2022
Parasites and Microbes Programme Overview

Our work

Who we are

Faculty

Associate faculty

International fellows

Honorary faculty

Programme support

Foreword

The Wellcome Sanger Institute has a proud history as a world leader in the genomics of eukaryotic, bacterial and viral pathogens. Over the past 30 years we have become firmly established as a global hub for pathogen and vector genome research and, more recently, for metagenomics and culturing of complex microbial communities.

The Parasites and Microbes (PaM) Programme has an ambitious and coherent scientific vision for the next decade. Our cutting edge science is built on a platform of established long-term national and international partnerships, developing open data tools and datasets relevant to basic science and disease control, as well as close links with local and international health organisations. We maintain a strong emphasis on endemic diseases of the developing world, and a long-term commitment to research training and capacity building in low- and middle-income countries. We also have leading roles in establishing global data sharing networks, such as the Malaria Genomic Epidemiology Network (MalariaGEN) and the Global Pneumoccocal Sequencing Project.

Genomic and metagenomic sequencing technologies are now sufficiently accessible, portable and affordable that we can work with research labs and public health bodies around the world to undertake prospective longitudinal analyses to better understand the evolutionary dynamics of species and complex microbial communities. Conducting studies over a timeframe of decades and at multiple levels of spatial resolution, ranging from local to global scales, allows us to characterise the intense evolutionary pressures applied by the use of drugs, vaccines, insecticides, and other public health interventions, as well as the impact of diet and lifestyle. This information will be increasingly vital to ensuring the effectiveness of strategies for tackling infectious disease and promoting health.

In addition to the incredible strength in depth among the PaM programme's teams of researchers, staff and technicians, an important element of our ongoing success has been a focus on collaborative research with scientists and public health bodies around the globe. This 'extended family' enables the programme to deliver impactful science at a scale well beyond the capacity of any individual research group within the programme. For example, we recently launched an Associate Faculty Programme in global pathogen surveillance, to which we have been fortunate to recruit four world-leading researchers. In addition we are privileged to be able to work with a cohort of world-class International Fellows and Honorary Faculty that, together with our Associate Faculty, provide strong collaborative ties and strategic links that will ensure the PaM Programme continue to have real-world impact in the years to come.
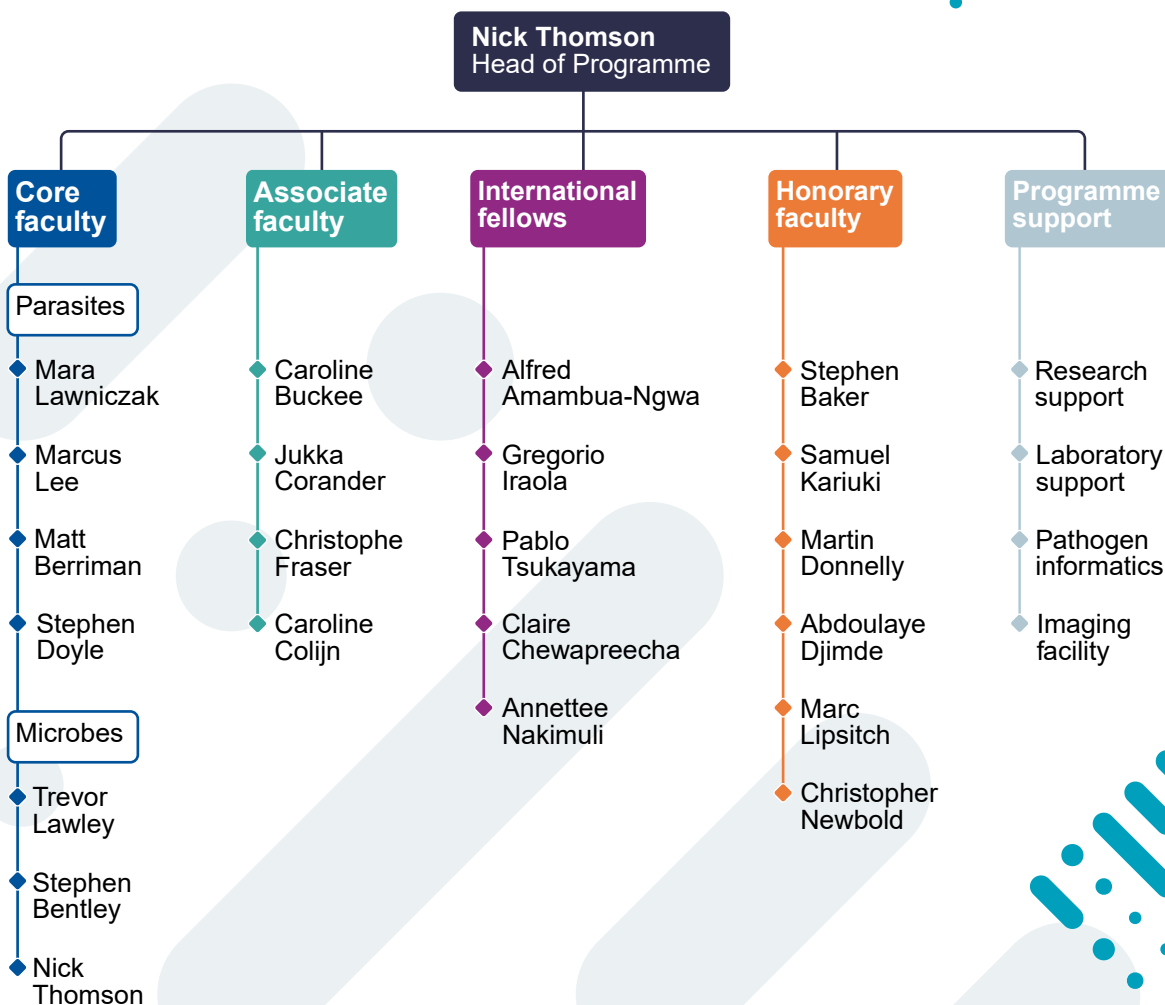
With the COVID-19 pandemic raising the profile of the benefits of genomic surveillance in public health settings, the next decade is set to be bright for the pathogen genomics and evolutionary dynamics fields. I am hugely pleased to be leading the PaM Programme as we enter this exciting next phase.

Nick Thomson

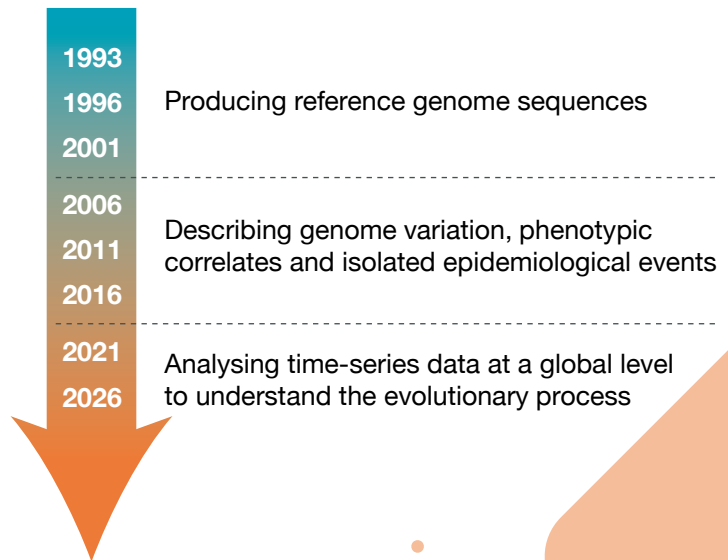Head of the Parasites and Microbes Programme

Programme summary


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              │   Nick Thomson      │
              │   Head of Programme │
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Core faculty	Associate faculty	International fellows	Honorary faculty	Programme support

Parasites

Core faculty
- Mara Lawniczak
- Marcus Lee
- Matt Berriman
- Stephen Doyle

Microbes
- Trevor Lawley
- Stephen Bentley
- Nick Thomson

Associate faculty
- Caroline Buckee
- Jukka Corander
- Christophe Fraser
- Caroline Colijn

International fellows
- Alfred Amambua-Ngwa
- Gregorio Iraola
- Pablo Tsukayama
- Claire Chewapreecha
- Annettee Nakimuli

Honorary faculty
- Stephen Baker
- Samuel Kariuki
- Martin Donnelly
- Abdoulaye Djimde
- Marc Lipsitch
- Christopher Newbold

Programme support
- Research support
- Laboratory support
- Pathogen informatics
- Imaging facility

The PaM Programme has an extensive collaborative network, with researchers and disease control programmes encompassing over 300 collaborating groups in 69 countries marked here in blue (low- and middle-income countries) and dark grey (high-income countries).
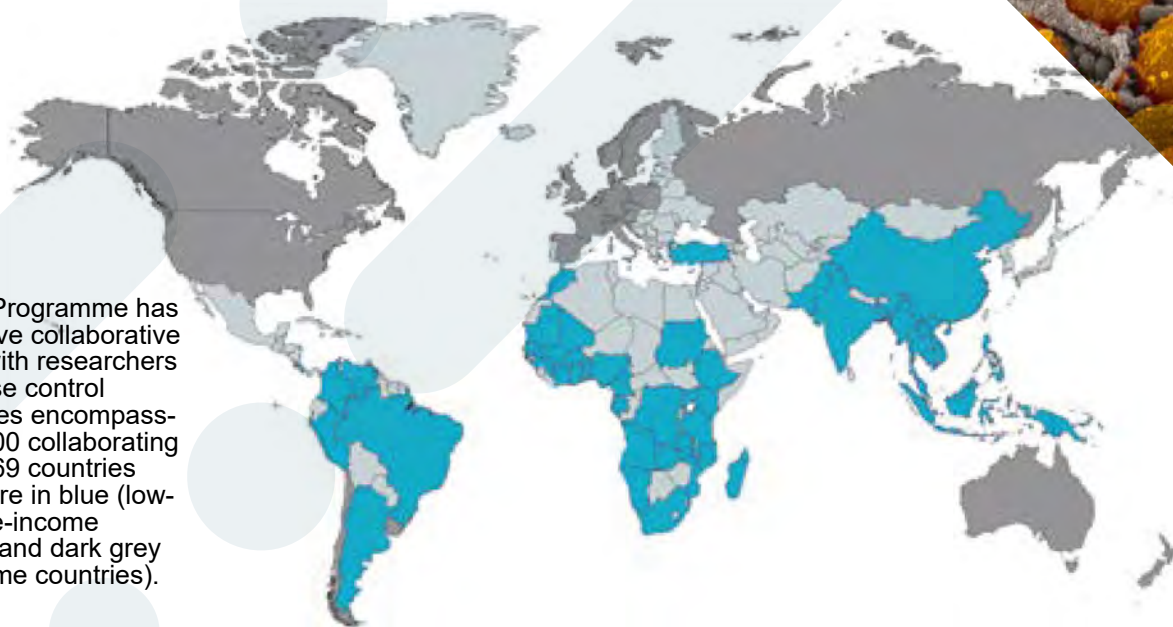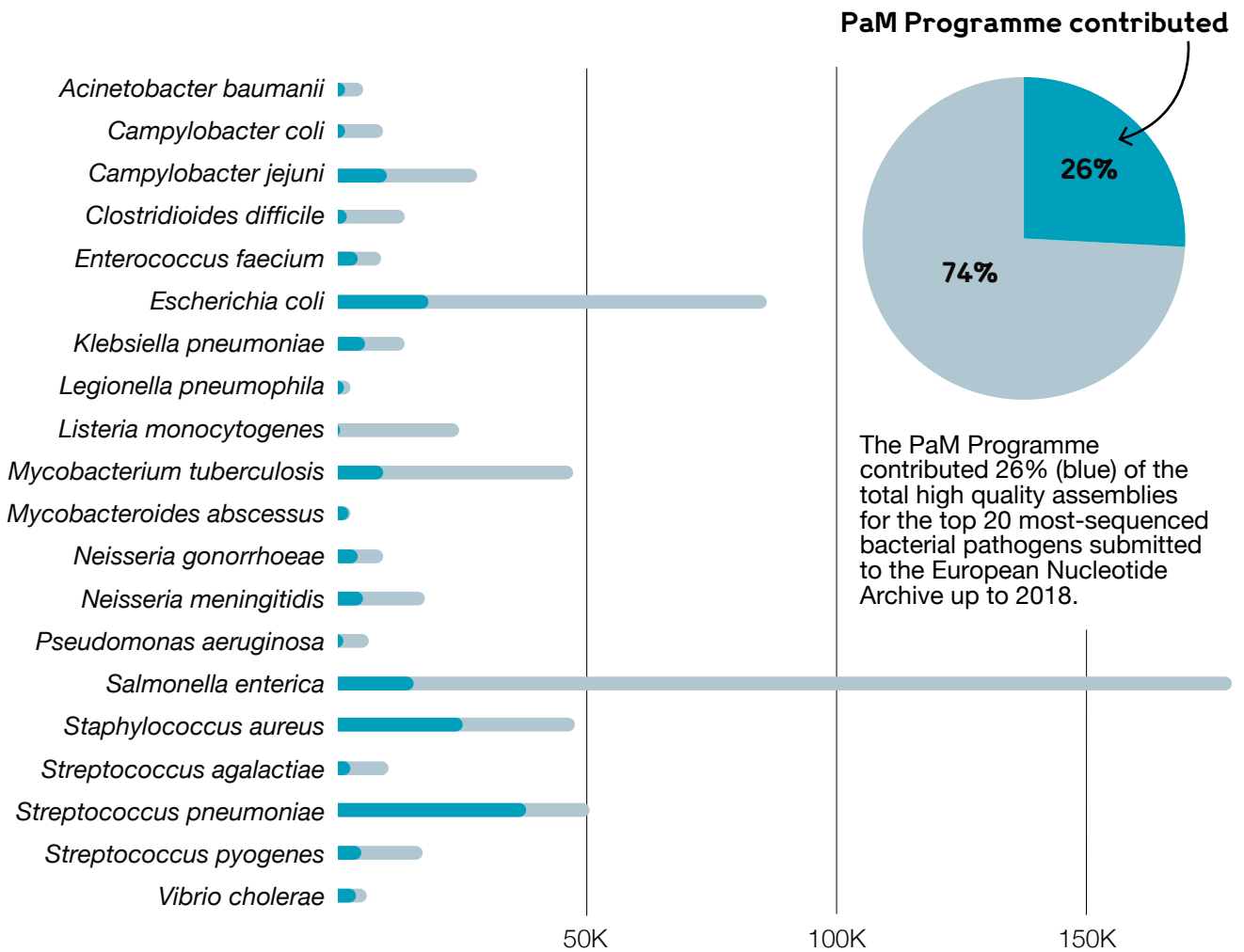
Sanger's contribution to research on parasites and microbes has evolved over time. Work in the PaM Programme in the coming years will increasingly focus on generating longitudinal datasets to investigate the evolutionary dynamics of pathogens, vectors and the human microbiome.

| 1993 | |
1996	Producing reference genome sequences
2001	
2006	
2011	Describing genome variation, phenotypic correlates and isolated epidemiological events
2016	
2021	Analysing time-series data at a global level
2026	to understand the evolutionary process

The PaM programme has a strong culture of cultivating the next generation of scientists, through training programmes for Masters & Doctoral researchers & career development opportunities offered to staff scientists. Numbers shown for 2014-2019.

8
MPhil

87
Postdoc

29
PhD
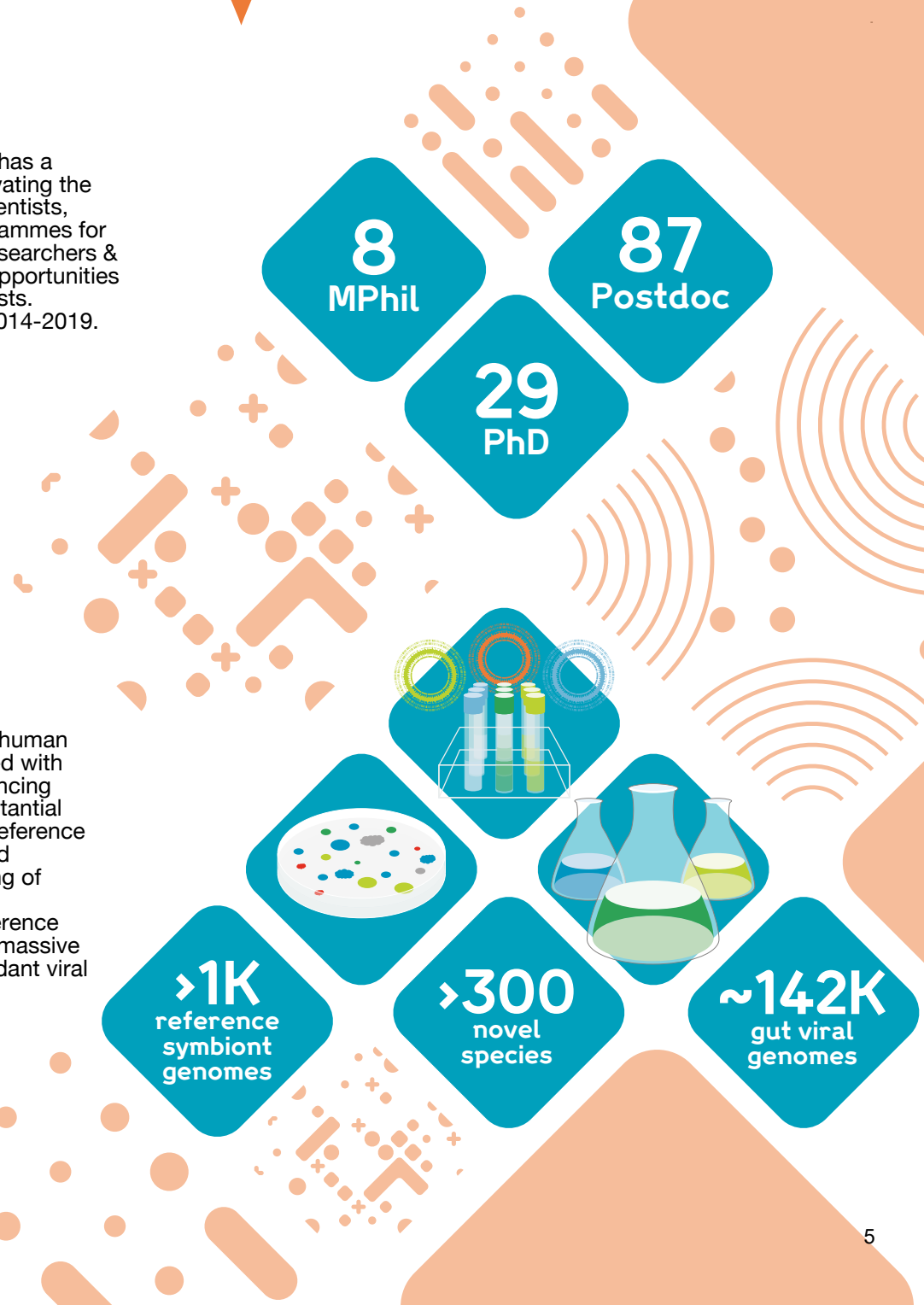
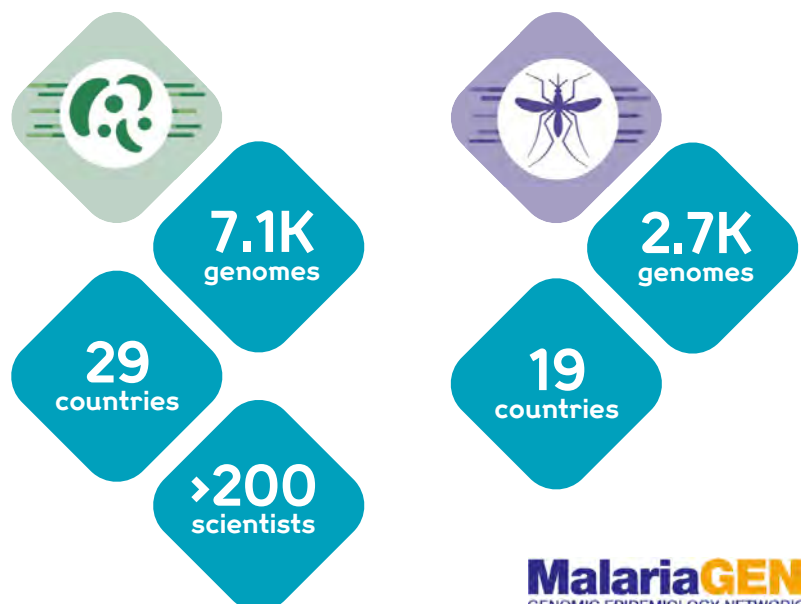Mass culturing of the human gut microbiota coupled with whole genome sequencing has resulted in a substantial increase in available reference genomes with cultured representatives. Mining of global human gut metagenome and reference genomes identified a massive number of non-redundant viral genomes (>10 kb).

