Postdoctoral Programme in Epidemiological and Evolutionary Dynamics

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WELLCOME GENOME CAMPUS

The Sanger Epidemiological and Evolutionary Dynamics (SEED) Postdoctoral Programme

The SEED Postdoctoral Programme offers the chance to develop and implement innovative methods for analysis of large-scale genomic datasets to address fundamental problems concerning the evolution, transmission dynamics and control of major infectious diseases.

Predefined projects

Below are a selection of projects and Faculty contact points that illustrate the research areas we envisage for the SEED Fellowships. However, we are keen to incorporate your own expertise and interests into these projects and so they provide a starting point only. If selected, we will work with you to develop a research project which you will present in the final stage of the SEED recruitment process. Projects will be co-supervised by at least one member of our Associate Faculty members and a Sanger Group Leader in the Sanger Parasites and Microbes Programme. Please apply via our job site

Self-proposed projects

You are welcome to propose a project of your own. This would need to be co-supervised by at least one member of our Associate Faculty members and a Sanger Group Leader in the Sanger Parasites and Microbes Programme. Please submit a brief outline proposal (approximately 500-1000 words) to the Group Leader and Associate Faculty member who you would like to work with via pam-recruit@sanger.ac.uk. Your proposal will need to be approved before you submit the application. Once approved, please apply via our job site.

SEED Projects for 2023

Respiratory metagenomics
Point of Contact: Josie Bryant and Ewan Harrison

The human gut microbiome is known to have significant and diverse impacts on host physiology. The lower respiratory tract has a surface area twice that of the gut and yet, until recently, has been considered to be sterile in the absence of lung disease. Next generation sequencing approaches have demonstrated colonisation of bacteria at even the most distal parts of the lung, however the ecological parameters and functional relevance of the respiratory microbiome remains unclear. The upper respiratory tract is the primary niche of a number of bacterial pathogens including Staphylococcus aureus and Streptococcus pneumoniae.

All microbes in the lung enter via the upper respiratory tract where bacterial densities are typically much higher. The microbes that enter the lungs of people with chronic lung diseases such as cystic fibrosis and chronic obstructive pulmonary disorder significantly contribute to disease progression. In addition, most acute respiratory infections such as pneumonia are caused by bacteria that are normal commensals of the upper respiratory tract. Therefore in order to fully understand the importance of the respiratory microbiome in disease, we need to understand the ecology of both upper and lower portions of the respiratory tract and the movements of microbes between them.

We are looking for a SEED fellow to study this ecosystem through metagenomic sequencing to provide a deep understanding of this niche. The Bentley, Bryant and Harrison teams are generating large scale microbiome data from samples taken from the respiratory tract (nose, throat and lung). Samples are collected from healthy donors, community samples from COVID-19 diagnostic testing as well as patients with a range of lung conditions including CF and COPD. These samples offer exciting opportunities to understand the fundamental biology of the respiratory microbiome and how it changes throughout life in health, disease and during infection.

By working between the Harrison and Bentley labs (upper respiratory tract) and the Bryant lab (lower respiratory tract), the fellow will be leading on analyses to bridge our understanding between these systems. The fellow will leverage methods developed by the Lawley lab for metagenomics of the gut microbiome, in addition to developing new analytical approaches to these large and complex datasets.

We are looking for a scientist with strong quantitative skills and an interest in understanding the ecology of microbial systems. The candidate will need to be able to work independently and collaboratively as they will be working between multiple faculty and external collaborators.

SEED Projects for 2023

Reconstructing the evolutionary history of pathogens during chronic infection
Point of Contact: Josie Bryant

Many bacterial infections of people with chronic lung disease are extremely difficult to treat, and therefore can last decades. These chronic respiratory infections present an evolutionary scenario where the length of colonisation allows the generation of a high level of within-patient diversity and the opportunity to continually adapt to the lung. This has documented for Pseudomonas aeruginosa[1], Burkholderia dolosa[2] and Mycobacterium abscessus[3,4] where processes such as hypermutation, selective sweeps and parallel genetic mutations are prevalent.

Previously, most bacterial whole genome studies have been primarily based on colony-purified samples; so have focused on calling consensus SNPs. This has meant there is little opportunity to investigate within-patient diversity through the detection of unfixed minority variants. As deep sequencing and metagenomics becomes more affordable – there is a need to develop methods to analyse these datasets. Phasing minority variants using short-read sequencing remains a problem.

In our lab we have developed methods based on those used to study tumour evolution[5], which allow us to reconstruct the evolutionary history of bacterial clones found within a patient[3]. However, our current approach is not statistically robust and is particularly sensitive to homoplasious variants – which are highly common in the context of drug resistance. Moreover, we require methods to detect and incorporate larger genomic variation (such as CNVs and INDELs) into these evolutionary reconstructions. The focus of this SEED fellowship will be to develop phylogenetically robust methods to infer the evolutionary history of bacterial infections within patients.

The SEED fellow will then apply these methods to a large deep sequencing dataset of P. aeruginosa infections longitudinally collected from people with chronic lung disease. By reconstructing the evolutionary history of the P. aeruginosa within patients, the fellow will be aiming to uncover evolutionary paths to drug resistance and increased virulence potential. A second aim is to use the daily shifts in subclonal dynamics to model the bacterial response to changes in drug regimen.

The successful candidate will have an interest in studying the evolutionary dynamics of pathogens, preferably with a background in phylogenetics and/or mathematical modelling.

