6A methylation have been shown to regulate translation efficiency and degradation kinetics, directly impacting T cell expansion and differentiation. Despite these advances, the interplay between LNP composition, mRNA modifications, and T cell immunodominance hierarchies—the preferential targeting of specific epitopes during immune responses—remains unexplored. This knowledge gap limits the rational design of vaccines capable of directing T cells against high-priority epitopes in infections or cancer.

Work Package 1: Systematic Screening of LNP Formulations on Antigen Presentation Objective: Identify LNP components that optimize DC uptake, mRNA translation, and epitope presentation. **Methodology:** Test 20+ LNP variants with variable ionizable lipids (C12-200, cKK-E12), helper lipids (DOPE vs. cholesterol/β-sitosterol ratios), and PEG content. Transfect bone marrow-derived DCs (BMDCs) with OVA- mRNA LNPs and quantify activation markers (CD40, CD86), IL-12 secretion, and MHC-I/II epitope presentation using mass spectrometry. Rank LNPs by their ability to induce cross-presentation of immunodominant vs. subdominant epitopes.

Work Package 2: mRNA Modification Engineering for Epitope-Specific Translation Objective: Determine how chemical modifications (ac4C, m6A) alter mRNA stability and ribosomal engagement to skew immunodominance. **Methodology:** Engineer OVA-mRNA with site-specific ac4C (via NAT10 co-delivery) or m6A modifications and encapsulate in top-performing LNPs from Work Package 1. Use ribosome profiling and RNA-seq in BMDCs to correlate modification patterns with epitope translation efficiency. Validate epitope hierarchy shifts using OT- I/CD8+ T cell proliferation assays and single-cell TCR sequencing.

Work Package 3: In Vivo Immunodominance Profiling and Functional Validation Objective: Evaluate how LNP-mRNA combinations alter epitope dominance in infection and tumour models.

Methodology: Immunize mice with top LNP-mRNA candidates and challenge with *Listeria*-OVA or E.G7-OVA tumors3. Map CD8+ T cell responses to 15 OVA-derived epitopes via tetramer staining and IFN-γ ELISpot. Deplete cDC1/cDC2 subsets to assess their roles in immunodominance using XCR1-DTR mice.

Training opportunities

This project will elucidate how LNP-mRNA design parameters govern T cell epitope selection, enabling precision engineering of vaccines with tailored immunodominance profiles and will provide training in human primary cell culture, advanced immune profiling techniques including spectral flow cytometry, RNAseq and mass spectrometry as well as molecular and chemical biology techniques.

Student Background

You should hold a first degree in a relevant discipline such as biomedical sciences or immunology or relevant field. A Master's degree in Immunology/ Cancer Science will be an advantage but is not a prerequisite. Previous laboratory experience in molecular biology and cellular immunology (e.g. mammalian cell culture, flow cytometry) will be an advantage but is not required, as the DPhil student will be trained and will have daily supervision as required by senior lab members and collaborators. Excellent communication skills and ability to work as part of a team are essential

References

1. Alameh MG, Tombácz I, Bettini E, Lederer K, Sittplangkoon C, Wilmore JR, Gaudette BT, Soliman OY, Pine M, Hicks P, Manzoni TB, Knox JJ, Johnson JL, Laczkó D, Muramatsu H, Davis B, Meng W, Rosenfeld AM, Strohmeier S, Lin PJC, Mui BL, Tam YK, Karikó K, Jacquet A, Krammer F, Bates P, Cancro MP, Weissman D, Luning Prak ET, Allman D, Locci M, Pardi N. Lipid nanoparticles enhance the efficacy of mRNA and protein subunit vaccines by inducing robust T follicular helper cell and humoral responses. Immunity. 2021 Dec 14;54(12):2877-2892.e7. doi: 10.1016/j.immuni.2021.11.001. Epub 2021 Nov 4. Erratum in: Immunity. 2022 Jun 14;55(6):1136-1138. doi: 10.1016/j.immuni.2022.05.007. PMID: 34852217; PMCID: PMC8566475.
2. Zeng Y, Escalona-Rayo O, Knol R, Kros A, Slütter B. Lipid nanoparticle-based mRNA candidates elicit potent T cell responses. Biomater Sci. 2023 Jan 31;11(3):964-974. doi: 10.1039/d2bm01581a. PMID: 36537916.

4.Discovery and Validation of Neoantigens for Immunoprevention of Colorectal Cancer – Eoghan Mulholland

Primary Supervisor: Eoghan Mulholland
Additional Supervisors: Simon Leedham and David Church

Abstract of the project
Colorectal cancer (CRC) develops over a prolonged period (typically 5 to 17 years) through a gradual accumulation of genetic and epigenetic changes that transform normal intestinal epithelium into malignant tissue. This extended window offers a unique opportunity to study early tumorigenesis and design immunopreventive strategies, including vaccines targeting pre-cancer-specific neoantigens.