›1K
reference symbiont genomes

›300
novel species

~142K
gut viral genomes

5

PaM Programme contributed

Species	
Acinetobacter baumanii	
Campylobacter coli	
Campylobacter jejuni	
Clostridioides difficile	
Enterococcus faecium	
Escherichia coli	
Klebsiella pneumoniae	
Legionella pneumophila	
Listeria monocytogenes	
Mycobacterium tuberculosis	
Mycobacteroides abscessus	
Neisseria gonorrhoeae	
Neisseria meningitidis	
Pseudomonas aeruginosa	
Salmonella enterica	
Staphylococcus aureus	
Streptococcus agalactiae	
Streptococcus pneumoniae	
Streptococcus pyogenes	
Vibrio cholerae	

Scale axis: 50K, 100K, 150K

Pie chart: 26% / 74%

The PaM Programme contributed 26% (blue) of the total high quality assemblies for the top 20 most-sequenced bacterial pathogens submitted to the European Nucleotide Archive up to 2018.

By the end of 2019, The Global Pneumoccocal Sequencing Project had sequenced >26K genomes as part of its worldwide survey of the impact of vaccination on the population of *Streptococcus pneumoniae*.
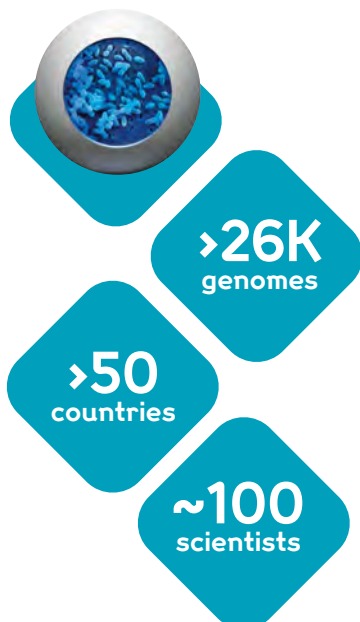
Through the MalariaGEN network, curated genome variation data has been released for >7K *Plasmodium falciparum* genomes, as well as a smaller but growing dataset of *P. vivax* genome variation. The *Anopheles gambiae* 1000 Genomes Project (Ag1000g) has released curated genome variation data on 2784 *Anopheles gambiae* specimens from 19 African countries, plus 297 specimens from laboratory crosses.

›26K genomes
›50 countries
~100 scientists

7.1K genomes
29 countries
›200 scientists

2.7K genomes
19 countries

MalariaGEN
GENOMIC EPIDEMIOLOGY NETWORK

226 programme members

6 Core faculty

14 Extended faculty

15 Postdoctoral fellows

16 MPhil & PhD students

14 Technicians

10 Staff scientists

28 IT & data science

39 Support & strategy

84 Visiting workers

Research of global importance

Insights only available through genomic sequencing are becoming increasingly vital for international efforts to tackle health priorities of global importance. Research being carried out by PaM faculty and their collaborative network are making critical contributions both to our understanding of the various intersections between microbial evolution and humanity, while also informing policy for controlling infectious disease and promoting health.

Global health

Infectious diseases do not respect international borders. As such the burden of striving to improve health and achieve equity in healthcare for people worldwide by tackling microbial pathogens needs to be shared at a global level. Not only is most research undertaken in PaM relevant to informing global health policy and outcomes, but numerous faculty are members of, or directly contribute to, a variety of national and international organisations that advise and support global initiatives to tackle infectious diseases and promote health.

Lawniczak
Lee
Berriman
Doyle
Thomson
Bentley
Lawley
Buckee
Corander
Fraser

Colijn
Nakimuli
Iraola
Chewapreecha
Amambua-Ngwa
Baker
Kariuki
Donnelly
Djimde

Vector-borne disease

Viruses and parasites that are transmitted by blood-feeding arthropod vectors account for more that 17% of all infectious diseases and more than 700K deaths annually. PaM faculty and their collaborators are developing the genomic and computational tools needed for large-scale analysis of genetic variation to understanding how human interventions drive evolutionary change in parasites, vectors, and human hosts. The insights gained will guide sustainable control strategies that drive down levels of drug and insecticide resistance.

Lawniczak
Lee
Doyle

Tropical disease

Malaria, and neglected tropical diseases found in large parts of Africa, Asia, and Latin America account for substantial morbidity and mortality. Many of these diseases can be controlled or eliminated through mass drug administration and other effective interventions. Insights from comparative genomics, and increasingly, large scale genomic surveillance programmes, now allow us to understand the evolutionary dynamics affecting these parasite populations, and to use these insights to inform control and elimination efforts.

Lawniczak
Lee
Berriman
Doyle
Buckee
Chewapreecha
Amambua-Ngwa
Kariuki
Donnelly

Djimde
Newbold

Antimicrobial resistance

Antimicrobial Resistance (AMR) is an urgent global problem, with widespread resistance to common antimicrobials increasing, while the pipeline for developing new drugs is essentially broken. AMR now claims hundreds of thousands of lives each year. Genome data is crucial to understanding the mechanisms underpinning AMR and its transmission. Researchers in the PaM programme undertake large-scale genomic surveillance of AMR in parasites and bacterial pathogens, to provide vital information for infectious disease control efforts.

Lee	Iraola
Doyle	Tsukayama
Thomson	Amambua-Ngwa
Bentley	Baker
Lawley	Kariuki
Corander	Donnelly
Fraser	Djimde
Colijn	Lipsitch

Genomic surveillance

Recent technological and computational advances, coupled with the decreasing costs of sequencing is enabling large-scale longitudinal genomic surveillance of bacterial, viral and parasite populations at local, regional and global scales. Such genomic insights into the evolutionary dynamics of pathogen populations in near real time, coupled with clinical and epidemiological data, allows PaM researchers to assess the influence of human interventions on pathogen populations, and use this information to advise on effective control strategies.

Lawniczak	Iraola
Doyle	Tsukayama
Thomson	Chewapreecha
Bentley	Amambua-Ngwa
Lipsitch	Baker
Buckee	Kariuki
Corander	Donnelly
Fraser	Djimde
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Epidemiology

Combining epidemiological approaches for surveying human populations with whole genome sequencing provides powerful new approaches for tackling infectious diseases and antimicrobial resistance. Epidemiological links that may previously have been missed can be identified by assessing the genetic relatedness of pathogen between infections or outbreaks. Conversely, genomic epidemiology can enable coincidental yet unrelated events to be disentangled, as well as providing insights into the efficacy of infection control measures.

Lawniczak	Kariuki
Thomson	Donnelly
Bentley	Djimde
Lipsitch	
Buckee	
Corander	
Fraser	
Colijn	
Baker	

Vaccines

Vaccination programmes prevent countless millions of infections and deaths each year. However, for any given pathogen, it is likely that some vaccine antigens are not expressed uniformly across the entire species. As such, using large-scale genomic analyses to understand how the introduction of a vaccine drives evolution at the population level, selecting for the expansion of vaccine-resistant lineages, is vital for ensuring that vaccinations can be updated such that they remain effective against the circulating pathogen population.

Baker
Chewapreecha
Bentley
Corander

Microbiomes & health

Recent years have seen a growing appreciation for the microbiome as a key determinant in human health and development, impacting a growing list of diseases and syndromes. We are only beginning to uncover the taxonomic and functional potential of the microbial communities contained on and within us, the majority of which have not been cultured. PaM faculty and collaborators are using advanced metagenomic sequencing, deep culturing and cutting-edge analytical tools to access and exploit this potential, to promote human health.

Lawley
Iraola
Baker
Tsukayama
Kariuki

Pathogenicity & virulence

Understanding the processes and molecular mechanisms that dictate whether an interaction between a microbe and a host (or vector) will be commensal, mutual or pathogenic is vital in developing new approaches to ameliorate the impacts of infectious disease and prevent infection and transmission. Research in the PaM programme uses comparative genomics and molecular genetic tools to identify the genes and pathways important for pathogenicity, virulence and antimicrobial resistance for a range of parasites and bacterial pathogens.
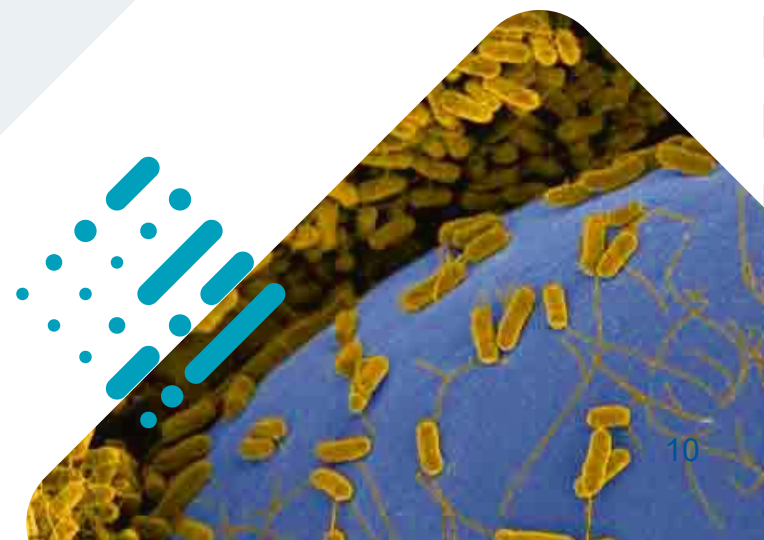
Berriman
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Amambua-Ngwa
Nakimuli

Iraola
Tsukayama
Baker
Lipsitch
Newbold

Pandemic preparedness

Given the enormous potential health and societal impact of novel pandemic pathogens, as aptly demonstrated by COVID-19, pandemic preparedness should be a high priority. Global networks for genomic surveillance can help to identify potential threats and inform pandemic prevention and response policy. Members of the PaM faculty and its collaborative network have been among the first-responders in establishing large-scale genomic sequencing for SARS-CoV-2, and in developing the infrastructure needed for wider genomic surveillance.

Lawniczak
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Fraser
Colijn

Iraola
Tsukayama
Chewapreecha
Amambua-Ngwa
Baker
Kariuki
Donnelly
Djimde

Dr Mara Lawniczak

✉ mara@sanger.ac.uk

Global health

Genomic surveillance

Epidemiology

Vector-borne disease

Tropical disease

Research

Mara Lawniczak is an evolutionary geneticist carrying out large scale whole genome sequencing projects on African *Anopheles* mosquito species as well as using single cell transcriptomics to investigate *Plasmodium* transmission dynamics. The Lawniczak group develops genomic tools and resources to deliver impact in malaria control while also enhancing our understanding of evolution. Mara and her team work on several MalariaGEN Vector Observatory projects ranging from amplicon sequencing to population genomics to building high quality reference genomes.

The group developed a targeted sequencing panel that sequences 62 short regions scattered across the generic *Anopheles* nuclear genome as well as two loci in the generic *Plasmodium* mitochondrial genome. The panel can be used on any *Anopheles* mosquito and reveals the species as well as if that mosquito carries malaria parasites and if so, which parasaite species. Beyond this, when many individuals of the same species are sequenced using the panel, it reveals population structure and can also identify cryptic populations/species. Over the 2022-2026, we will work with MalariaGEN Vector Observatory partners to study half a million mosquitoes to better understand the true diversity of malaria vectors.

Partnered with researchers across Africa, they also lead the *Anopheles funestus* population genomics project, to evaluate diversity and selection in this important but often overlooked species. As part of this endeavour, the team is also looking back in time at mosquito specimens collected over the past century (representing one thousand or more generations) of *Anopheles* evolution through Project Neandersquito, which is successfully generating whole genome sequencing data from historic pinned mosquitoes without destroying the specimen.

Supported by funding from the Bill and Melinda Gates Foundation, the team is also generating high quality reference genomes for a diverse set of *Anopheles* species. High quality genomes underpin our ability to understand the evolutionary trajectory of these important organisms and are critical to developing novel control tools, including for example gene drive approaches.

Through funding from the MRC, Mara and her team have created the Malaria Cell Atlas, which displays how any gene is expressed at any point across the entire life cycle of parasites in a freely available and interactive manner. Nucleotide variants from transcriptional data are used to assign genetic identity to each cell, thereby deconvolving natural mixed infections for the first time. Work is now underway to incorporate wild parasites from *P. falciparum*, *P. malariae*, and *P. ovale* into the Atlas. Finally the Lawniczak group use single cell RNAseq to study the behaviour of *P. falciparum* parasites from natural infections and to determine how malaria parasites behave inside of the human host to enhance their probability of transmission. In particular, using single cell approaches, they interrogate the relationship of the asexual and sexual parasites in a given infection, assess whether parasites mate non-randomly inside the mosquito. This work is ongoing with our collaborators from Djimde Abdoulaye's group in Mali, where we have installed a 10X Chromium controller to support scRNAseq research in West Africa.

Mara is also involved in the Darwin Tree of Life Project, which aims to generate reference genomes for all 60,000 or so British eukaryotic species in the next decade.

Collaborative projects

The Malaria Cell Atlas (MCA) includes data from multiple collaborative projects that have optimised and then applied methods to generate single cell transcriptomes for malaria parasites. The MCA includes single cell RNA-sequencing data covering all stages of the life cycle in both *Anopheles* vector and mammalian host tissues, spans both cell sorting and droplet-based scRNAseq and includes four *Plasmodium* species, including three human pathogens. It also includes the first single cell data from parasites isolated directly from clinical samples. In the MCA, users can explore how genes are expressed over thousands of individual parasites from several different

Plasmodium species and across all life stages. The MCA is beneficial to all malaria researchers, from those focused on particular gene families, to those developing novel drugs and vaccines. The *Anopheles gambiae* 1000 Genome project is a global collaboration using whole genome deep sequencing to provide a high-resolution view of genetic variation in natural populations of *Anopheles gambiae*, the principal vector of *Plasmodium falciparum* malaria in Africa.

Personal bio

Mara completed her PhD in Population Biology at the University of California Davis studying the female side of sexual conflict and arms race dynamics in *Drosophila* in the lab of David Begun. Continuing to work on this study system, she moved to Tracey Chapman's lab in London for a postdoc where she generated transgenic flies lacking seminal fluid proteins and studied fitness consequences of these losses. She took a year away from science after this postdoc and then returned to London for another postdoc with Fotis Kafatos and George Christophides at Imperial College London, where she switched to working on *Anopheles* mosquitoes. In 2012 she was awarded an MRC Career Development Fellowship and in 2014 she moved to Sanger to form her group focused on vector population genomics, where she has played a leading role in the Malaria Cell Atlas and the *Anopheles gambiae* 1000 genomes projects.
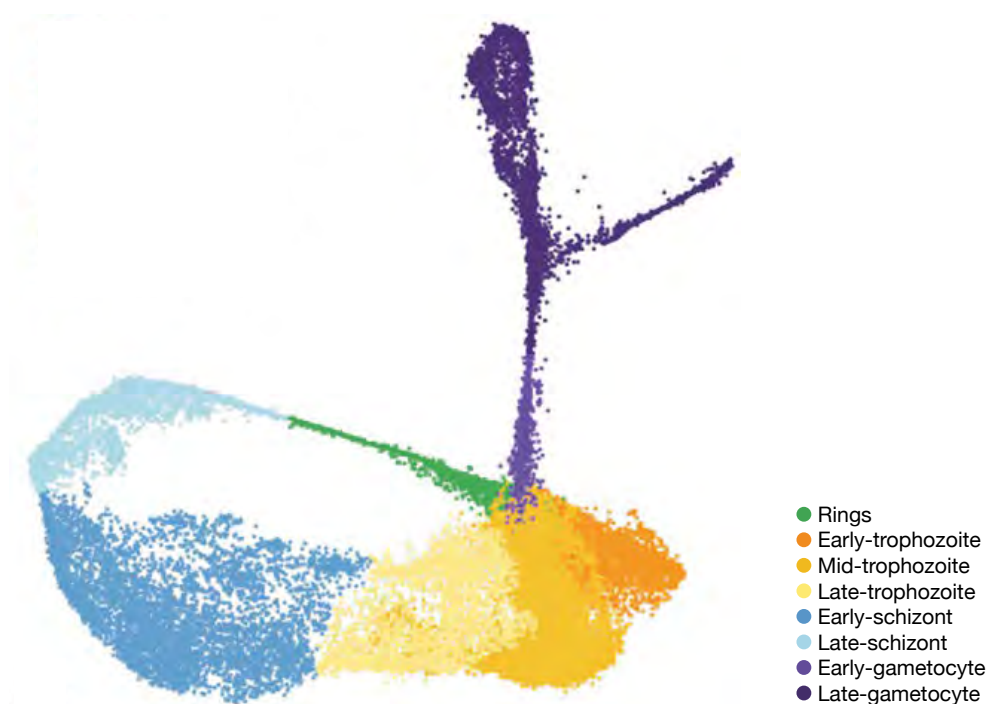

- ● Rings
- ● Early-trophozoite
- ● Mid-trophozoite
- ● Late-trophozoite
- ● Early-schizont
- ● Late-schizont
- ● Early-gametocyte
- ● Late-gametocyte

Figure: More than 30,000 *Plasmodium falciparum* single cell transcriptomes reveal the departure of the sexual parasites from the asexual cycle.

