Sanger Excellence Fellowship Projects 2025

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Sanger Excellence Fellowship

2025 Excellence Fellowship Candidates:

- **Can either i) apply to pre-defined projects (see below), or ii) co-develop a project that combines their own interests and expertise with those of a preferred (or matched) Sanger Supervisor**
- **Must complete the Expression of Interest process before approaching potential supervisors about co-developing a project, this is to confirm your eligibility to participate in the call (and if co-developing a project, to support you engaging with a Sanger supervisor).**

Pre-defined projects

See below for a selection of pre-defined Postdoc projects spanning Sanger's scientific programmes:

1. Deciphering the regulatory landscape of the developing immune system - with Muzz Haniffa (Cellular Genomics Programme)
2. Developing a multiomic predictive model of disease response in Inflammatory Bowel Disease (IBD) - with Carl Anderson (Human Genetics Programme)
3. Developing machine learning models to predict human genetic interactions in different cellular contexts - with Mathew Garnett (Cancer, Ageing & Somatic Mutation Programme)
4. High-throughput multimodal profiling of immune cell morphology and transcriptomes for pooled variant-to-function screens - with Gosia Trynka (Human Genetics Programme)
5. Modelling Driver Mutations with Skin Organoids to Elucidate their Contribution to Cell Fate Decisions in Skin Cancer - with Dave Adams (Cancer, Ageing & Somatic Mutation Programme)
6. Multimodal 3D Mapping of Tissue Cell Ecosystems via Histology-Driven Transcriptomics - Mo Lotfollahi (Cellular Genomics Programme)
7. Predicting cancer evolution and resistance to therapy - with Matt Coelho (Cancer, Ageing & Somatic Mutation Programme)
8. Spatial transcriptomics of tuberculosis lung infections from the pre-antibiotic era - with Josie Bryant (Parasites & Microbes Programme)
9. Surveying the somatic mutational landscape and cancer risk in the upper gastrointestinal tract following chemoprevention therapy - with Ayesha Noorani (Cancer, Ageing & Somatic Mutation Programme)

- Candidates may apply to one of the projects below (or pursue the alternative route of co-developing a project with a Sanger Supervisor). If you are applying to one of the pre-defined projects below, you should note that:
- The lead supervisor will triage applicants, progressing up to 2 candidates per project to the shortlisting stage
- The Excellence Fellowship Review Panel will then shortlist candidates for interview and expects to invite no more than 1 candidate per project to interview
- Feedback will be available for unsuccessful candidates.

Projects for 2025

Project 1: Deciphering the regulatory landscape of the developing immune system

Lead supervisor: Muzz Haniffa (Cellular Genomics Programme)

Co-supervisor(s): Jussi Taipale (Generative & Synthetic Genomics Programme) and Mo Lotfollahi (Cellular Genomics Programme)

Human immune system development is a tightly regulated, multi-layered process that forms a key branch of prenatal hematopoiesis. It begins in the yolk sac, progresses through the aorta-gonad-mesonephros (AGM) region and fetal liver, and ultimately consolidates in the bone marrow. This progressive determination of immune cell identities and lineage specification is driven by coordinated actuation of cis regulatory elements by combinatorial binding of transcription factors resulting in regulation of specific gene expression programs. While the resultant expression landscape is well studied the preceding chromatin landscape is not well understood. This project aims to elucidate the interplay of chromatin and transcriptional landscapes using 10x Multiome and Fiber-seq using deep learning multi expert sequence modelling to uncover how chromatin architecture regulates gene expression during prenatal immune system development across diverse organs and timepoints.

You will be working primarily within the Haniffa lab, in close collaboration with two dynamic and interdisciplinary teams: the Lotfallahi and Taipale Groups.

You will generate a gestational hematopoietic and immune multiome atlas in human development for the first time, gaining state-of-art expertise in computational biology, genomics, protein-DNA structure-function relationship, and deep learning methods pertaining to sequence modelling and protein representations. You will be provided with training and opportunities to develop your early leadership skills by supervision of rotation PhD and masters students. You will also be actively encouraged to increase your scientific footprint by attending and presenting in international conferences, contributing to scientific proposals to expand the work and writing manuscripts for publication.