SEED Projects for 2023

Respiratory virus dynamics

Point of Contact: Ewan Harrison

Building on the large-scale sequencing of SARS-CoV-2 at the Sanger Institute, the Respiratory Virus and Microbiome Initiative (RVI) aims to develop methods for routine sequencing of all clinically important respiratory virus (Flu, RSV, Parainfluenza, etc) and then to sequence at scale from community samples and from patients in hospital, both prospectively and from historical samples collected as part of mass testing during COVID-19 pandemic.

We are looking for a SEED fellow to analyse data generated by the RVI - example projects that the fellow might work on include:

1. Conducting comparative phylogenetic analysis of the different respiratory viruses at a national level to understand the dynamics of seasonal transmission and within-country spatial movement.

2. Combining sequencing data generated from samples collected as part of mass testing during COVID-19 pandemic with epidemiological and contact data, to attempt to characterise how much contact is necessary for transmission to be sustained for different viruses. This may differ by age, as the age patterns and relative infectiousness vary across respiratory viruses. During the pandemic, we have information about which measures were in place over time, and therefore in which age groups and in which types of activities contact was likely taking place. Linking this information with when and where respiratory viruses began to have sustained transmission is likely to be informative for future characterization of the joint dynamics of respiratory viruses.

3. The RVI data will be a rich and high-resolution view into the co-infection dynamics of respiratory viruses: do they compete with each other? Is there any evidence of one raising the risk of others? These interactions are key potential drivers of the overall burden of respiratory seasons and important inputs for any forecasting models that attempt to describe co-circulating respiratory viruses and the changing population dynamics and selection that shape respiratory seasons

Together these analyses will generate novel insights about the transmission of respiratory viruses and provide estimates of the effectiveness of contact tracing and other non-pharmaceutical interventions - information of importance to public health policy makers for future epidemic and pandemic preparedness.

We are looking for a scientist with strong quantitative skills and ideally a background in phylogenetic analysis. The candidate will need to be able to work independently and collaboratively as they will be working between multiple faculty and external collaborators.

Role Profile

Current job title:	Postdoctoral Fellow
Reports to:	Associate Faculty/Sanger group leader

Core Accountabilities [in approximate order of importance to role purpose]:
1. To plan a programme of research that is original but fits within the general research area of the team, taking into account the relevant literature, own experience, and advice from the team leader and other appropriate scientists.
2. To carry out the research, developing the practical skills required for successful completion.
3. To analyse data and write up results for publication, and to deal with all aspects of the publication process.
4. To communicate the results through other relevant means, such as talking or presenting posters at scientific meetings
5. To seek appropriate training, including taking an active part in any training programmes organised for post-doctoral training fellows. This will include transferable skills training.
6. To take a full part in the general duties of the team, and to pass on skills and knowledge to other team members and visitors. To take part in wider Sanger Institute activities as appropriate.
7. To complete training period in a timely manner, publish the research and document any unpublished data and materials before moving on to a new position.

Interacts with	Purpose of the interaction
Own team and others	Transfer of knowledge, skills, in both directions
Collaborators and other scientists worldwide as appropriate to project	Seeking and passing on knowledge, reagents

Describe the most complex/challenging aspects of the role

Planning and carrying out research, and striking an appropriate balance between fitting in with the goals of the team and developing their own independent research projects.

Knowledge, skills and experience required:

- PhD in a relevant subject area (E)

- Knowledge of a range of research techniques and methodologies in experimental/computational areas (E)

- Research expertise in an area that will complement and enhance the Institute's research strategy and goals (E)

- Ability to develop research objectives, projects and proposals for own and joint research, with the assistance of a mentor if required (E)

- Experience of carrying out both independent and collaborative research (E)

- Ability to plan and prioritise own work in order to meet deadlines, including using initiative to plan research programmes (E)

- Highly developed communication skills to engage effectively with a wide-ranging audience, both orally and in writing, using a range of media (E)

- Interest in and enthusiasm for the subject matter of the project (E)

- Commitment to personal development and updating of knowledge and skills (E)

- Working collaboratively with others and building working relationships with stakeholders at all levels (E)

- Demonstrates inclusivity and respect for all (E))

- Respects and demonstrates our core competencies outlined in our Behavioural Competency Framework (E)

- Experience working with international collaborators (D)

- Experience of handling and analysing computationally intensive datasets (D)

Equality, Diversity and Inclusion

Our global reputation for excellence is strengthened by our commitment to developing and maintaining a positive, fair and healthy working environment – our Equality, Diversity and Inclusion (EDI) Programme is about valuing our people and supporting them to be their best. Our leaders play a key role in nurturing a positive and inclusive culture where everyone can thrive and diversity is celebrated.

We have developed an ambitious programme of activity that drives organisational culture change, empowers our leadership and ensures that equity and inclusion principles are embedded across all of our processes – from recruitment, promotion, reward, to accessing career development opportunities

In order to further reinforce our commitment to being a fully inclusive workplace, we became Stonewall Diversity Champions in 2020 to support LGBT+ inclusion. We are also signatories of the Race at Work Charter and Disability Confident scheme and are working towards these principles.

Our broader Wellcome Genome Campus-wide EDI initiatives include our LGBT+, Race Equity, Neurodiversity and Parent and Carers' Staff Engagement Networks. These bring people together, raise awareness, provide specific and relevant support and development opportunities and are safe spaces for people to be themselves.

We are committed to providing equal opportunities for everyone, regardless of their background. We acknowledge that people from certain backgrounds are under-represented in our sector and we are committed to doing what we can to correct this. We positively encourage applications from candidates regardless of sex, race, disability, age, sexual orientation, gender reassignment, religion or belief, marital status, or pregnancy and maternity status.

For more information about EDI at GRL see our Equality in Science Programme.

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Our strength lies in the diversity of our people, skills and ideas."