Selected publications

Korlević *et al*. (2021) A minimally morphologically destructive approach for DNA retrieval and whole genome shotgun sequencing of pinned historic Dipteran vector species. Genome Biol. Evol. evab226

Makunin *et al*. (2021) A targeted amplicon sequencing panel to simultaneously identify mosquito species and *Plasmodium* presence across the entire *Anopheles* genus. Mol. Ecol. Resour.

Real *et al*. (2021) A single-cell atlas of *Plasmodium falciparum* transmission through the mosquito. Nat. Commun. 12 (1): 3196

Heaton *et al*. (2020) Souporcell: robust clustering of single-cell RNA-seq data by genotype without reference genotypes. Nat. Methods 17 (6): 615-620

Horwick *et al*. (2019) The Malaria Cell Atlas: Single parasite transcriptomes across the complete *Plasmodium* life cycle. Science. 365: 6455

Kingan *et al*. (2019) A High-Quality De novo Genome Assembly from a Single Mosquito Using PacBio Sequencing. Genes. 10 (1): 62

Reid *et al*. (2018) Single-cell RNA-seq reveals hidden transcriptional variation in malaria parasites. eLife. 7: e33105

Anopheles gambiae 1000 Genomes Consortium (2017) Genetic diversity of the African malaria vector *Anopheles gambiae*. Nature. 552 (7683): 96-100

Professor Marcus Lee

✉ marcus.lee@sanger.ac.uk

Global health

Vector-borne disease

Tropical disease

Antimicrobial resistance

Research

Marcus Lee is interested in the molecular basis of drug resistance in the human malaria parasite *Plasmodium falciparum*, and in developing molecular genetics tools to interrogate gene function in this important pathogen.

Of the >5000 genes in the genome of the malaria parasite, a sizable number have unknown function and lack homologs outside of *Plasmodium* species. A deeper understanding of their roles and essentiality would provide biological insight as well as suggest new therapeutic targets.

An individual malaria infection can be driven by more than 100 billion parasites at the peak of the disease cycle. Over the course of a chronic infection, the parasite has the potential to mutate at rates that suggest the capacity to develop vast genetic diversity. This latent variability has troubling implications for the ease with which the parasite might develop resistance to drug treatment, both current and future. Understanding the mechanisms available to the malaria parasite to develop resistance, which often comes at a cost in terms of fitness in the absence of drug

pressure, can guide the development and prioritization of future therapeutic targets and provide fundamental biological insights into critical parasite pathways.

To identify new drugs, several large-scale screening campaigns have tested over 6 million compounds in cell-based screens against the blood stage of *P. falciparum*, yielding thousands of chemically diverse active drug scaffolds. However a major challenge is to leverage these compounds to identify targets that are either particularly vulnerable to perturbation, or refractory to resistance. The Lee group are developing new molecular genetics approaches that harness CRISPR/Cas to enable rapid systems-level analysis of multiple aspects of antimalarial compound action, including the identification of potential targets or mechanisms of resistance, cross-resistance profiles, and fitness costs associated with resistance. This will allow the prioritization of compounds that may have novel mechanisms of action or that antagonise the generation of resistance.

Collaborative projects

The Malaria Drug Accelerator (MALDA) Consortium is an innovative target-guided discovery platform linking phenotypic hits to function for malaria. MALDA is a collaboration of 17 scientific laboratories funded by the Bill and Melinda Gates Foundation

to use state-of-the-art *Plasmodium*-adapted technology platforms to advance the development of new antimalarial drugs in a manner that complements the existing ways malaria drugs are discovered.

Personal bio

Marcus Lee received his PhD from the University of Melbourne, Australia, where he studied plant defence proteins. He subsequently undertook his postdoctoral training, first in yeast cell biology with Randy Schekman at the University of California Berkeley, and subsequently with David Fidock at Columbia University Medical Center, where he worked on mechanisms of
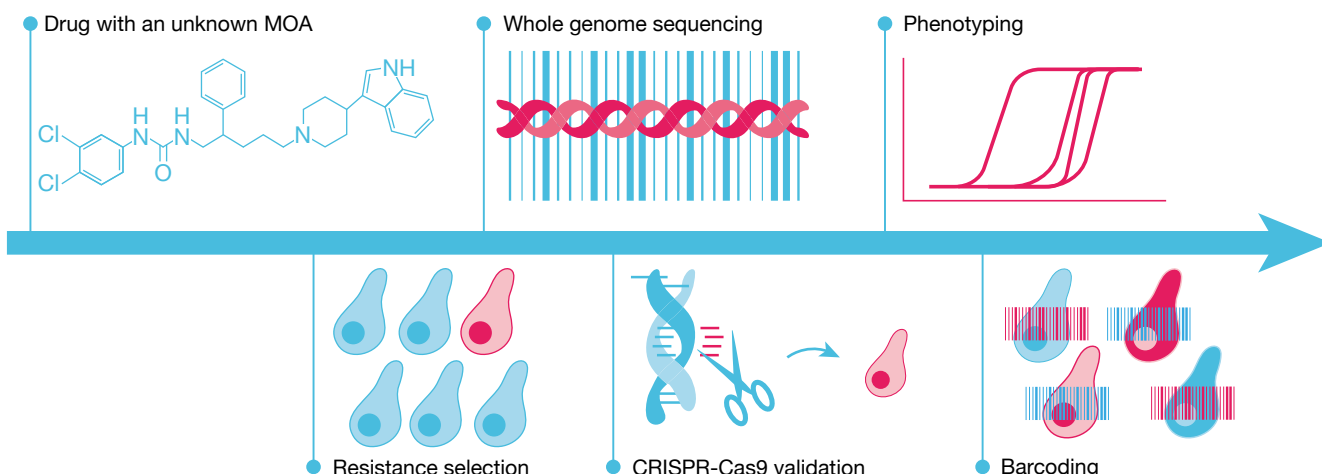
resistance to novel antimalarial compounds. Marcus joined the Malaria Programme at the Wellcome Sanger Institute in 2015. His current work continues to focus on drug resistance, and to complement these investigations, he has been developing novel methods to manipulate the parasite genome.

Drug with an unknown MOA · Whole genome sequencing · Phenotyping · Resistance selection · CRISPR-Cas9 validation · Barcoding

Selected publications

Rocamora *et al*. (2021) PfMFR3: A Multidrug-Resistant Modulator in *Plasmodium falciparum*. ACS Infect. Dis. 7 (4): 811-825

Carrasquilla *et al*. (2020) Defining multiplicity of vector uptake in transfected *Plasmodium* parasites. Sci. Rep. 10 (1): 10894.

Vanaerschot *et al*. (2020) Inhibition of Resistance-Refractory *P. falciparum* Kinase PKG Delivers Prophylactic, Blood Stage, and Transmission-Blocking Antiplasmodial Activity. Cell Chem. Biol. 27 (7): 806-816

Karpiyevich *et al*. (2019) Nedd8 hydrolysis by UCH proteases in *Plasmodium* parasites. PLOS Pathog. 15 (10): e1008086

Lee *et al*. (2019) Cutting back malaria: CRISPR/Cas9 genome editing of *Plasmodium*. Brief. Funct. Genomics 18 (5): 281-289

Cowell *et al*. (2018) Mapping the malaria parasite druggable genome by using in vitro evolution and chemogenomics. Science 359 (6372): 191-199

Lim *et al*. (2016) UDP-galactose and acetyl-CoA transporters as *Plasmodium* multidrug resistance genes. Nat. Microbiol. 1: 16166

Corey *et al*. (2016) A broad analysis of resistance development in the malaria parasite. Nat. Commun. 7: 11901

Baragaña *et al*. (2015) A novel multiple-stage antimalarial agent that inhibits protein synthesis. Nature 522 (7556): 315-20

McNamara *et al*. (2013) Targeting *Plasmodium* PI(4) K to eliminate malaria. Nature 504 (7479): 248-253

Straimer *et al*. (2012) Site-specific genome editing in *Plasmodium falciparum* using engineered zinc-finger nucleases. Nat. Methods 9 (10): 993-8

Rottmann *et al*. (2010) Spiroindolones, a potent compound class for the treatment of malaria. Science 329 (5996): 1175-80
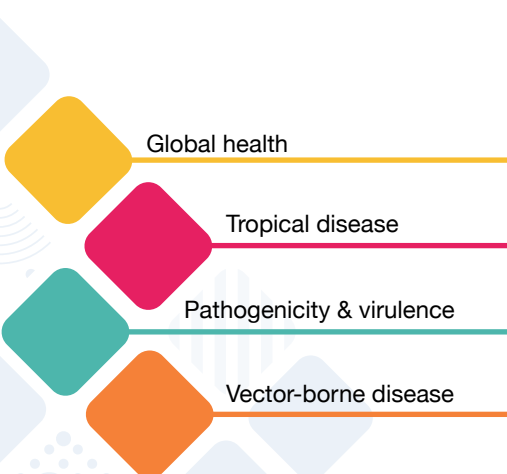
Lee *et al*. (2005) Sar1p N-terminal helix initiates membrane curvature and completes the fission of a COPII vesicle. Cell 122 (4): 605-17

Dr Matt Berriman

✉ mb4@sanger.ac.uk

🐦 @Berriman_mb4

- Global health
- Tropical disease
- Pathogenicity & virulence
- Vector-borne disease

Research

Matt Berriman leads the parasite genomics group who study the parasites that cause malaria and neglected tropical diseases. Parasites have an enormous impact on human health. The Berriman group is interested in the genes that underpin key differences between parasite lineages. These genes are often involved with pathogenesis processes and interactions between parasites and their hosts. They are particularly interested in helminths, including schistosomes, tapeworms, whipworms, threadworms and hookworms, which cause some of the most neglected diseases and collectively infect more than a billion people.

The Berriman group use comparative genomics to sift through the vast numbers of uncharacterised genes and identify those that are limited to, or evolving more rapidly in, specific groups of parasites. In the groups largest study (the 50 Helminth Genomes project), they compare draft genomes to gain a broad overview of most of the major roundworm and flatworm lineages that impact human health. In other studies, they use finer-grained comparisons to drill into the details of parasite evolution within individual clades.

The group also investigate natural genome variation of neglected parasites to understand their epidemiology and evolution, and exploit laboratory-models of parasite life-cycles established in house to create functional genomics data-sets that identify genes, and their regulation, involved in host-pathogen interactions or key stages of parasite development.

Matt's earlier work at the Sanger Institute focussed on analysing the accurate reference genomes that now form the cornerstones of large-scale comparisons– for species of malaria, leishmania and trypanosome parasites. For malaria parasites, the Berriman group have now produced accurate genome sequences from across the *Plasmodium* genus and are particularly interested in the organisation and function of the subtelomeric regions of chromosomes. These regions comprise 10-15% of the parasite's genomes, contain large repertoires of host-interacting genes and play important roles in the establishment and maintenance of infections.

Collaborative projects

The 50 Helminth Genomes Project (50HGP), surveys the genomes of the parasitic worms that have the greatest impact on human, agricultural and veterinary disease and cause significant global health issues, particularly in the developing world. Helminth infections account for morbidity equivalent to that of malaria or tuberculosis and more than one billion people are infected globally every year. However, despite their importance, parasitic helminth research remained relatively untouched by genomics compared to other infectious disease agents. In collaboration with the McDonnell Genome Institute at Washington University and Edinburgh Genomics, the 50 Helminth Genomes project is working to produce new draft helminth genomes, to populate the phylogenetic space around current high quality reference helminth genomes, and to identify major differences between parasite lineages.

The Building Upon the Genome (BUG) Consortium is a BBSRC-funded project to exploit genomic approaches to understand anthelminthic drug resistance in GI nematodes of small ruminants. Through a combination of a genetic cross and population genomics of worms in UK sheep flocks, the BUG Consortium aims to use the recently published genome of the sheep parasite *Haemonchus contortus* to identify the genetic changes that allow worms to survive drug treatment.

The Flatworm Functional Genomics Initiative (FUGI) consortium is funded by a Wellcome Trust Strategic Award to develop game-changing research tools for the study and manipulation of parasitic flatworm species responsible for the devastating diseases echinococcosis (hydatid disease) and schistosomiasis (bilharzia). These tools include the establishment of stem cell systems, reverse genetic toolkits, and immortal cells lines for *Schistosoma mansoni* and *Echinococcus multilocularis*.

In collaboration with the Guinea worm eradication programme, the

Berriman group is using genome analysis to determine the epidemiological link between the growing number of canine cases and the persistence of "sporadic" human cases.

Personal bio

Matt undertook a PhD with Professor Alan Fairlamb at the London School of Hygiene and Tropical Medicine and the University of Dundee, characterising a putative drug target for the malaria parasite *Plasmodium falciparum*. After being awarded a Wellcome Trust Travelling Prize Fellowship, Matt moved to the laboratory of Professor George Cross at Rockefeller University in New York to study trypanosome telomeres. At the end of 2000, he joined the Wellcome Sanger Institute as a Senior Computational Biologist in the pathogen genomics unit. From 2003, Matt took over leadership of more than 20 eukaryotic pathogen sequencing projects primarily focussed on important Ampicomplexan and Kinetoplastid protozoa. Matt joined the faculty in 2008 and leads a programme in the genomics of Neglected Tropical Disease parasites, including helminths such as schistosomes, tapeworms, roundworms, hookworms, threadworms and whipworms.
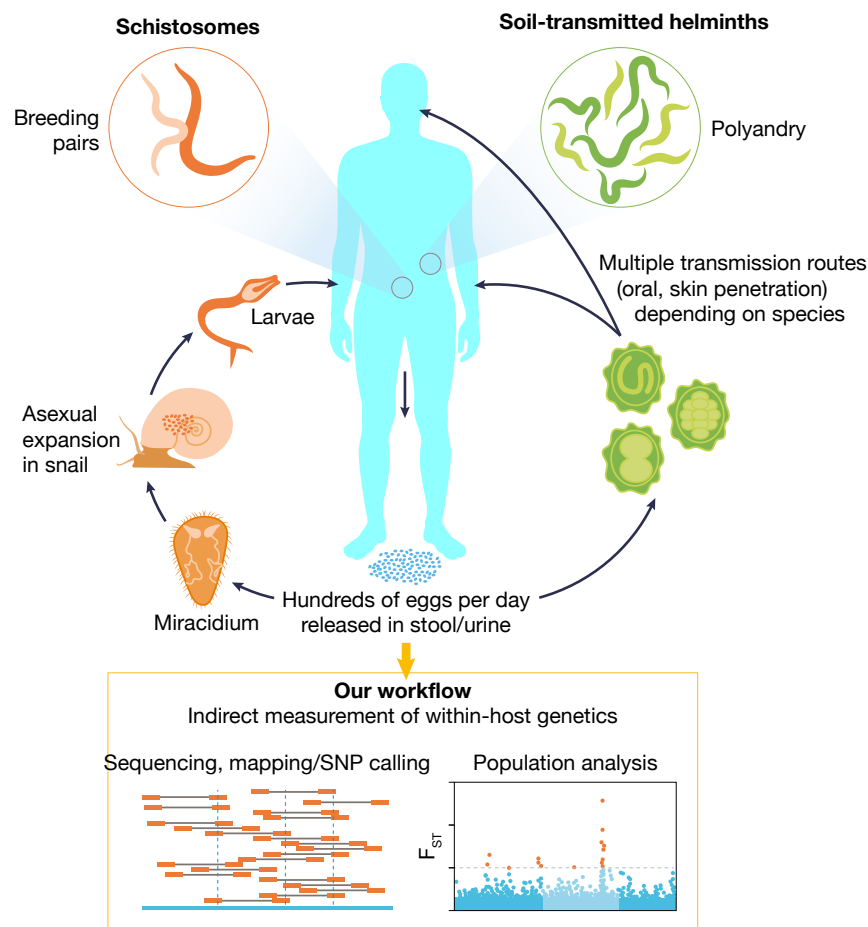
Selected publications

Duque-Correa *et al*. (2019) Exclusive dependence of IL-10Rα signalling on intestinal microbiota homeostasis and control of whipworm infection. PLOS Pathogens 15 (1) e1007265

International Helminth Genomes Consortium. (2018) Comparative genomics of the major parasitic worms. Nature Genetics 51 (1) 163-174

Otto *et al*. (2018) Genomes of all known members of a *Plasmodium* subgenus reveal paths to virulent human malaria. Nature Microbiology 3 (6) 687-697

Böhme *et al*. (2018) Complete avian malaria parasite genomes reveal features associated with lineage-specific evolution in birds and mammals. Genome Research 28 (4) 547-560

Cotton *et al*. (2016) The genome of *Onchocerca volvulus*, agent of river blindness. Nature Microbiology 2; 16216

Imamura *et al*. (2016) Evolutionary genomics of epidemic visceral leishmaniasis in the Indian subcontinent. eLife 5; e12613

Hunt *et al*. (2016) The genomic basis of parasitism in the *Strongyloides* clade of nematodes. Nature Genetics 48 (3) 299-307

Tsai *et al*. (2013) The genomes of four tapeworm species reveal adaptations to parasitism. Nature 496 (7443) 57-63

Berriman *et al*. (2009) The genome of the blood fluke *Schistosoma mansoni*. Nature 460 (7253) 352-8

Dr Stephen Doyle

✉ stephen.doyle@sanger.ac.uk

Global health

Genomic surveillance

Tropical disease

Antimicrobial resistance

Research

Stephen Doyle is a molecular and computational biologist with a broad interest in understanding genetic change over time. Stephen's research has largely focused on characterising genome-wide genetic variation in parasite populations that respond differently to anthelmintic drug treatment, the primary means to control these parasites, and to identify genes responsible for resistance to this treatment. This work also includes building high-quality genomic resources and reference genomes for a number of helminth species for the community to use. Much of this research has focused on the parasitic helminth *Haemonchus contortus*, which infects sheep and goats and causes a huge economic and animal health burden on the farming community around the world. While drugs against *H. contortus* are available, resistance is common owing to the parasite's ability to evolve in response to selective pressure from drugs. *H. contortus* represents a genetically tractable model parasite for understanding drug resistance in other parasites, including those that infect humans; these same drugs are used in mass drug administration campaigns to control helminths that infect over 1 billion people worldwide.