Project 2: Developing a multiomic predictive model of disease response in Inflammatory Bowel Disease (IBD)

Lead supervisor: Carl Anderson (Human Genetics Programme)

Inflammatory bowel disease (IBD) is composed of two major forms, Crohn's Disease and Ulcerative Colitis, both characterized by severe and debilitating inflammation of the gut. To reveal the molecular processes that accompany IBD progression, we have conducted large-scale analysis of scRNA sequencing data collected from healthy and diseased donors across multiple anatomical sites (Krzak et al., MedRxiv 2024; Ramirez-Navarro et al., MedRxiv 2025), correlating this with susceptibility genetics (Alegbe, Harris et al., medRxiv 2025). While useful in understanding drivers of disease, this does not address the significant clinical heterogeneity observed between patients. In recent years, a wide range of new therapies, including biologics and small molecules, have been approved for IBD.

Despite this, clinical trial and real-world data show primary non-response affects up to 40% of patients across all therapeutic classes and unfortunately, in those with an initial symptomatic benefit, 40% may subsequently lose response. A better understanding of who is likely to respond to each treatment would therefore be of significant clinical use.

To this end, we designed the IBD Response project with the goal of developing a multiomic predictive model of disease response. The project has assembled a longitudinal cohort of over 1,000 IBD patients from across the UK, generating a rich and unique multiomic dataset. This includes:

- Whole-genome sequencing data
- Longitudinal single-cell RNA sequencing and proteomic profiles from blood samples pre- and post-treatment
- Longitudinal metagenomic sequencing from stool samples at three timepoints
- Extensive clinical, drug response, and dietary information

You will work with a nationwide collaborative team of experts in genetics, genomics, immunology, metagenomics, nutritional sciences, and gastroenterology to draw causal insights into disease pathogenesis and drug response.
In conjunction with the other large-scale transcriptomic datasets, you will have the opportunity to address key research questions, including:

- How do different treatments impact single-cell transcriptomic and/or proteomic profiles over time?
- Which cell types are involved in treatment-associated gene expression changes?
- Can baseline transcriptomic/proteomic features predict individual response to specific therapies?
- How does regulatory variation (e.g quantitative trait loci) influence these trajectories?

This project provides a unique opportunity to contribute to the development of personalised treatment strategies in IBD by leveraging integrative, multi-layered biological data.

Project 3: Developing machine learning models to predict human genetic interactions in different cellular contexts

Lead supervisor: Mathew Garnett (Cancer, Ageing & Somatic Mutation Programme)

Co-supervisor(s): Saroor Patel (Cancer, Ageing & Somatic Mutation Programme)

Seminal genetic interaction (GI) studies in model organisms (e.g. yeast) have provided knowledge on mechanistic connections between genes. However, it has not yet been possible to comprehensively map GIs in human cells due to technical limitations. Furthermore, the lack of large-scale systematic screening of human GIs limits systems-level approaches, such as machine learning (ML), for accurate GI prediction.

Using an innovative CRISPR/Cas9 perturbation platform, we are assembling a large scale human GI mapl. Whilst this is a unique and rich dataset of unprecedented scale, it is not able to elucidate how GIs vary across different contexts, necessitating new powerful approaches for GI prediction. This computational project proposes to leverage the human GI map, along with other smaller scale GI datasets available in our lab, to develop ML models to accurately predict GIs in untested cellular contexts, providing deeper insights into gene regulatory mechanisms.

Human GI mapping will enhance understanding of how genetic information impacts on cellular phenotypes. Being able to predict GI maps in different cellular contexts will have applications for understanding GIs in Mendelian diseases and complex diseases, such as cancer. We anticipate the methodology arising from this project will be published in journals and presented at international conferences. Beyond our own findings, we will release the data for the community to analyse and use, amplifying the impact. We expect wide use of our findings and data, similar to DepMap (our cancer dependency map dataset in collaboration with the Broad Institute). We anticipate our data will provide training and benchmarking datasets for ML models across broad applications in human genetics, including developing new ML tools to predict GIs in different contexts (as proposed here) and thereby providing wide-ranging insights on gene regulatory networks.