This DPhil project focuses on the discovery and functional validation of neoantigens arising in pre-cancerous colorectal lesions. Our aim is to identify and characterise tumour-specific antigens from serrated, conventional, and familial adenomatous polyposis (FAP)-associated lesions using whole-genome sequencing (WGS) and long-read RNA sequencing, integrating these data with immune profiling and spatial biology. Ultimately, this work will inform the development of precision cancer vaccines for CRC prevention.

Resources available include:

- A comprehensive biobank of human pre-cancer lesions.
- Advanced human organoid and non-human in vivo models.
- Proprietary spatial statistics platform (MuSpAn).
- Expertise in organoid culture, multi-omics, and histopathology.

Research objectives and proposed outcomes
Identify CRC-specific neoantigens arising during early tumour evolution using high-resolution genomic and transcriptomic profiling. Characterise the immune landscape across distinct polyp subtypes and tissue compartments. Test antigenic drivers in vivo, evaluating their immunogenicity and therapeutic potential in mouse models of intestinal pre-cancer.

Work Package 1: Neoantigen Discovery through Multi-Omics Integration

Objective: Identify and prioritise pre-cancer-specific neoantigens in colorectal polyps.
Approach:

- Perform **whole-genome sequencing (WGS)** and **long-read RNA sequencing** on human polyp subtypes (serrated, conventional, and FAP-associated).
- Detect **somatic mutations**, **alternative splicing events**, and **fusion transcripts** to generate a comprehensive catalogue of candidate neoantigens.
- Integrate genomic and transcriptomic data using **neoantigen prediction pipelines** and correlate with immunopeptidome data from matched samples.
  Outcome: A refined list of high-confidence, lesion-specific neoantigens for downstream validation.

Work Package 2: Immune Profiling and Spatial Contextualisation

Objective: Characterise the immune landscape and spatial organisation of immune–epithelial interactions in pre-cancerous lesions.
Approach:

- Apply **spatial transcriptomics** and **multiplex proteomic imaging** to human polyp tissues.
- Quantify immune cell phenotypes, their abundance, and spatial distribution using our in-house **MuSpAn spatial analysis platform**.
- Compare immune architecture across distinct histological and mutational subtypes.
  Outcome: A spatially resolved immune atlas of early CRC lesions, revealing how neoantigen emergence correlates with immune editing and evasion.

Work Package 3: Functional Validation of targets and their context using human organoids and non-human model systems.

Objective: Validate neoantigen immunogenicity and assess how oncogenic signalling pathways influence antigen presentation and responses.
Approach:

- Modulate key pathways (**Wnt, MAPK, IFNγ**) using genetic or pharmacological tools ex vivo with human polyp organoid systems.
- Use **non-human models of intestinal polyposis** (e.g., *ApcMin*, inducible models) to test how key pathway modulation impacts in vivo systems.
- Explore **immune cell recruitment**, and **TME remodelling** over time in these models.
  Outcome: Mechanistic insights into how pathway dysregulation alters immune visibility, supporting rational design of immunoprevention strategies.

Translational potential
Each year, around 42,000 people in the UK face a life-changing diagnosis: colorectal cancer. For up to half of those who respond poorly to treatment, the disease spreads further leading to distant metastases and more aggressive outcomes. By developing our understanding of pre-cancerous lesions, we're working toward the development of preventative vaccines that could stop colorectal cancer before it starts.

Training opportunities
This interdisciplinary project is based at the Centre for Human Genetics and provides a rich array of training opportunities. The student will gain hands-on experience in genetic data analysis, tissue sample preparation for histopathological examination, and access to a collection of spatial transcriptomic datasets. In addition, they will be trained in fundamental wet lab techniques, develop a strong understanding of tumour biology, and explore key concepts in vaccine development.

Student Background
This project aims to identify and validate neoantigens arising in pre-cancerous colorectal lesions to inform the development of preventive cancer vaccines. Using whole-genome and long-read RNA sequencing, combined with immune profiling and spatial biology, it will characterise tumour-specific antigens across serrated, conventional, and FAP-associated polyps. Spatial transcriptomics and proteomics will map immune–epithelial interactions, while ex vivo models will assess neoantigen immunogenicity and the impact of oncogenic pathways on immune recognition. By integrating genomics, immunology, and spatial data, the project advances understanding of early colorectal tumorigenesis and supports the development of precision immunoprevention strategies targeting a major digestive cancer.

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