The Doyle group is using the genomic analysis of controlled genetic crosses between drug susceptible and resistance worms in natural host/parasite system to understand how this parasite changes over time in response to drug treatments, which could lead to a better understanding of not just *H. contortus*, but all helminth species, including how to treat and manage these parasites that infect both animals and humans. His group uses genomic approaches ranging from population-wide to single-cell resolution seek to understand the genetic basis for the evolutionary success and future potential of parasitic worms, and identify evolutionary constraints that may be exploited to develop novel ways to control them.

Collaborative projects

The Building Upon the Genome (BUG) Consortium is a BBSRC-funded project to exploit genomic approaches to understand anthelminthic drug resistance in GI nematodes of small ruminants. Through a combination of a genetic cross and population genomics of worms in UK sheep flocks, the BUG Consortium aims to use the recently published genome of the sheep parasite *Haemonchus contortus* to identify the genetic changes that allow worms to survive drug treatment.

Personal bio

Stephen completed his PhD in the Department of Genetics at La Trobe University studying molecular strategies to investigate and treat human mitochondrial disorders. In a switch of field, he moved to Warwick Grant's lab at La Trobe as a postdoc to lead genome-wide analyses of sub-optimal responses to ivermectin treatment of the human-infective filarial nematode *Onchocerca volvulus*, the causative agent of River Blindness (onchocerciasis) in Africa. In 2015, Stephen moved to the Wellcome Sanger Institute to join a BBSRC-funded collaboration – the BUG Consortium - to build genomic resources to develop novel interventions to control endemic gastrointestinal parasites of small ruminants. This work resulted in a highly-resolved reference genome for *Haemonchus contortus* and the mapping of known and novel causal variants associated with multidrug resistance in this species. In 2020, Stephen was awarded a UKRI Future Leaders Fellowship to form his group at Sanger where they continue to develop high-quality genomic resources for the parasitological community, and develop genomic and computational approaches to detect and monitor helminth parasites of human and veterinary importance.
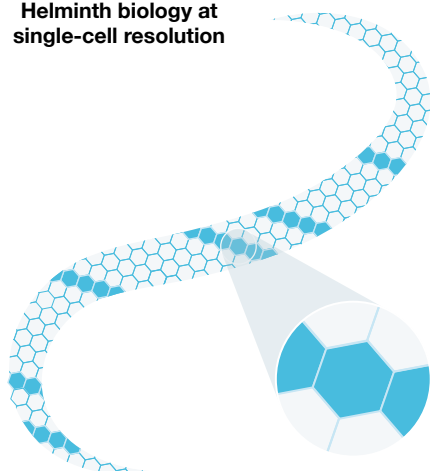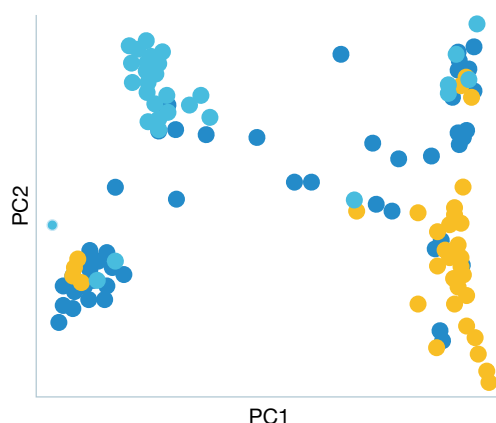
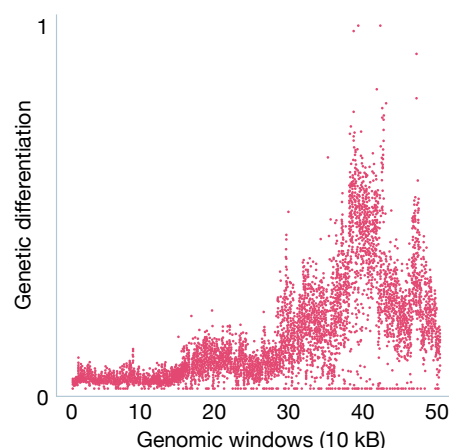**Helminth biology at
single-cell resolution**

Building genomic resources

**Defining genetic relationships
at local and global scales**

**Understanding genome-wide variation
associated with genetic traits**

Selected publications

Doyle *et al*. (2020) Genomic and transcriptomic variation defines the chromosome-scale assembly of *Haemonchus contortus*, a model gastrointestinal worm. Commun. Biol. 3 (1): 656

Diaz Soria *et al*. (2020) Single-cell atlas of the first intra-mammalian developmental stage of the human parasite *Schistosoma mansoni*. Nat. Commun. 11 (1): 6411

Kotze *et al*. (2020) Challenges and opportunities for the adoption of molecular diagnostics for anthelmintic resistance. Int. J. Parasitol. 14: 264-273

Durrant *et al*. (2020) Population genomic evidence that human and animal infections in Africa come from the same populations of *Dracunculus medinensis*. PLOS Negl. Trop. Dis. 14 (11): e0008623

Doyle *et al*. (2019) Population genomic and evolutionary modelling analyses reveal a single major QTL for ivermectin drug resistance in the pathogenic nematode, *Haemonchus contortus*. BMC Genomics 20 (1): 218

Doyle & Cotton (2019) Genome-wide Approaches to Investigate Anthelmintic Resistance. Trends in Parasitol. 35 (4): 289-301

International Helminth Genomes Consortium. (2018) Comparative genomics of the major parasitic worms. Nat. Genet. 51 (1): 163-174

Doyle *et al*. (2017) Genome-wide analysis of ivermectin response by *Onchocerca volvulus* reveals that genetic drift and soft selective sweeps contribute to loss of drug sensitivity. PLOS Negl. Trop. Dis. 11 (7): e0005816

Choi *et al*. (2017) Genomic introgression mapping of field-derived multiple-anthelmintic resistance in *Teladorsagia circumcincta*. PLOS Genet. 13 (6): e1006857

Cotton *et al*. (2016) The genome of *Onchocerca volvulus*, agent of river blindness. Nat. Microbiol. 2: 16216

Professor Nick Thomson

✉ nrt@sanger.ac.uk

🐦 @nrt_thomson

- Global health
- Genomic surveillance
- Epidemiology
- Antimicrobial resistance
- Pathogenicity & virulence

Research

Nick Thomson is a microbiologist and bioinformatician interested in bacterial evolution and spread with a focus on sexually transmitted and diarrhoeal diseases. He is Head of the Parasites and Microbes Programme at the Wellcome Sanger Institute and also Professor of Bacterial Genomics and Evolution at the London School of Hygiene and Tropical Medicine.

Under Nick's leadership, the Bacterial Genomics and Evolution group, uses genomic approaches to explore questions of basic science relating to the evolution and spread of bacterial pathogens in both humans and animals. The group uses genomic data to understand the phylogeography of how pathogens have moved, and continue to move, through populations and across continents, providing high-resolution insights aimed at tracking and limiting their spread. The group focuses on diseases such as cholera and dysentery that continue to cause significant mortality and morbidity in low-income countries, as well as the number one bacterial STI in the world, *Chlamydia trachomatis*. A major theme in the groups work is the understanding of antimicrobial resistance (AMR) in driving the evolution and transmission of these major bacterial pathogens.

Their research primarily uses whole-genome sequencing approaches to study the patterns and drivers for historical and ongoing pathogen genome evolution, which they combined with high throughput screens in whole cells or model organisms to understand the phenotypic consequences of the evolutionary changes observed. They use phylogenomics of isolates competing within their natural host to identify novel and known factors associated with 'fitness', to characterise how these factors drive transmission between countries and within communities, and to identify new opportunities for intervention to interrupt transmission. Their research encompasses all aspects of pathogen variation, natural or induced, and incorporates the host component to infectious disease.

The Thomson group has a history of developing novel approaches for accessing genomic and transcriptomic data, for example to enable direct sequencing of genomes from swab, opening up new areas for study especially for bacteria that are fastidious, or difficult to culture.

Collaborative projects

The Global Task Force on Cholera Control (GTFCC) is a partnership of more than 50 non-governmental organizations, UN agencies, academic institutions and donors committed to supporting countries to control cholera. The Thomson group provide advice on the use of genomic data to GTFCC working groups focussed on cholera epidemiology and regional surveillance, as well as to the WHO Independent Review panel advising on national cholera plans for control or elimination.

Personal bio

Nick graduated in Microbiology and Microbial Technology from Warwick University in 1991 and then went on to earn a PhD in global regulation of virulence and secondary metabolism in enteric bacteria. After receiving his Doctorate in 1995, Nick worked as a Postdoctoral Fellow at the University of Cambridge Biochemistry Department and L'Institut National des Sciences Appliquées (INSA) de Lyon, France. In 1999, Nick moved to the Wellcome Sanger Institute as a Senior Computer Biologist, subsequently became a Principal Staff Scientist and was promoted to Group Leader and member of Faculty.

Nick holds an honorary chair at the University of St Andrews, School of Medicine. At the end of 2013 Nick took up a joint appointment between the Wellcome Sanger Institute and the London School of Hygiene and Tropical Medicine (LSHTM), where he is Chair of Bacterial Genomics and Evolution. These appointments are at the heart of Nicks approach to research: multidisciplinary teams bringing together scientists, modelers and clinicians, with a broad global reach and focus. In April 2021, Nick became Head of the Parasites and Microbes Programme at the Wellcome Sanger Institute.
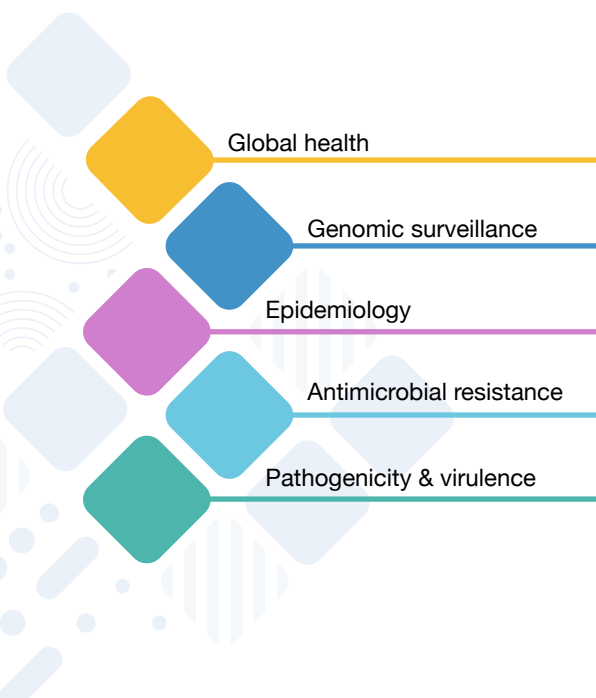
Much of his work involves extended international networks of scientist, clinicians and clinical scientists. To support these collaborations and increase access to genomic data Nick, along with the Wellcome Trust Advanced Courses and LSHTM, has established and continues to develop numerous widely attended genomics courses.
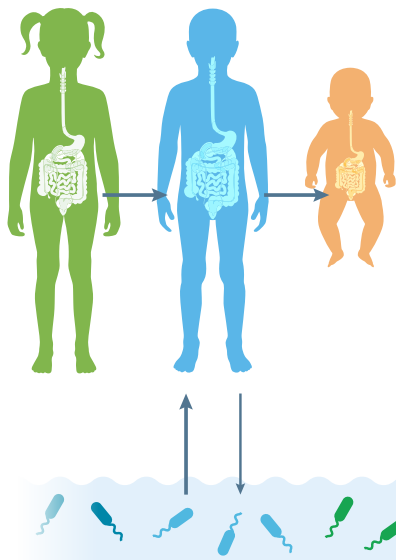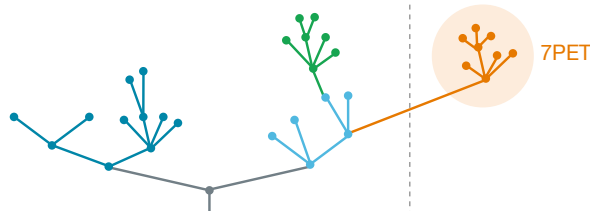
Endemic lineages | **Epidemic lineages**
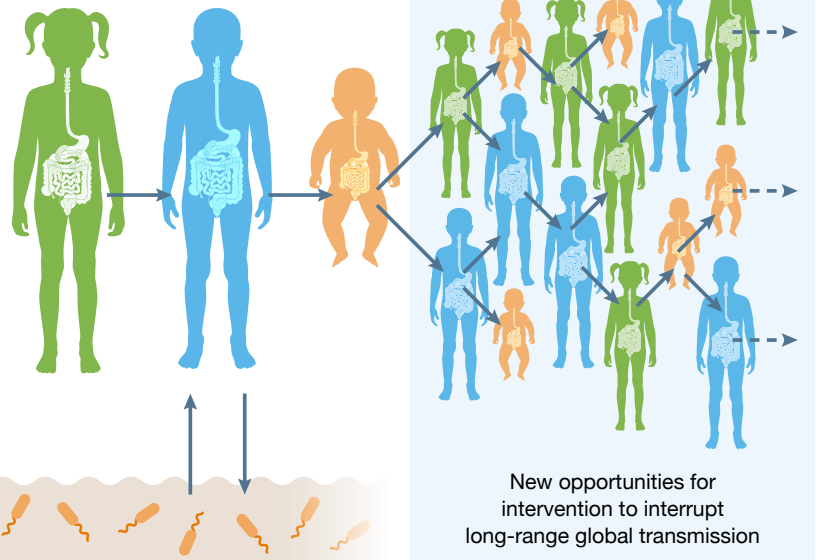
New opportunities for intervention to interrupt long-range global transmission

7PET

Selected publications

Dorman, Thomson & Campos (2021) Genomic contextualisation of ancient DNA molecular data from an Argentinian fifth pandemic *Vibrio cholerae* infection. Microb. Genom. 7 (6): e000580

Dorman *et al*. (2020) Genomics of the Argentinian cholera epidemic elucidate the contrasting dynamics of epidemic and endemic *Vibrio cholerae*. Nat. Commun. 11 (1): 4918

Horesh *et al*. (2020) Type II and type IV toxin-antitoxin systems show different evolutionary patterns in the global *Klebsiella pneumoniae* population. Nucleic Acids Res. 48 (8): 4357-4370

Ellington *et al*. (2019) Contrasting patterns of longitudinal population dynamics and antimicrobial resistance mechanisms in two priority bacterial pathogens over 7 years in a single center. Genome Biol. 20 (1): 184

Criscuolo *et al*. (2019) The speciation and hybridization history of the genus *Salmonella*. Microb. Genom. 5 (8): e000284

Beale *et al*. (2019) Genomic epidemiology of syphilis reveals independent emergence of macrolide resistance across multiple circulating lineages. Nat. Commun. 10 (1): 3255

Connor *et al*. (2015) Species-wide whole genome sequencing reveals historical global spread and recent local persistence in *Shigella flexneri*. eLife 4: e07335

Holt *et al*. (2015) Genomic analysis of diversity, population structure, virulence, and antimicrobial resistance in *Klebsiella pneumoniae*, an

urgent threat to public health. Proc. Natl Acad. Sci. USA 112 (27): E3574-81

Baker *et al*. (2015) Intercontinental dissemination of azithromycin-resistant shigellosis through sexual transmission: a cross-sectional study. Lancet Infect. Dis. 15 (8): 913-21

Baker *et al*. (2014) The extant World War 1 dysentery bacillus NCTC1: a genomic analysis. Lancet 384 (9955): 1691-7

Mather *et al*. (2014) Bacillary dysentery from World War 1 and NCTC1, the first bacterial isolate in the National Collection. Lancet 384 (9955): 1720

Gillespie *et al*. (2014) Genomic Investigations unmask *Mycoplasma amphoriforme*, a new respiratory pathogen. Clin. Infect. Dis. 60 (3): 381-8

Reuter *et al*. (2014) Parallel independent evolution of pathogenicity within the genus *Yersinia*. Proc. Natl Acad. Sci. USA 111 (18): 6768-73

Seth-Smith *et al*. (2013) Generating whole bacterial genome sequences of low-abundance species from complex samples with IMS-MDA. Nat. Protocols 8 (12): 2404-12

Mather *et al*. (2013) Distinguishable epidemics of multidrug-resistant *Salmonella* Typhimurium DT104 in different hosts. Science 341 (6153): 1514-7

Mutreja *et al*. (2011) Evidence for several waves of global transmission in the seventh cholera pandemic. Nature 477 (7365): 462-5

Professor Stephen Bentley

✉ stephen.bentley@sanger.ac.uk

🐦 @StephenBentley5

- Global health
- Genomic surveillance
- Epidemiology
- Pandemic preparedness
- Pathogenicity & virulence
- Antimicrobial resistance
- Vaccines

Research

Stephen Bentley's research uses genomics to understand the patterns of colonisation, transmission and disease for bacterial pathogens that cause pneumonia, meningitis and neonatal sepsis and have a major impact on infant and neonate mortality in resource-poor settings. Our main foci are *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Streptococcus agalactiae*, with a view to informing strategies for treatment and prevention.

The most effective way of preventing infection is through vaccination and several very effective vaccines are currently in use around the world. Unfortunately, some vaccine antigens are not expressed across the entire pathogen species raising the risk of vaccine evasion. The Bentley group identified vaccine-insensitive variants *S. pneumoniae*, generated through homologous recombination prior to the introduction of the vaccine, that were able to expand in the post vaccine period. Through the Global Pneumococcal Sequencing (GPS) project, they showed how a circulating population of bacteria adapts to vaccine introduction by expanding existing lineages to fill the niche vacated by the vaccine susceptible strains. This population bounce-back is highly dynamic and the Bentley group are using the GPS datasets to characterise adapting populations, with the ultimate aim of being able to predict the outcome of applying new vaccines and other interventions, including antibiotics.