The project will be supported through a collaboration with Fabian Theis (Helmholtz Munich), a world-leading expert in ML and existing collaborator. There may be an opportunity for you to receive ML training in the Theis lab during the course of the project. The approaches developed will be generalisable and we therefore anticipate the Fellow will be involved in preparing grants to seek additional funding to extend the scope of data generation, thereby gaining experience in grant writing.

Project 4: High-throughput multimodal profiling of immune cell morphology and transcriptomes for pooled variant-to-function screens

Lead supervisor: Gosia Trynka (Human Genetics Programme)

Co-supervisor(s): Omer Bayraktar (Cellular Genomics Programme) and Andrew Bassett (Cellular and Gene Editing Research, Scientific Operations)

Cell function is regulated through interconnected molecular layers, including signalling, transcription, gene expression, metabolism, and morphology. These layers do not act in isolation but are tightly co-regulated. We developed TGlow, a high-content imaging assay that quantifies T cell morphology and function at scale. To extend its utility for large-scale CRISPR screens and population studies of genetic variation, this project will integrate TGlow with pooled optical screening methods that enable guide RNA detection and multiplexed transcript detection for direct coupling of morphology, gene expression and genotype information. This approach will enable creating a multimodal platform that captures both morphological and transcriptional responses to perturbations in immune cells. It will allow us to systematically map how immune disease variants and gene perturbations reshape cellular programs, revealing the flow of regulatory information across molecular layers. Ultimately, this work aims to establish a scalable strategy for linking genetic variation to immune cell function through integrated, high-throughput multimodal phenotyping.

You will acquire expertise in high-throughput microscopy, multiplexed fluorescence imaging, spatial transcriptomics, and assay automation. You will gain hands-on experience designing and executing CRISPR-based perturbation screens in primary human immune cells and develop protocols tailored for morphological and spatial readouts. You will also build computational skills in image analysis, feature extraction, spatial barcode decoding, and statistical modelling to uncover structure-function relationships in T cells. Throughout, you will benefit from mentorship and collaboration across the Wellcome Sanger Institute and Wellcome Genome Campus communities, such as Open Targets and spatial genomics technology research groups. You will also benefit from local and international collaborations, including with the Broad Institute, Human Technopole and the University of Cambridge. These interactions will support scientific exchange, career development, and visibility within a vibrant international network.

Overall, this Fellowship will drive innovation in how we translate genetic discoveries into mechanistic understanding and prepare you for an independent career at the intersection of functional genomics, imaging, and immune biology.

Project 5: Modelling Driver Mutations with Skin Organoids to Elucidate their Contribution to Cell Fate Decisions in Skin Cancer

Lead supervisor: Dave Adams (Cancer, Ageing & Somatic Mutation Programme)

Co-supervisor: Muzz Haniffa (Cellular Genomics Programme)

Understanding how genetic mutations drive changes in cell behaviour and differentiation is central to advancing our knowledge of cancer biology. This project applies a novel skin organoid-based approach, originally developed to build a time-resolved atlas of human skin development to model the functional consequences of mutations curated in the Dermatlas project which is analysing rare skin cancers of unmet need.

By integrating single-cell RNA sequencing and immunofluorescence the project will enable detailed dissection of transcriptional and regulatory networks across skin cell types and developmental stages and will reveal an understanding the association between tumour specific genetic events and the biology of these conditions.

The project aims to adapt the above mentioned platform to introduce and characterise mutations found in Dermatlas using CRISPR-based genome editing in pluripotent stem cell-derived skin organoids. The approach provides a scalable system to trace how individual mutations, or combinations thereof, influence regulatory states, lineage commitment, and differentiation trajectories. Key cell populations—including melanocytes, keratinocytes, Schwann cells, and dermal fibroblasts will be analysed over multiple time points, with single-cell resolution, to determine how specific mutations perturb normal skin development and possibly trigger neoplastic transformation.

By combining precise mutational modelling with rich regulatory and phenotypic data, this work will offer a powerful framework for systematically linking genotype to cellular behaviour in a human context. Given the breadth of mutations catalogued in Dermatlas and the complexity of skin tissue, the scale of this project has the potential to transform how we understand the origins and progression of skin cancers. It will also establish a foundation for future efforts to identify key drivers, biomarkers, and therapeutic targets grounded in developmental biology and single-cell insight.

Project 6: Multimodal 3D Mapping of Tissue Cell Ecosystems via Histology-Driven Transcriptomics

Lead supervisor: Mo Lotfollahi (Cellular Genomics Programme)

Co-supervisor(s): Muzz Haniffa (Cellular Genomics Programme), Omer Bayraktar (Cellular Genomics Programme), Vijaya Baskar Mahalingam Shanmugiah (Haniffa Group), Amirhossein Vahidi (Lotfollahi Group), Arpit Merchant (Lotfollahi Group)

Spatial transcriptomics (ST) has revolutionised our understanding of the tissue cellular ecosystem. It has allowed us to dissect tissues by their constituent cell types and analyze how gene expression patterns are structured within their native spatial context. However, most spatial transcriptomic approaches remain inherently two-dimensional, providing only partial insight into the three-dimensional architecture of developing or complex organs. Understanding the 3D spatial organisation of gene expression is particularly crucial in the context of developing embryos, where tightly regulated spatial and temporal cues govern organogenesis and spatial patterning.

To this end, the goal of this Fellowship is to advance our understanding of organs as whole transcriptional entities by designing novel graph-based learning methods for complete 3D reconstruction of the organ at high cellular resolution of the tissue-wide transcriptome. Using unique ST datasets spanning interleaving sagittal sections of a developing human embryo at 6-7 post-conception weeks and lesional and nonlesional sections of skin tissue from patients with eczema, and shed valuable insights into the three dimensional development of cellular ecosystems in developing and diseased tissues.

You will benefit from interdisciplinary collaboration across labs at Sanger, gaining state-of-the-art expertise in computational genomics as well as deep-learning based AI pertaining to spatial transcriptomics modelling and graph representations. You will be provided with training and opportunities to develop your early leadership skills via supervision of rotation PhD and masters students. You will also be actively encouraged to increase your scientific footprint by reviewing for leading scientific journals, writing manuscripts, participating in grant and funding proposals, and attending and presenting your research at international conferences.

Project 7: Predicting cancer evolution and resistance to therapy

Lead supervisor: Matt Coelho (Cancer, Ageing & Somatic Mutation Programme)

Co Supervisor: Mathew Garnett (Cancer Ageing & Somatic Mutation Programme)

Drug resistance is a major challenge in the treatment of cancer. Accurately predicting resistance and identifying which patients will respond to a given drug is critical to improve cancer patient treatment outcomes. However, such precision medicine approaches are currently limited by our incomplete understanding of the function of DNA variants within cancer genomes.

Cutting-edge gene editing technologies such as base and prime editing enable the programmed installation of DNA variants at unprecedented scale. Coupling this to single-cell transcriptomics has the exciting potential to make mechanistic insights into how these mutations shape cancer evolution and resistance to therapy. The resulting single-cell transcriptomics datasets from cells harbouring thousands of different engineered cancer variants will be used to build predictive models of cancer drug resistance. You will use these unique datasets to explore novel ways to reverse or prevent drug-resistant cellular programmes. Overall, this project aims to improve treatment outcomes for patients with cancer. Secondly, it will build a new technology platform, sc-Prime-seq, for the investigation of variant function in cancer and other genetic diseases.