Large-scale population genomic datasets have opened the way to performing well powered analyses to detect genes and variants that are significantly associated with aspects of the natural biology of the organism. The Bentley group use such datasets to study patterns of gene presence/absence, SNPs and k-mers, uncovering genetic associations with clonal expansion, progression to meningitis, antibiotic resistance, colonisation efficiency and invasiveness.

Understanding how such pathogens such as *S. pneumoniae* transmit between healthy individuals, and onwards across wide geographic areas can inform strategies to control the spread of disease causing strains. In collaboration Professor Paul Turner (Cambodia-Oxford Medical Research Unit), the Bentley group are studying person-to-person transmission in a deeply sampled pneumococcal carriage cohort. Having previously conducted a large genomic study of this cohort to identify likely transmission events, they are now using deep sequencing to detect within host variation over relatively short time scales. These analyses allow population bottlenecks to be measured and the influence of antibiotic usage and resistance on the outcome of transmission to be assessed.

Collaborative projects

The JUNO project is a global genomic surveillance study of *Streptococcus agalactiae* (aka Group B Streptococcus), an opportunistic pathogen and a major cause of neonatal invasive disease, with a particular impact on infant mortality in low- and middle-income countries (LMICs). Whole genome sequencing of GBS isolates from across a broad geographical and temporal span is being undertaken to better understand pathogen diversity, pathogen genetic association with the disease and pathogen transmission. Key outputs of JUNO will be assessment of the risk of evasion of vaccines that are currently undergoing clinical trials and measurement of the influence of pathogen genetics on the manifestations of early and late onset disease.

Over the last decade, the Global Pneumococcal Sequencing (GPS) project has created a global picture of *Streptococcus pneumoniae* (aka the pneumococcus) evolution during vaccine introductions using whole-genome sequencing. The pneumococcus is the leading cause of pneumonia, septicaemia and meningitis in young children. Pneumococcal conjugate vaccine (PCV) targets the capsule surrounding pneumococcal cells and has proven to be effective in reducing pneumococcal disease. However, there are at least 100 different forms of capsule, or serotypes. The current PCVs are only able to target some serotypes and the population overall is able to evolve to evade the vaccine. The GPS project coordinates the genomic analysis of large number of isolates, prioritising low- and middle-income countries where disease burden are high, to
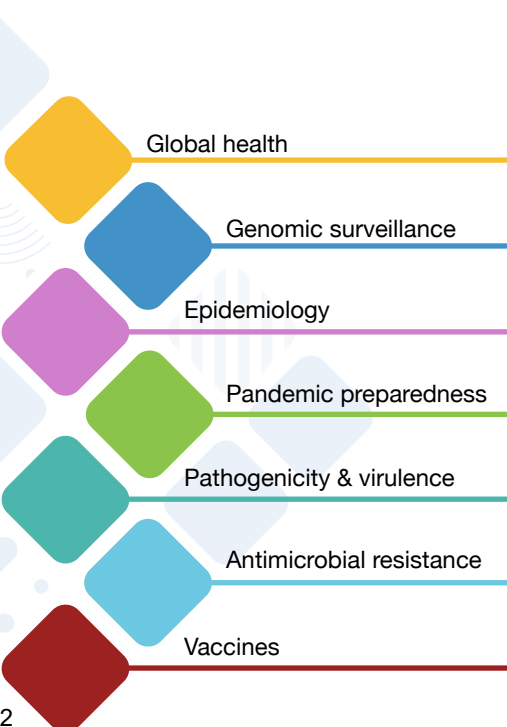
enable ongoing genomic surveillance and the monitoring of vaccine evasion globally. Findings from GPS are crucial to the strategy for the ongoing development of future vaccine formulations.

Personal bio

Stephen is a Principal Staff Scientist and Team Leader at the Wellcome Sanger Institute. He completed PhD and postdoctoral work on the molecular genetics of cell division and virulence gene expression with Professor George Salmond at the Universities of Warwick and Cambridge. In 1998, Stephen joined the Sanger Institute to work on the annotation and analysis of bacterial genomes. His early work focused on the antibiotic-producing soil bacterium *Streptomyces coelicolor* and the rare human pathogen Tropheryma whipplei, providing insights into horizontal gene transfer, antigenic variation and the antibiotic production. This was followed by research into *Streptococcus pneumoniae* and *Neisseria meningitidis* showing that gene and genome variation between loci and species was due to common and differing mechanisms of variation. His work to sequence the capsular biosynthesis genes for all known serotypes of *S. pneumoniae* enabled molecular methods for determining serotype which have brought important new understanding of pneumococcal colonisation and transmission. Since the development of high throughput sequencing, Stephen's research has focused on population genomics, revealing patterns of international spread, vaccine escape and the acquisition of antimicrobial resistance.
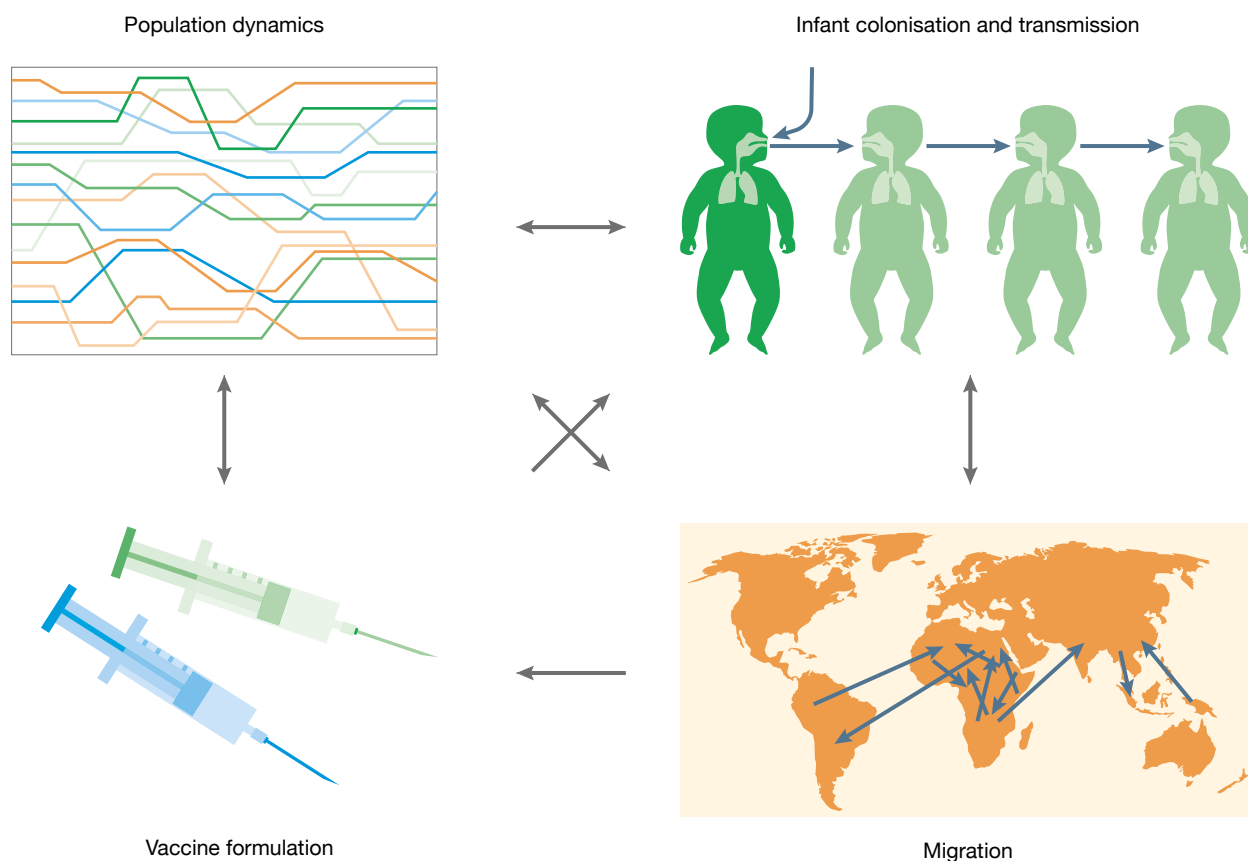
Population dynamics

Infant colonisation and transmission

Vaccine formulation

Migration

Selected publications

Chewapreecha *et al*. (2014) Dense genomic sampling identifies highways of pneumococcal recombination. Nat. Genet. 46 (3): 305-309

Croucher *et al*. (2013) Population genomics of post-vaccine changes in pneumococcal epidemiology. Nat. Genet.. 45 (6): 656-63

Harris *et al*. (2012) Whole-genome sequencing for analysis of an outbreak of meticillin-resistant *Staphylococcus aureus*: a descriptive study. Lancet Infect. Dis. 13 (2): 130-6

Croucher *et al*. (2011) Rapid pneumococcal evolution in response to clinical interventions. Science. 331 (6016): 430-4

Harris *et al*. (2010) Evolution of MRSA during hospital transmission and intercontinental spread. Science. 327 (5964): 469-74

Bentley *et al*. (2006) Genetic analysis of the capsular biosynthetic locus from all 90 pneumococcal serotypes. PLOS Genet. 2 (3): e31
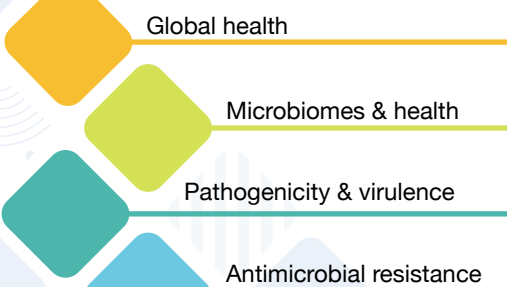
Bentley *et al*. (2002) Complete genome sequence of the model actinomycete *Streptomyces coelicolor* A3(2). Nature 417 (6885): 141-7

Dr Trevor Lawley

✉ trevor.lawley@sanger.ac.uk

🐦 @LawleyLab

Global health

Microbiomes & health

Pathogenicity & virulence

Antimicrobial resistance

Research

Research in the Host-Microbiota Interactions Lab led by Trevor Lawley is focussed on using advanced metagenomic sequencing, deep culturing, cutting-edge analytical tools and technology development to investigate the microbial communities contained on and within host organisms. The human microbiome is now established as a key determinant in human health and development, and a growing list of diseases and poorly characterised syndromes. The microbiome also impacts clinical response to a growing list of life saving drugs. Remarkably, the majority of microbes found within our microbiota have not been cultured, nor described, which is a major limitation for phenotypic and mechanistic studies to understand the basic functions of our microbiota in determining the host's health or disease status.

The Lawley group have been pioneers in developing reference genome-based mapping approaches in human microbiome studies, with cheaper and faster metagenomic analysis and higher taxonomic precision and comprehensiveness compared to *de novo* assembly of short read sequences. Importantly, the clinical-grade microbiome analysis platform that they have developed also has the unique advantage of being linked to a curated microbial culture collection to enable biological discovery and the development of biomarkers and therapeutics. Their platform is also capable for pathogen surveillance directly from microbiome samples.

A particular research focus for the Lawley group is on the study of the early-life microbiome, and how birth-mode and clinical interventions, impact microbiome acquisition and assembly. At birth, babies are rapidly colonised by microbes from both the mother and local environment, ultimately leading to a diverse, adult-like microbiome by the age of 3-5 years. Microbiome acquisition and assembly over the first months and years of life is thought to be the result of deep human genome-microbiome co-evolution that selected for beneficial microbes to shape the longer term immunological, metabolic and cognitive development of the baby. Perturbations in the acquisition and assembly of a baby's microbiome, owing to modern clinical practices, infections, diet and environmental transmission of AMR pathogens, have been linked with diseases in childhood and later in life. Through the Global Babybiome project, the Lawley group are using both data-driven microbiome discovery and hypothesis-driven functional validation approaches to study the early life microbiomes of babies from around the world, with a particular focus on low- and middle-income countries (LMICs). Their aim is to define the ecology and evolution of maternal and environmental transmission to understand how a baby's gut microbiome assembles and protects the child from conditions such as enteric infections, growth stunting, obesity and asthma. In addition, the Lawley group are expanding their capabilities beyond analysis of the gut to other body ecosystems (such as the oral cavity, respiratory tract and urogenital tract), and starting to integrate human microbiome data with other rich and heterogenous datasets, including human genetics, metatranscriptomics, metabolomics and diet using machine learning tools and other data mining methods. Their ultimate goal is to develop live bacterial therapeutics for use in LMIC settings for the treatment and prevention of growth stunting, and other debilitating conditions.

Collaborative projects

The Global BabyBiome is a growing international network, based out of the Lawley group and comprised of key strategic and clinical partners (Latinobiota, OpenBiome, Gates Foundation, CHAIN, UCL and KEMRI). The key aim of Global Babybiome is to identify opportunities for using microbiome-based approaches to intervene and reduce infections, AMR pathogen colonisation and growth stunting in children from a variety of settings and cultures.

Microbiotica was founded by Dr Trevor Lawley, Prof Gordon Dougan FRS and Dr Mike Romanos in December 2016 to build on fundamental advances made at the Wellcome Sanger Institute in addressing barriers to the translation of the microbiome. Microbiotica has advanced capabilities in microbiome analysis

linked to patient phenotype and preclinical development of bacterial products. Microbiotica has a pipeline of clinically--derived products including Live Bacterial Therapeutics and Biomarkers in IBD, Immuno-oncology and Gut Epithelial Bar-rier Repair. It has collaborations with Cancer Research UK and Cambridge University Hospitals in Immuno-oncology, Genentech/Roche in IBD, and University of Adelaide in Ulcerative Colitis.

Personal bio

Trevor obtained his PhD from the University of Alberta, Canada, in the Laboratories of Professors Diane Taylor and Laura Frost, where he studied the mechanisms that pathogenic bacteria use to disseminate antibiotic resistance genes. After his PhD Trevor was awarded a Canadian Institutes of Health Research post-doctoral fellowship to work in the Laboratories of Professors Stanley Falkow and Denise Monack at Stanford University, where he studied the impact of antibiotic treatment on *Salmonella* disease and transmission. In 2007 Trevor received a Royal Society of London Award – sponsored by Professor Gordon Dougan – to start a research programme on *Clostridium difficile* disease and transmission at the Wellcome Sanger Institute. In 2010, Trevor was appointed as a Career Development Fellow in the Sanger Institute Faculty and was promoted to Faculty Group Leader in 2014 and a Senior Group Leader in 2021. Trevor has pioneered many aspects of the bacteriotherapy concept where defined mixtures of bacteria are used to cure intestinal diseases linked to pathological imbalances in the intestinal microbiota. Trevor also is a co-founder and the Chief Scientific Officer of Microbiotica.
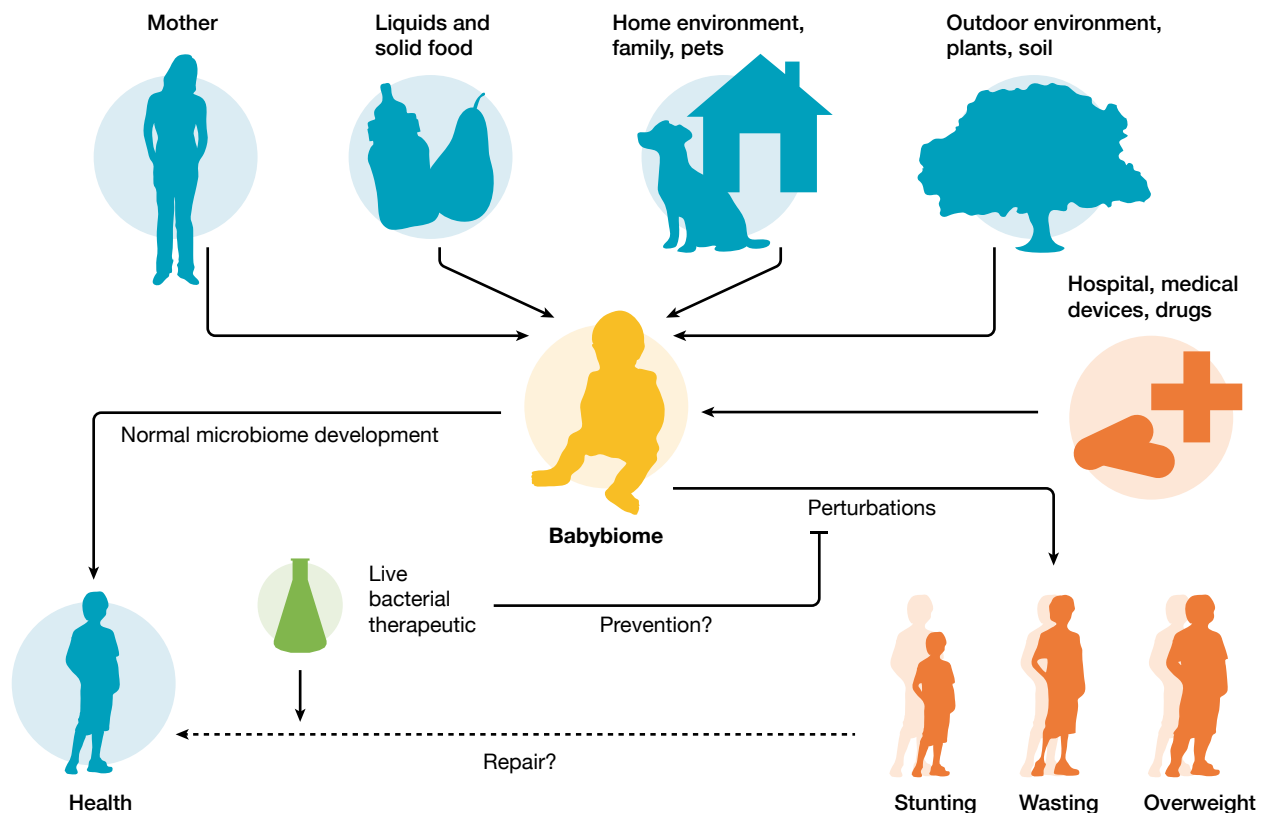
Selected publications

Camarillo-Guerrero *et al*. (2021) Massive expansion of human gut bacteriophage diversity. Cell 184 (4): 1098-1109.e9

James *et al*. (2020) Distinct microbial and immune niches of the human colon. Nat. Immunol. 21 (3): 343-353

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Pham *et al*. (2014) Epithelial IL-22RA1-mediated fucosylation promotes intestinal colonization resistance to an opportunistic pathogen. Cell Host & Microbe 16 (4): 504-16

Lawley *et al*. (2012) Targeted restoration of the intestinal microbiota with a simple, defined bacteriotherapy resolves relapsing *Clostridium difficile* disease in mice. PLOS Path. 8 (10): e1002995

COVID-19 Genomic Surveillance

The Sanger Institute's large-scale genome sequencing capabilities have been deployed to work on the COVID-19 pandemic. SARS-CoV-2 viral genome sequence data are being used, in real-time, to inform public health measures and help save lives.