Anticipated outputs include a high-impact publication and models that will be widely used by the cancer research community. This project will be an excellent platform to build a generative model for therapeutic intervention, attracting further grant funding and building relationships with external collaborators. For example, you will be a part of the international Multiplexed Assays of Variant Effect (MAVE) and Atlas of Variant Effect Alliance (AVE) scientific communities, attending international conferences to present your findings. Your datasets will be made available to the scientific community as a public resource through the Perturbation Catalogue (EBI-Open Targets) and MAVE Database.
The project has wet- and dry-lab components, meaning you will develop skills in generating and analysing high-content perturbation data. Wet-lab skills will include NGS and advanced CRISPR techniques and screening, perturb-seq. Dry-lab skills will include single-cell RNA seq analysis and machine learning (ML) approaches. Furthermore, you will develop expert domain knowledge in cancer biology and drug resistance. You will be part of a dynamic and diverse lab environment (www.coelho-lab.com). Our team has a translational focus and is chiefly funded by Cancer Research UK, with close links with pharma and biopharma start-ups (BASE Rx). You will also be involved in mentoring and training graduate students in the team.

Project 8: Spatial transcriptomics of tuberculosis lung infections from the pre-antibiotic era

Lead supervisor: Josie Bryant (Parasites & Microbes Programme)

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is the leading cause of death from infectious disease. TB affects the lungs and is characterized by granulomas—complex immune structures formed to contain the infection. While animal models have provided insights into granuloma biology, significant differences from humans remain, leaving gaps in our understanding of host-Mtb interactions. Spatial transcriptomics is a powerful tool for mapping cell types and interactions in tissues, offering new avenues to study these complex dynamics. The Bryant lab has adapted this technology to capture mycobacterial and human transcripts in lung granulomas. However, modern samples often come from treated patients with low microbial loads, limiting the study of host-pathogen interactions.

This project will apply spatial transcriptomics to rare archival lung tissue from TB patients treated between 1930 and 1950, prior to the introduction of antibiotics. These historical samples offer a unique opportunity to explore host-Mtb interactions and granuloma architecture.

You will lead the bioinformatic analysis and interpretation of data generated as part of this project, likely becoming the lead author on the key publications coming out of this work. You will interact with many different teams across the institute (such as CellGen, SGP) as part of this project, gaining exposure to many different technologies and expertise. We anticipate this project will lead to a longer-term collaborative effort to understand TB biology in-situ and we are planning to apply for larger collaborative grants for which you would be a key contributor. The project involves close collaboration with immunologists and pulmonologists at the University of Bergen (Norway) and you may have the opportunity to visit our collaborators in Norway.

In summary, the project involves applying state of the art technology to a highly unique sample collection, which we anticipate will lead to the discovery of novel biology and multiple high impact publications. You will be encouraged to present this research at international tuberculosis conferences, thereby establishing themselves within the infectious disease field. By developing bioinformatic approaches to both human spatial transcriptomics data and microbial omics data, you will be in a highly unique position within the infectious disease landscape allowing you to carve out a unique niche for your future career.

Project 9: Surveying the somatic mutational landscape and cancer risk in the upper gastrointestinal tract following chemoprevention therapy

Lead supervisor: Ayesha Noorani (Cancer, Ageing & Somatic Mutation Programme)

Co-supervisor(s): Inigo Martincorena (Cancer, Ageing & Somatic Mutation Programme)

Oesophageal adenocarcinoma (OAC) is the sixth most common cancer worldwide and is deemed a ‘less survivable cancer’ because of its poor five-year survival of less than 20%.

There is an unmet need to use chemopreventive strategies in aggressive cancers like OAC that often present at non-curative stages. Using state-of-the art sequencing technologies to characterise the effect of these drugs on the clonal landscape will provide invaluable insights into how these medications work, often synergistically to alter cancer risk. In the longer term, this could be leveraged to develop cancer prevention strategies more widely, across cancer types.

This is a relatively new area of research that is incredibly exciting as we now have a way to profile the effect of various interventions on the normal epithelium to see if they alter cancer risk. We anticipate that this work will form a blueprint for interrogating the effect of drugs on the clonal landscape of the normal epithelium. We are focusing on the oesophagus, but there is scope for future work to be across tissue types so that the impact is even broader rather than restricted to one cancer type.

This work is highly novel and we anticipate it will result in publications in high impact journals and presentations at international cancer prevention and genomic conferences. This work could form the basis of further collaborations, including the set up of further trials with translational analysis. As a skill set, you will gain access to histopathology skills, laser capture microdissection and computational skills by working closely with our dedicated pathologist, and computational team within the Programme.