At the start of the pandemic, the Sanger Institute, together with UK Public Health Agencies, academic partners and NHS organisations across the country, formed the COVID-19 Genomics UK Consortium (COG-UK) to sequence and analyse virus genomes. This sequence data is being used to trace the virus as it spreads and to identify chains of transmission, super spreading events and potential variants of concern.

The institute's logistics, software, laboratory, technical and scientific teams worked together to rapidly set up, validate and run processes for handling and sequencing coronavirus samples. Thousands of samples are received on site every day from the laboratories that are undertaking COVID-19 tests in communities across the country. These samples consist of the residues of positive and negative diagnostic swab tests, with the positive ones being picked out for processing and sequencing. The team have handled tens of millions of samples, and sequenced hundreds of thousands of them. In addition, they have refined existing laboratory protocols and developed new ones, meaning that much of the process has been automated and the Institute now has the capacity to sequence 50,000 virus samples a week.

Initial funding for the work, totalling £20 million, was contributed by the Sanger Institute, the Department of Health and Social Care, and UK Research and Innovation. Subsequent investment has enabled the Institute to help develop a national real-time genomic surveillance system of COVID-19 to help tackle the pandemic.

The viral genome data from COG-UK are also combined with clinical and epidemiological datasets to help guide UK public health interventions and policies. COG-UK tools and data are used by public health agencies and researchers to monitor for new variants. Data and analysis are immediately made freely available, and information is passed directly to public health authorities and others who need it.

Sanger's COVID-19 programme is a truly institute-wide effort, involving more than 300 staff from all areas of the organisation.

As of Apr 2022
2.1M+
virus genomes read

300+
staff involved

**More than**
100 million
samples handled by Sanger

Some of the PaM Programme members involved

Alan Keith, Aleksei Makunin, Anastasia Hernandez-Koutoucheva, Callum Saint, Carmen Diaz Soria, Catherine Ludden, Christen Smith, Christoph Puethe, Christopher Jacob, Claire Nathwani, Cristina Ariani, Danielle Walker, Dee Toombs, Dorota Jamrozy, Duncan Berger, Eleanor Drury, Georgia Whitton, Gerry Tonkin-Hill, Ian Wright, Jason Oakes, John Sillitoe, Jon Keatley, Katherine Rowlands, Kathryn Murie, Krzysztof Kluczynski, Leanne Kane, Liam Prestwood, Mara Lawniczak, Matt Berriman, Matthew Beale, Matthew Dorman, Matthew Sinnott, Mozam Ali, Nicholas Thomson, Petra Korlevic, Roberto Amato, Sally Kay, Sarah Kay Buddenborg, Shavanthi Rajatileka, Sonia Goncalves, Stephanie Lo, Sunil Dogga, Tanya Brooklyn, Tim Stickland, Will Hamilton

Professor Caroline Buckee

✉ cbuckee@hsph.harvard.edu

Global health

Genomic surveillance

Epidemiology

Tropical disease

Pandemic preparedness
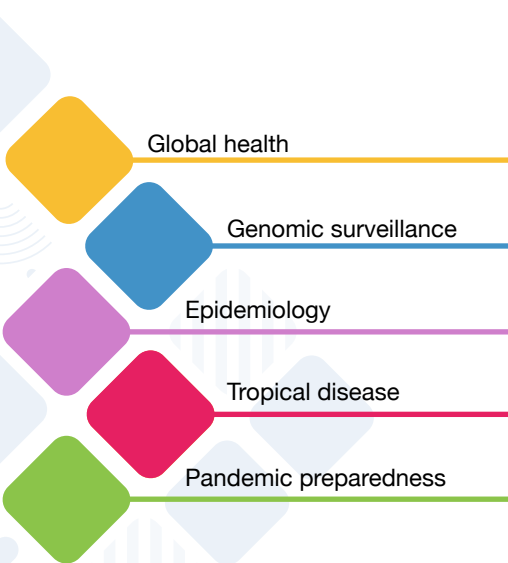
Research

Caroline Buckee is an Associate Professor at Harvard T.H. Chan School of Public Health and an Associate Faculty member at the Wellcome Sanger Institute. The Buckee lab uses a range of mathematical models, experimental and pathogen genomic data, and "Big Data" from mobile phones and satellites to determine the transmission of infectious diseases through populations in an effort to understand the spatial dynamics of disease transmission and how it might be controlled. A major focus of the group is the human malaria parasite, *Plasmodium falciparum*, which is still a major global killer of children under 5 years. The Buckee lab's work spans both the within-host processes that determine pathogenesis in individual hosts, and the population processes that sustain transmission and disease, working with vector biologists to understand the impacts of novel vector control approaches, and with mobile phone operators to track the migration patterns of people that import infections and drug resistant parasites when they travel. The group is also interested in how to predict and contain the spatial spread of emerging epidemics.

Collaborative projects

Buckee co-leads the COVID-19 Mobility Data Network, a coalition of infectious disease epidemiologists from over a dozen universities working to understand the COVID-19 pandemic. The network is now utilising mobility data to understand the impact of social distancing measures and to utilise for contact tracing and disease forecasting.

Personal bio

Caroline Buckee received her BSc degree in zoology from the University of Edinburgh and then attended the University of York where she received her Master of Research (MRes) degree in Bioinformatics. She moved to the University of Oxford to study mathematical epidemiology working under the mentorship of Professor Sunetra Gupta, receiving her PhD in 2006. Following graduate school, Buckee became a postdoctoral researcher, supported by the Wellcome Trust, at the Kenya Medical Research Institute. There, she began working with mobile phone location data to understand the effect human migration patterns and on malaria disease transmission. She then became an Omidyar Fellow at the Santa Fe Institute, to continue this work. Caroline joined Harvard T.H. Chan School of Public Health in the summer of 2010 as an Assistant Professor of Epidemiology, and was promoted to Associate Professor in 2017. In 2013, Dr. Buckee was named the Associate Director of the Center for Communicable Disease Dynamics.

Selected publications

Taylor *et al*. (2017) Quantifying connectivity between local *Plasmodium falciparum* malaria parasite populations using identity by descent. PLOS Genetics. 13 (10): e1007065

Peak *et al*. (2017) Comparing nonpharmaceutical interventions for containing emerging epidemics. Proc. Natl Acad. Sci. USA. 114 (15): 4023-4028

Childs *et al*. (2016) Disrupting Mosquito Reproduction and Parasite Development for Malaria Control. PLOS Pathog. 12 (12): e1006060

Wesolowski *et al*. (2015) Quantifying seasonal population fluxes driving rubella transmission dynamics using mobile phone data. Proc. Natl Acad. Sci. USA. 112 (35): 11114-9

Larremore *et al*. (2015) Ape parasite origins of human malaria virulence genes. Nat. Comm. 6: 8368

Wesolowski *et al*. (2015) Impact of human mobility on the emergence of dengue epidemics in Pakistan. Proc. Natl Acad. Sci. USA. 112 (38): 11887-92

Wesolowski *et al*. (2012) Quantifying the Impact of Human Mobility on Malaria. Science 338 (6104): 267-70

Professor Jukka Corander

✉ jukka.corander@medisin.uio.no

Global health

Genomic surveillance

Epidemiology

Antimicrobial resistance

Pathogenicity & virulence

Vaccines

Research

Jukka Corander is a Professor at the Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Norway, and an Associate Faculty member at the Wellcome Sanger Institute. The Corander lab focuses on microbial evolution and transmission modeling, statistical machine learning, population genomics and inference algorithms for the large-scale genomic surveillance of microbial pathogens. The group has developed multiple methods for statistical population genomics in bacteria, including population structure estimation (BAPS, hierBAPS, fastbaps), GWAS (SEER, pyseer) and GWES (SuperDCA, SpydrPick). They are currently coordinating the development of the ELFI software for likelihood-free inference for computer simulator-based models. The statistical methods developed by the Corander group have led to numerous discoveries on the evolution, resistance, virulence and transmission of pathogenic bacteria and viruses.

Collaborative projects

The BATTALION project aims to develop systems biology level understanding about mechanisms behind colonization success, acquisition of resistance elements and their dissemination dynamics in *E. coli*. The project uses systematic longitudinal surveys of isolates from infections, combining short- and long-read sequencing of DNA, with population RNA-seq and experimental techniques to reach its ambitious goals.

The CARDAMOM project in collaboration with prof. Paul Turner from the University of Oxford, which aims to understand the effects of hospital visits and antibiotic treatment on the pathogenic bacteria colonizing the nasopharynx and gut of infants in a low-resource setting.

Personal bio

Jukka Corander received a PhD at Stockholm University in 2000, where he studied Bayesian learning of graphical models. Following a period as a senior lecturer at the University of Helsinki, Jukka became a Professor in statistics in the Department of Mathematics at Åbo Akademi University. In 2016 Jukka became a Professor of biostatistics at the Faculty of Medicine, University of Oslo, Norway and, since 2009, has also been a Professor of statistics at University of Helsinki, Finland.

Selected publications

Gladstone *et al*. (2021) Emergence and dissemination of antimicrobial resistance in *Escherichia coli* causing bloodstream infections: a nationwide longitudinal microbial population genomic study in Norway between 2002-2017. Lancet Microbe. 2 (7): E331-E341

Pöntinen *et al*. (2021) Apparent nosocomial adaptation of *Enterococcus faecalis* predates the modern hospital era. Nat Commun. 12 (1): 1523

Kantele *et al*. (2021) Prospective study of intestinal multidrug-resistant bacteria contracted by visitors to a high-endemic setting: daily real-time sampling abroad to analyse acquisition rates and dynamics of colonisation. Lancet Microbe. 2 (4): E151-E158

Lees *et al*. (2020) Improved Prediction of Bacterial Genotype-Phenotype Associations Using Interpretable Pangenome-Spanning Regressions. mBio. 11 (4): e01344-20

Corander *et al*. (2017) Frequency-dependent selection in vaccine-associated pneumococcal population dynamics. Nat. Ecol. Evol. 1 (12): 1950-1960
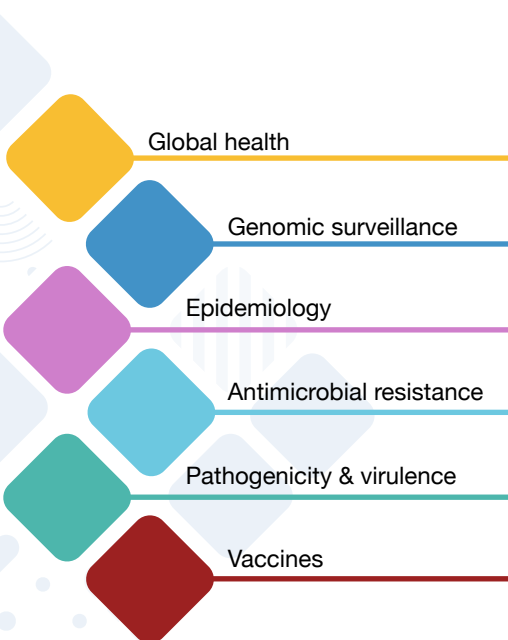
Colijn, Corander & Croucher (2020) Designing ecologically optimized pneumococcal vaccines using population genomics. Nat. Microbiol. 5 (3): 473-485

Pensar *et al*. (2019) Genome-wide epistasis and co-selection study using mutual information. Nucleic Acids Res. 47 (18): e112

Tonkin-Hill *et al*. (2019) Fast hierarchical Bayesian analysis of population structure. Nucleic Acids Res. 47 (11): 5539-5549

Lees *et al*. (2016). Sequence element enrichment analysis to determine the genetic basis of bacterial phenotypes. Nat. Commun. 7: 12797

Hanage *et al*. (2009) Hyper-recombination, diversity and antibiotic resistance in the pneumococcus. Science. 324 (5933): 1454-1457

Professor Christophe Fraser

✉ christophe.fraser@bdi.ox.ac.uk

- Global health
- Genomic surveillance
- Epidemiology
- Pandemic preparedness
- Antimicrobial resistance

Research

Christophe Fraser is a Senior Group Leader in Pathogen Dynamics at the Big Data Institute, Professor in the Nuffield Department of Medicine at the University of Oxford. The Fraser group is interested in studying the population dynamics and epidemiology of pathogens, and translating this knowledge to public health. The primary tools used in the group are mathematical modelling and pathogen genomics. Their current topics of interest include: HIV virulence, genomics and treatment, pneumococcal genomics, antibiotic resistance and outbreak responses. In response to the COVID-19 pandemic, since January 2020, the Fraser group has been working on the development of a variety of contact tracing innovations and have been members of the COVID-19 Genomics UK (COG-UK) consortium.

Collaborative projects

BEEHIVE (Bridging the Epidemiology and Evolution of HIV in Europe) is a cross-European study of HIV genomics and virulence amongst seroconverters that aims to assemble 4500 viral sequences from HIV patients across Europe and use this data to discover and characterise viral mutations or combinations of mutations that influence the severity of disease.

HPTN071 PopART (Population Effects of Antiretroviral Therapy to reduce HIV Transmission) is a cluster-randomized trial of HIV prevention (the largest HIV trial conducted to date), including universal test and treat in a population of 1.2 million people at high risk in 21 communities in Zambia and South Africa.

PANGEA (Phylogenetics and Networks for Generalised HIV Epidemics in Africa) is a consortium using modern molecular epidemiology and phylodynamics to map HIV-1 genomic diversity and link to prevention modelling across sub-Saharan Africa. The first phase of the project centred on sample collection and sequencing, the second phase focusses on data analysis and providing datasets for policy evaluation.

AMPHEUS (Analytics and Microbiology for Precision Health and Epidemiology - A Unified Solution) aims to deliver a single integrated platform for clinical microbiology, real-time epidemiology and intervention research to fight infectious pathogens in low income settings.

Personal bio

Christophe trained in theoretical particle physics at the University of Edinburgh and the University of Swansea, where he received a doctorate in 1997. After his PhD, Christophe converted to mathematical biology, becoming a Lecturer, Reader, Royal Society University Research Fellow and then Chair of Theoretical Epidemiology in the Department of Infectious Disease Epidemiology at Imperial College. In 2016, Christophe moved to the University of Oxford to become a Senior Group Leader in Pathogen Dynamics at the Big Data Institute, and Professor in the Nuffield Department of Medicine.

Selected publications

Ferreti *et al*. (2020) Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science 368 (6491): eabb6936

Hayes *et al*. (2019) Effect of Universal Testing and Treatment on HIV Incidence - HPTN 071 (PopART). N. Engl. J. Med. 381 (3): 207-218

Ratmann *et al*. (2019) Inferring HIV-1 transmission networks and sources of epidemic spread in Africa with deep-sequence phylogenetic analysis. Nat. Commun. 10 (1): 1411

Fraser *et al*. (2014) Virulence and pathogenesis of HIV-1 infection: an evolutionary perspective. Science 343 (6177): 1243727
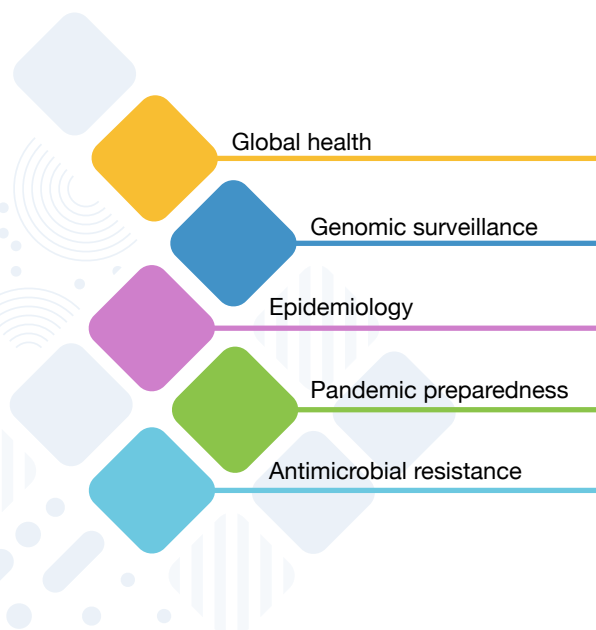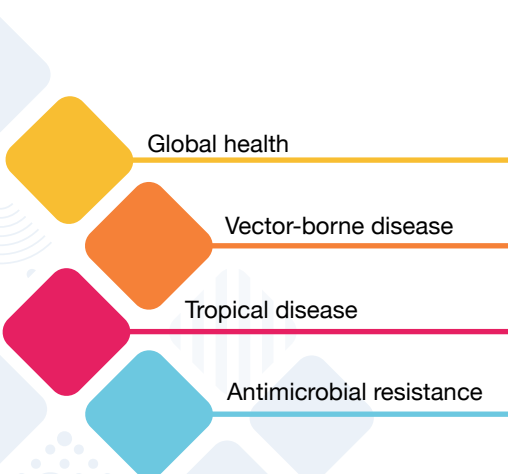
Professor Caroline Colijn

✉ ccolijn@sfu.ca

🐦 @CarolineColijn

Global health

Vector-borne disease

Tropical disease

Antimicrobial resistance

Research

Caroline Colijn is a Canada 150 Research Chair at Simon Fraser University, and an Associate Faculty member at the Wellcome Sanger Institute. She leads the MAthematics, Genomics and Prediction in Infection and Evolution (MAGPIE) group, which develops the necessary mathematical tools to connect sequence data to the ecology and evolution of infections. The group have a long-standing interest in the dynamics of diverse interacting pathogens. For example, they seek to understanding how the interplay between co-infection, competition and selection drives the development of antimicrobial resistance and how genomic data for diverse infections can be used to design better interventions, controlling resistance or vaccine strain replacement. The MAGPIE group builds new approaches to analyzing and comparing phylogenetic trees derived from sequence data, studying tree space and branching processes, and developing ecological and epidemiological models with diversity in mind. Alongside their own research, the group support public health bodies with pandemic modelling, including case-forecasting, vaccination parameter estimation, genomic epidemiology and other topics in relation to COVID-19.

Personal bio

Caroline earned an undergraduate degree from the University of British Columbia, a Master's degree in environmental studies at York University, and a PhD from the University of Waterloo. She completed her post-doctoral training with Michael Mackey at McGill University and later studied epidemiology with Megan Murray at the Harvard T.H. Chan School of Public Health. Following her post-doctoral training, Caroline joined the University of Bristol's Department of Engineering Maths until 2011 when she moved to Imperial College London. In 2017, Caroline was recruited to Simon Fraser University as one of four Canada 150 research chairs, where her research focuses on making connections between mathematics and public health, using diverse data to understand how pathogens adapt and spread.

Selected publications

Colijn, Corander & Croucher (2020) Designing ecologically optimized pneumococcal vaccines using population genomics. Nat. Microbiol. 5 (3): 473-485

Stimson *et al*. (2019) Beyond the SNP Threshold: Identifying Outbreak Clusters Using Inferred Transmissions. Mol. Biol. Evol. 36 (3): 587–603

Walter *et al*. (2019) Genomic variant identification methods alter *Mycobacterium tuberculosis* transmission inference. bioRxiv. doi:10.1101/733642

Xu *et al*. (2019) Transmission analysis of a large TB outbreak in London: mathematical modelling study using genomic data. Microb. Genom. 6 (11): mgen000450

Kendall *et al*. (2018) Estimating transmission from genetic and epidemiological data: a metric to compare transmission trees. Stat. Science 33 (1): 70-85

Hall & Colijn (2018) Transmission trees on a known pathogen phylogeny: enumeration and sampling. Mol. Biol. Evol. 36 (6): 1333-1343

Lees *et al*. (2018) Evaluation of phylogenetic reconstruction methods using bacterial whole genomes: a simulation based study. Wellcome Open Res. 3: 33
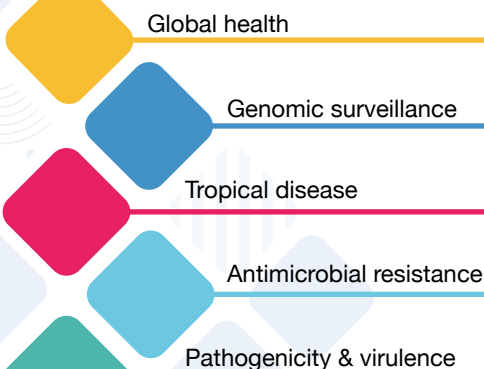
Colijn & Plazzotta (2017) A metric on phylogenetic tree shapes. Syst. Biol. 67 (1): 113-126

Didelot *et al*. (2017) Genomic infectious disease epidemiology in partially sampled and ongoing outbreaks. Mol. Biol. Evol. 34 (4): 997-1007

Professor Alfred Amambua-Ngwa

✉ angwa@mrc.gm

- Global health
- Genomic surveillance
- Tropical disease
- Antimicrobial resistance
- Pathogenicity & virulence

Research

Alfred Amambua-Ngwa is a Cameroonian biochemist at the MRC unit The Gambia at LSHTM. He applies molecular cell biology, population genetics and genomics to understand the evolution and transmission of infectious pathogens and developing new disease interventions. Research in the Amambua-Ngwa group focus on phenotype-genotype association, human *Plasmodium* parasite evolution and transmission tracking in natural populations of malaria. The group uses *in vitro* malaria parasite culture assays, human and parasite population genomics, parasite and vector genomic surveillance and epidemiology to understand antimalarial drug and insecticide resistance development, malaria susceptibility and transmission across Africa. The Amambua-Ngwa group collaborate with the MalariaGEN programme to sequence malaria parasite and Anopheline vector genomes and with colleagues in Ghana on the genomic surveillance of malaria in West Africa. They are also developing forward genetic approaches in collaboration with Dr Marcus Lee, to functionally characterise the role of novel polymorphisms in African *P. falciparum* populations in antimalarial drug tolerance.

Collaborative projects

Pan-African Malaria Genetic Epidemiology Network (PAMGEN) is a team of African scientists studying how genetic changes in humans and malaria parasites impact on the disease in individuals and communities in different ecological environments within seven African countries.

The Malaria Genomic Epidemiology Network (MalariaGEN) is a data-sharing community working to develop new tools to control malaria by integrating epidemiology with genome science.

Personal bio

Alfred obtained BSc, MSc and PhD degrees in Biochemistry from the University of Buea, Cameroon. His research experience began in 1998 with studies on host-parasite interactions in blinding helminthiasis from infection with *Onchcocerca volvulus*. Since 2004 he has been involved in malaria research cutting across disciplines; epidemiology, immunity, cell biology and population genetics. In 2006 he was appointed as scientist at MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, pioneering microarray and genome sequencing to determine signatures of selection across the genome of the deadliest malaria parasite, *Plasmodium falciparum* in Africa. Alfred was the first scientist to hold the prestigious MRC Career Development Award and is co-Principal investigator in several research and capacity building programs in cell biology, genomics and bioinformatics of infectious pathogens in Africa.

Selected publications

Hamid-Adiamoh *et al*. (2021) Influence of insecticide resistance on the biting and resting preferences of malaria vectors in the Gambia. PLOS One. 16 (6): e0241023

Amambua-Ngwa *et al*. (2019) Long-distance transmission patterns modelled from SNP barcodes of *Plasmodium falciparum* infections in The Gambia. Sci. Rep. 9 (1): 13515

Amambua-Ngwa *et al*. (2019) Major subpopulations of *Plasmodium falciparum* in sub-Saharan Africa. Science. 365 (6455): 813-816

MalariaGEN *Plasmodium falciparum* Community Project. (2016) Genomic epidemiology of artemisinin resistant malaria. Elife. 5: e08714

Ghansah *et al*. (2014) Monitoring parasite diversity for malaria elimination in sub-Saharan Africa. Science. 345 (6202): 1297-1298

Dr Gregorio Iraola

✉ giraola@pasteur.edu.uy

🐦 @goyoiraola

- Global health
- Genomic surveillance
- Microbiomes & health
- Antimicrobial resistance
- Pathogenicity & virulence

Research

Gregorio Iraola is Head of the Microbial Genomics Laboratory at the Institut Pasteur Montevideo in Uruguay, and an Adjunct International Professor at the Center for Integrative Biology in the Universidad Mayor of Santiago de Chile in Chile. The Iraola group applies high-throughput sequencing, bioinformatics and culturing to investigate the evolutionary patterns of human and animal bacterial pathogens, to understand the variability of the human microbiome and to assess the role of the environment in the dissemination of antimicrobial resistance. In particular, the group seek: to understand how genome variability in bacterial pathogens is involved in host-adaptation, acquisition of antibiotic resistance and virulence; to characterize microbiome diversity in healthy Latin American populations and how this is altered during pathogenic conditions; and to integrate genomic information from pathogens circulating in nosocomial settings with microbiome data from human populations and the urban environment to uncover bacterial dynamics and evolution under a one-health concept. The Iraola group approach is based on the application and development of bioinformatic strategies that are fed with genomic and metagenomic data generated by second- and third-generation sequencing technologies, and complemented with classical microbiology methods.

Collaborative projects

As an International Fellow at the Wellcome Sanger Institute, Gregorio is leading Latinbiota, a continental initiative to characterize the gut microbiome of healthy populations from urban, rural and native origins in different Latin American countries.

Personal bio

Gregorio graduated from the Universidad de la República of Uruguay in 2010 with a Bachelor in Biological Sciences specialized in Evolutionary Genetics. He then started a Masters in Bioinformatics and obtained a PhD in Biology with focus on computational microbiology and bacterial genomics. Gregorio worked as an Associate Researcher in the Bioinformatics Unit at the Institut Pasteur Montevideo until 2018, before being promoted as a Junior Group Leader to launch the Microbial Genomics Lab. He has been also a visiting worker at the Wellcome Sanger Institute since 2015, developing several projects in collaboration with Trevor Lawley involving whole-genome sequencing of global pathogen collections and analysis of human microbiome data. Gregorio is committed to building research capacities in Latin America.

Selected publications

Costa *et al*. (2020) Polyclonal *Campylobacter fetus* infections among unrelated patients, Montevideo, Uruguay, 2013-2018. Clin. Infect. Dis. 70 (6): 1236-1239

Ferrés, Fresia, & Iraola (2020) simurg: simulate bacterial pangenomes in R. Bioinformatics. 36 (4): 1273-1274

Fresia *et al*. (2019) Urban metagenomics uncover antibiotic resistance reservoirs in coastal beach and sewage waters. Microbiome. 7 (1): 35

Costa & Iraola (2019) Pathogenomics of emerging *Campylobacter* species. Clin. Microbiol. Rev. 32 (4): e00072-18

Grecco *et al*. (2018) Inter- and intra-continental migrations and local differentiation have shaped the contemporary epidemiological landscape of canine parvovirus in South America. Virus Evol. 4 (1): vey011

Thibeaux *et al*. (2018) Deciphering the unexplored *Leptospira* diversity from soils uncovers genomic evolution to virulence. Microb. Genom. 4 (1): e000144

Ferrés & Iraola (2018) MLSTar: automatic multilocus sequence typing of bacterial genomes in R. PeerJ. 6: e5098

Iraola *et al*. (2017) Distinct *Campylobacter fetus* lineages adapted as livestock pathogens and human pathobionts in the intestinal microbiota. Nat. Commun. 8 (1): 1367
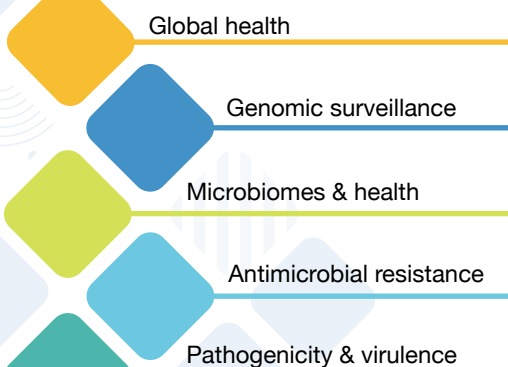
Dr
Pablo
Tsukayama

✉ pablo.tsukayama@upch.pe

Microbiomes & health

Genomic surveillance

Pathogenicity & virulence

Antimicrobial resistance

Research

Pablo Tsukayama is a Peruvian microbiologist with a long-standing interest in infectious diseases affecting Latin American populations. The Microbial Genomics Laboratory at Cayetano Heredia University combine methods in clinical microbiology, genomics, bioinformatics, and infectious disease epidemiology to study infectious diseases in Peru and to generate evidence that guides policy and interventions to help reduce the disease burden in local communities. In particular the group focuses on genomic epidemiology of human pathogens, studies of human and environmental microbiomes, and optimization of methods for genome sequencing and analysis. As a Sanger International Fellow, Pablo and collaborators have set up a SARS-CoV-2 genomic surveillance platform to study local transmission and evolution. His group also conducts surveillance studies on drug-resistant *Mycobacterium tuberculosis* in Lima, a major TB hotspot in Latin America. The group is also interested in the basic biology of *Bartonella bacilliformis*, the agent of Carrion's Disease, a neglected disease endemic to high-altitude communities in the Peruvian Andes.

Personal bio

Pablo obtained his PhD in Molecular Microbiology at Washington University in St. Louis, working with Professor Gautam Dantas. Later, as a Chevening Scholar, he did an MSc in Public Health in Developing Countries at the London School of Hygiene and Tropical Medicine. In 2017, he returned to Peru as an Assistant Professor of Microbiology at Universidad Peruana Cayetano Heredia, where he started his undergraduate training 15 years earlier.

Selected publications

Salvatierra *et al*. (2021) Market Chickens as a Source of Antibiotic-Resistant *Escherichia coli* in a Peri-Urban Community in Lima, Peru. Front. Microbiol. 12: 635871

Lezameta *et al*. (2020) Draft Genome Sequence of a New Delhi Metallo-β-Lactamase (NDM-1)-Producing *Providencia stuartii* Strain Isolated in Lima, Peru. Microbiol. Resour. Announc. 9: e00788-20

Nadimpalli *et al*. (2020) Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission. Nat. Microbiol. 5, 787–795

Dichter *et al*. (2020) Complete Genome Sequence of *Bartonella bacilliformis* Strain KC584 (ATCC 35686). Microbiol. Resour. Announc. 9 (1): e01377-19

Tsukayama *et al*. (2018) Characterization of wild and captive baboon gut microbiota and their antibiotic resistomes. mSystems. 3 (3): e00016-18

Pehrsson *et al*. (2016) Interconnected microbiomes and resistomes in low-income human habitats. Nature. 533 (7602): 212–216

Tsukayama *et al*. (2013) A FRET-based real-time PCR assay to identify the main causal agents of New World tegumentary leishmaniasis. PLOS Negl Trop. Dis. 7 (1): e1956

Henderson *et al*. (2009) Quantitative Metabolomics Reveals an Epigenetic Blueprint for Iron Acquisition in Uropathogenic *Escherichia coli*. PLOS Pathog. 5 (2): e1000305

Tsukayama, Lucas & Bacon (2009) Typing of four genetic loci discriminates among closely related species of New World *Leishmania*. Int. J. Parasitol. 39 (3): 355-362
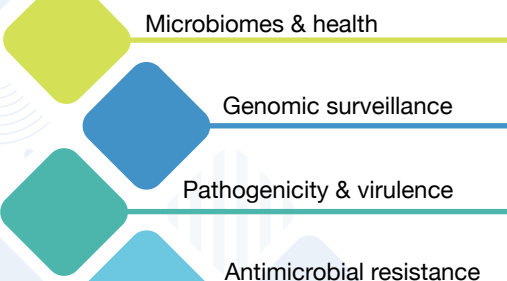
Dr Claire Chewapreecha

✉ claire@tropmedres.ac

🐦 @chewapreecha

Research

Claire Chewapreecha is a computational biologist based at the Mahidol-Oxford Tropical Medicine Research Unit (MORU) in Thailand. Her research group is particularly interested in Melioidosis, a rapidly progressing and frequently fatal neglected tropical infectious disease caused by a soil bacterium *Burkholderia pseudomallei*. Healthy individuals living in disease hotspots such as northeast Thailand develop serological evidence of exposure from early childhood. However, not all exposure leads to disease and infections can have variable outcomes, suggesting that there may be bacterial, host, or environmental components that influence disease acquisition and severity.

Research in the Chewapreecha group is focussed on using genomics to identify B. pseudomallei genetic factors that determine disease severity, to identify host biomarkers associated with susceptibility to Melioidosis and disease severity, and to construct models to predict disease outcome.

With a strong research network, the Chewapreecha group aims to help develop translational approaches that rationalise vaccine design by targeting the most harmful bacteria and most susceptible individuals. Their long-term goal is to build a sustainable genomic research programme for melioidosis and other infectious diseases in Thailand, and to link newly formed bioinformatics teams, Wellcome research units in Southeast Asia, Wellcome Sanger Institute, and the global research partners.

Collaborative projects

Claire is part of an ongoing NIHR Global Research project on development of a vaccine to prevent death from melioidosis in people with type 2 diabetes mellitus in LMICs.

Her team develops host-pathogen OMIC resource that provides genetic and molecular signatures of protective immune response for predicting vaccination outcomes.

Personal bio

Claire studied for an undergraduate degree at the University of Cambridge. She earned a PhD from the Wellcome Sanger Institute and University of Cambridge, where her research in the laboratory of Stephen Bentley focussed on using genomics to understand the evolution and transmission of *Streptococcus pneumoniae*. She was awarded a Sir Henry Wellcome Postdoctoral Fellowship, which facilitated her transition from the UK to Thailand, and is currently a Wellcome International Intermediate Fellow at the Mahidol-Oxford Tropical Medicine Research Unit (MORU) in Bangkok, where she leads the Melioidosis Genomic Group.

- Global health
- Genomic surveillance
- Pathogenicity & virulence
- Tropical disease
- Vaccines

Selected publications

Chewapreecha *et al*. (2022) Co-evolutionary signals identify *Burkholderia pseudomallei* survival strategies in a hostile environment. Mol. Biol. Evol. 39 (1): msab306

Chewapreecha *et al*. (2019) Genetic variation associated with infection and the environment in the accidental pathogen *Burkholderia pseudomallei*. Commun. Biol. 2: 428

Pensar *et al*. (2019) Genome-wide epistasis and co-selection study using mutual information. Nucleic Acids Res. 47 (18): e112

Skwark *et al*. (2017) Interacting networks of resistance, virulence and core machinery genes identified by genome-wide epistasis analysis. PLOS Genet. 13 (2): e1006508

Chewapreecha *et al*. (2017) Global and regional dissemination and evolution of *Burkholderia pseudomallei*. Nat. Microbiol. 2: 16263

Lees *et al*. (2016) Sequence element enrichment analysis to determine the genetic basis of bacterial phenotypes. Nat. Commun. 7: 12797

Chewapreecha *et al*. (2014) Dense genomic sampling identifies highways of pneumococcal recombination. Nat Genet. 46 (3): 305-309

Köser *et al*. (2012) Rapid whole-genome sequencing for investigation of a neonatal MRSA outbreak. N. Engl. J. Med. 366 (24): 2267-75

Dr Annettee Nakimuli

✉ annette.nakimuli@gmail.com

Global health

Pathogenicity & virulence

Research

Annettee Nakimuli is an Associate Professor and the Chair of the Department of Obstetrics and Gynaecology at Makerere University, in Uganda. She is a leading maternal health researcher and also clinically active. Her clinical expertise is high risk obstetrics (complicated pregnancies) and works at Mulago Hospital which is the main teaching Hospital for Makerere University and has the greatest number of annual births of any hospital in sub-Saharan Africa (30,000 births per year). Her research group's primary research interest is pre-eclampsia, a major cause of maternal morbidity and mortality in sub-Saharan Africa. In particular, the group is interested in identifying genetic and other risk factors for pre-eclampsia in order to improve pregnancy outcomes in Ugandan mothers. Her group is also interested in functional characterization of other pregnancy complications common in Ugandan women such as fetal growth restriction, preterm birth, intrauterine fetal death and pathogen infections during pregnancy.

Collaborative projects

Annette is working with Dr Roser Vento-Tormo in the Vento-Tormo research group, with the Cellular Genetics Programme at the Wellcome Sanger Institute. She serves on several national and international committees, including the Uganda Maternal and Newborn Technical working group, Steering Committee of the MultiOmics for Mothers and Infants (MOMI) Consortium at the Bill & Melinda Gates Foundation established to understand the biological drivers of adverse pregnancy outcomes in low resource settings.

Personal bio

Annette trained as a medical doctor with specialist training in Obstetrics and Gynaecology at Makerere University, Kampala, graduating in 2005. As an obstetrician and gynaecologist she became interested in pre-eclampsia, a major cause of death and morbidity in sub-Saharan Africa. Her PhD research on pre-eclampsia was the first genetic case-control study on pre-eclampsia among indigenous Africans, despite African ancestry being a predisposing factor to pre-eclampsia. Her post-doctoral research extended these studies to recruit more mothers and babies with a wider range of pregnancy disorders such as fetal growth restriction, preterm birth and intrauterine fetal death. Now an Associate Professor and Chair of the Department of Obstetrics and Gynaecology at Makerere University, Annettee is committed to building maternal and new-born research capacity in Africa. Her aim is, with East African and International colleagues, to establish a multidisciplinary centre for African maternal and neonatal health research located at Makerere University. Annettee currently serves as the Vice President of the East Central and Southern Africa College of Obstetrics and Gynaecology (ECSACOG) which was established in 2017.

Selected publications

Vousden et al. (2020) Incidence and characteristics of pregnancy-related death across ten low and middle-income geographical regions: secondary analysis of a cluster randomised controlled trial. BJOG. 127 (9): 1082-1089

Smith & Nakimuli (2020) Ultrasound estimation of gestational age in late pregnancy in low-income countries: made to measure or off-the-peg? Lancet Glob. Health. 8 (4): e462–e463

Blokhuis et al. (2017) KIR2DS5 allotypes that recognize the C2 epitope of HLA-C are common among Africans and absent from Europeans. Immun. Inflamm. Dis. 5 (4): 461-468

Professor
Stephen
Baker

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✉ sgb47@cam.ac.uk

🐦 @Baker_Lab_Cam

Global health

Genomic surveillance

Epidemiology

Microbiomes & health

Pathogenicity & virulence

Antimicrobial resistance

Vaccines

Research

Stephen Baker is a molecular microbiologist with an interest in the microbiology, genetics, epidemiology and treatment of enteric infections in developing countries, with an emphasis on focal pathogens that include Norovirus, *Shigella* spp. and *Salmonella* Typhi, the causative agents of diarrhoea, dysentery and typhoid fever. The Baker group use various genomic and laboratory approaches to understanding how bacteria and viruses that cause infectious disease in humans in low and middle income countries (LMICs) evolve and spread. In particular they are interested in understanding the phylogeography of enteric bacteria, and looking more closely at evolutionary adaptation and clonal replacement of gastrointestinal pathogens in endemic settings through cohort studies and hospital surveillance. In addition they are interested in the impact of antimicrobial access and treatment on the gut microbiota and the generation of drug resistant pathogens. Their work maintains an international focus, with the ultimate goal to develop new interventions for treating and preventing infections cause by antimicrobials resistant pathogens.

Collaborative projects

The Global Typhoid Genomics Consortium aims to engage with the global typhoid research community to aggregate *S.* Typhi genome data to monitor the emergence and spread of drug resistance and inform targeted public health action.

The Strategic Typhoid alliance across Africa and Asia (STRATAA) and the Typhoid Vaccine Acceleration Consortium (TyVAC) seek to accelerate the introduction of vaccines in low-income countries and facilitate access in the most at-risk and marginalized communities.

The RESISTANT programme for developing new therapeutics for *Shigella*.

Personal bio

Stephen obtained his PhD from Imperial College, London in 2005 studying *Salmonellae* genomic diversity. He spent 12 years researching the epidemiology, genomics, and diagnostics of enteric and zoonotic infections as part of the Wellcome Trust Major Overseas Programme in Ho Chi Minh City, Vietnam. In 2019, Stephen returned to the UK to become Director of Research For Global Health in the Department of Medicine at the University of Cambridge, an honorary professor at the University of Oxford, and honorary faculty at the Wellcome Sanger Institute. He is a Wellcome senior research fellow and gave the 2017 microbiology society Fleming prize lecture.

Selected publications

Park *et al*. (2018) The phylogeography and incidence of multi-drug resistant typhoid fever in sub-Saharan Africa. Nature. 9 (1): 5094

de Alwis *et al*. (2018) The Role of Maternally Acquired Antibody in Providing Protective Immunity Against Nontyphoidal *Salmonella* in Urban Vietnamese Infants: A Birth Cohort Study. J. Infect. Dis. 219 (2): 295-304

Mather *et al*. (2018) New Variant of Multidrug-Resistant *Salmonella enterica* Serovar Typhimurium Associated with Invasive Disease in Immunocompromised Patients in Vietnam. mBio. 9 (5): e01056-18

Andrews *et al*. (2018) NCTyphoid conjugate vaccines: a new tool in the fight against antimicrobial resistance. Lancet Infect. Dis. 19 (1): e26-e30

Thi Quynh Nhi *et al*. (2018) Quantifying antimicrobial access and usage for paediatric diarrhoeal disease in an urban community setting in Asia. J. Antimicrob. Chemother. 73 (9): 2546-2554

Professor Samuel Kariuki

✉ skariuki@kemri.org

- Global health
- Genomic surveillance
- Epidemiology
- Microbiomes & health
- Tropical disease
- Antimicrobial resistance

Research

Sam Kariuki is a microbiologist, epidemiologist and expert in antimicrobial surveillance and monitoring. His research group utilises molecular tools to investigate the field epidemiology of major enteric infections, and antimicrobial resistance (AMR) ecology and transmission in Kenya and the region. They focus on infections caused by *E. coli*, invasive non-typhoidal *Salmonella* disease, cholera, typhoid and dysentery, using genomic surveillance to inform improvements in food hygiene. In order to develop novel treatment methods for enteric infections, the Kariuki group also use genomics for understanding the microbiome in health and disease.

Collaborative projects

Sam leads a Wellcome Trust funded project with partners from Emory University and Ohio State University (OSU) for accelerating cholera prevention, preparedness and control in East Africa through hotspot mapping, genotyping, modelling transmission, exposure assessment, WASH and oral cholera vaccine interventions.

With the Robert Koch Institute and OSU, Sam leads projects examining the role of carriage in endemic settings in Kenya for i) multidrug-resistant invasive non-typhoidal *Salmonella* (NTS) disease in children and ii) multidrug-resistant *Salmonella* Typhi infections. These projects aim at mapping hotspots of disease to inform public health interventions.

Sam co-leads a sustainable one health research training capacity project that focuses on the molecular epidemiology of zoonotic foodborne and waterborne pathogens in East Africa. This is a Fogarty International Centre grant aimed at PhD and post-doc training.

Personal bio

Sam obtained a Bachelor degree in Veterinary Medicine and an MSc in Pharmacology and Toxicology from the University of Nairobi. In 1997 he obtained a PhD in Tropical Medicine from the Liverpool School of Tropical Medicine and then rose through the ranks to become a Chief Research Officer at Kenya Medical Research Institute (KEMRI). Sam is currently the Director of Research and Development at KEMRI. He is a Fellow of the African Academy of Sciences and an Honorary Faculty Member at Sanger. He is a visiting Professor of Tropical Microbiology at the University of Oxford and a member of the Kenyan National Antibiotic Stewardship Interagency Committee (NASIC) advising on one-health approaches to tackling AMR. He is also a member of the WHO Strategic and Technical Advisory Group on AMR and the Technical Advisory Group East Africa on AMR surveillance and monitoring. In 2012, Sam won the prestigious Royal Society Pfizer Prize for African Scientist of the Year.

Selected publications

Kariuki *et al*. (2021) Multiple introductions of multidrug-resistant typhoid associated with acute infection and asymptomatic carriage, Kenya. Elife 10: e67852
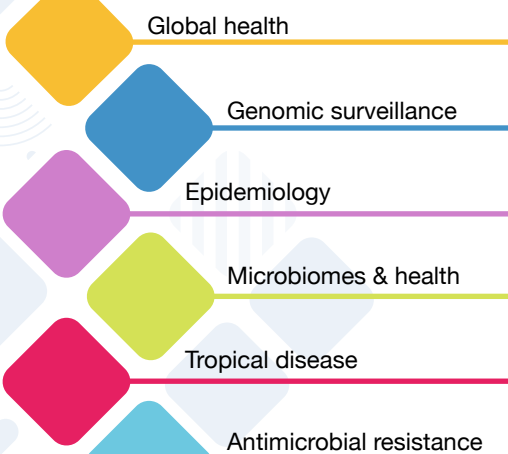
Kariuki *et al*. (2021) Antimicrobial Resistance in endemic enteric infections in Kenya and the region, and efforts towards addressing the challenges. J. Infect. Dis. jiab457

Kariuki *et al*. (2020) High relatedness of invasive multi-drug resistant non-typhoidal *Salmonella* genotypes among patients and asymptomatic carriers in endemic informal settlements in Kenya. PLOS Negl. Trop. Dis. 14: e0008440

Mulinge *et al*. (2021) *Entamoeba* species infection in patients seeking treatment for diarrhea and abdominal discomfort in Mukuru informal settlement in Nairobi, Kenya. Food Waterborne Parasitol. 23: e00122

Kariuki & Kiiru (2021) Detection and Characterization of *Salmonella enterica* Serotypes by Simple PCR Technologies. Methods Mol. Biol. 2182: 161-177

Kariuki & Owusu-Dabo (2020) Research on iNTS disease and developments towards better understanding of epidemiology, management, and control strategies. Clin. Infect. Dis. 71 (Supplement_2): S127-S129

Professor Martin Donnelly

✉ martin.donnelly@lstmed.ac.uk

🐦 @MartinDonnelly8

- Global health
- Genomic surveillance
- Epidemiology
- Antimicrobial resistance
- Tropical disease

Research

Martin Donnelly's group studies the evolutionary genetics of insect disease vectors. A major area of interest is the evolution of insecticide resistance in the malaria mosquito *Anopheles gambiae*. The Donnelly group leverage the power of next-generation sequencing technologies to address aspects of the biology of *Anopheles gambiae* that impact upon the sustainable control of malaria. This includes genome wide association studies (GWAS) to identify genetic loci associated with insecticide resistance and population genetic studies to describe population sub-structuring. They are also interested in understanding the impact of insecticide resistance on malaria epidemiology, through observational studies and randomized control trials.

Collaborative projects

Much of this work in the Donnelly group is conducted jointly with Dr David Weetman and team. In addition the Donnelly group collaborate with a range of other researchers in the UK and Africa.

The Malaria Genomic Epidemiology Network (MalariaGEN) is a data-sharing community working to develop new tools to con-trol malaria by integrating epidemiology with genome science.

The *Anopheles gambiae* 1000 Genome project is a global collaboration using whole genome deep sequencing to provide a high-resolution view of genetic variation in natural populations of *Anopheles gambiae*, the principal vector of *Plasmodium falciparum* malaria in Africa.

Personal bio

Martin Donnelly trained at Girton College, Cambridge University (MA) and the Liverpool School of Tropical Medicine (MSc, PhD). He was then awarded an American Society of Microbiology Fellowship and spent two years in the laboratory of Dr Tovi Lehmann at the Centers for Disease Control and Prevention (CDC) in Atlanta, USA. He re-joined the Liverpool School of Tropical Medicine in 2001, and is a Professor of Evolutionary Genetics and Head of the Vector Biology Department. Martin is an Honorary Faculty Member of the Wellcome Trust Sanger Institute.

Selected publications

Grau-Bové *et al*. (2020) Evolution of the Insecticide Target Rdl in African *Anopheles* Is Driven by Interspecific and Interkaryotypic Introgression. Mol. Biol. Evol. 37 (10): 2900-2917

Lucas *et al*. (2019) Whole genome sequencing reveals high complexity of copy number variation at insecticide resistance loci in malaria mosquitoes. Genome Res. 29 (8): 1250-1261

The *Anopheles gambiae* 1000 Genomes Consortium. (2017) Genetic diversity of the African malaria vector *Anopheles gambiae*. Nature. 552 (7683): 96–100
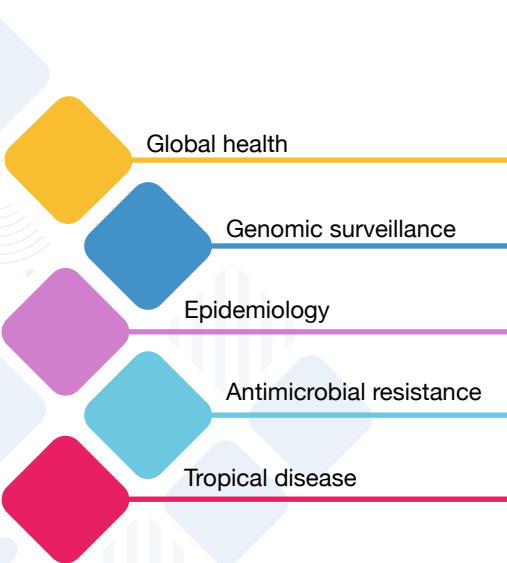
Clarkson *et al*. (2014) Adaptive introgression between *Anopheles* sibling species eliminates a major genomic island but not reproductive isolation. Nat. Commun. 5: 4248

Mitchell *et al*. (2012) Identification and validation of a gene causing cross-resistance between insecticide classes in *Anopheles gambiae* from Ghana. Proc. Natl Acad. Sci. USA. 109 (16): 6147-52

Staedke *et al*. (2020) Effect of long-lasting insecticidal nets with and without piperonyl butoxide on malaria indicators in Uganda (LLINEUP): a pragmatic, cluster-randomised trial embedded in a national LLIN distribution campaign. Lancet 395 (10232): 1292-1303

Abong'o *et al*. (2020) Impact of indoor residual spraying with pirimiphos methyl (Actellic 300CS®) on entomological indicators of transmission and malaria case burden in Migori County, western Kenya. Sci. Rep. 10 (1): 4518

Kleinschmidt *et al*. (2018) Implications of insecticide resistance for malaria vector control with long-lasting insecticidal nets: a WHO-coordinated, prospective, international, observational cohort study. Lancet Infect. Dis. 18 (6): 640-649

Professor Abdoulaye Djimde

✉ adjimde@icermali.org

🐦 @djimdeab

- Global health
- Genomic surveillance
- Epidemiology
- Antimicrobial resistance
- Tropical disease

Research

Abdoulaye Djimdé is a leading malaria researcher based in Mali. His group works primarily on the genetic epidemiology of antimalarial drug resistance in West Africa. They conduct field and laboratory based analyses to understand how variations in the genomes of the malaria parasite, the human host, and the mosquito vector relate to disease outcomes like the spread of antimalarial drug resistance.

Collaborative projects

The Malaria Genomic Epidemiology Network (MalariaGEN) is a data-sharing community working to develop new tools to control malaria by integrating epidemiology with genome science.

Personal bio

After receiving a pharmacy doctorate in 1988 from the University of Bamako, Mali, Djimdé started a private pharmacy and learnt first-hand about the need for more effective ways of treating and preventing malaria. He began volunteering as a research assistant with the Late Prof. Ogobara Doumbo at the Malaria Research and Training Centre in Bamako, and decided to undertake a PhD under Christopher V. Plowe at the University of Maryland and Thomas E. Wellems at the National Institutes of Health. Since 2002, Djimdé has been at The University of Science, Techniques and Technologies of Bamako, Mali, where he is CAMES Professor of Parasitology and Mycology and Chief of the Molecular Epidemiology and Drug Resistance Unit at the Malaria Research and Training Centre. Djimdé was instrumental in the formation of the Worldwide Antimalarial Drug Resistance Network, on whose Scientific Advisory Board he served. He has also been Chair of the Multilateral Initiative on Malaria Task Force within the World Health Organization Tropical Disease Research Programme. He currently serves as coordinator of the West African Network for Clinical Trials of Antimalarial Drugs, Leader of the Pathogens genetic Diversity Network-Africa (PDNA) and Director Developing Excellence in Leadership and Genetic Training for Malaria Elimination in sub-Saharan Africa (DEL-GEME). He is also the Founding President of the African Association for research and control of AntiMicrobial Resistance (AAAMR). Djimdé has won a number of prestigious awards during his career and is a Fellow of the African Academy of Science, the Malian Academy of Sciences and The World Academy of Sciences.

Selected publications

Djimde, Ranque & Thera. (2019) Building a center of excellence in biomedical research in an unfavorable environment: the Malaria Research and Training Center in Mali. Med Sante Trop. 29 (4): 343-347

Ghansah *et al*. (2019) Targeted Next Generation Sequencing for malaria research in Africa: current status and outlook. Malar. J. 18 (1): 324

Amambua-Ngwa *et al*. (2019) Major sub-populations of *Plasmodium falciparum* in sub-Saharan Africa. Science. 365 (6455): 813-816

West African Network for Clinical Trials of Antimalarial Drugs (2018). Pyronaridine-artesunate or dihydroartemisinin-piperaquine versus current first-line therapies for repeated treatment of uncomplicated malaria: a randomised, multicentre, open-label, longitudinal, controlled, phase 3b/4 trial.

Lancet. 391 (10128): 1378-1390

Kamau *et al*. (2014) K13-Propeller Polymorphisms in *Plasmodium falciparum* Parasites From Sub-Saharan Africa. J. Infect. Dis. 211 (8): 1352-5

Ghansah *et al*. (2014) Monitoring parasite diversity for malaria elimination in sub-Saharan Africa. Science. 345 (6202): 1297-8

Djimde *et al*. (2010) A molecular map of chloroquine resistance in Mali. FEMS Immunol. Med. Microbiol. 58 (1): 113-8

Djimde *et al*. (2001) Application of a molecular marker for surveillance of chloroquine-resistant *falciparum* malaria. Lancet. 358 (9285): 890-891

Djimdé A *et al*. (2001). A molecular marker for chloroquine-resistant *falciparum* malaria. N. Engl. J. Med. (344):257-63
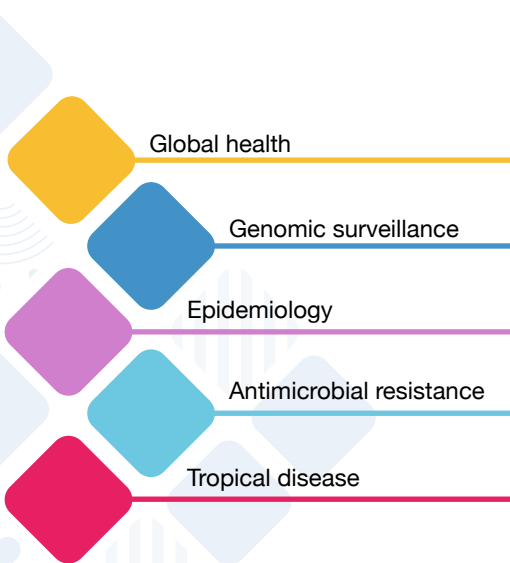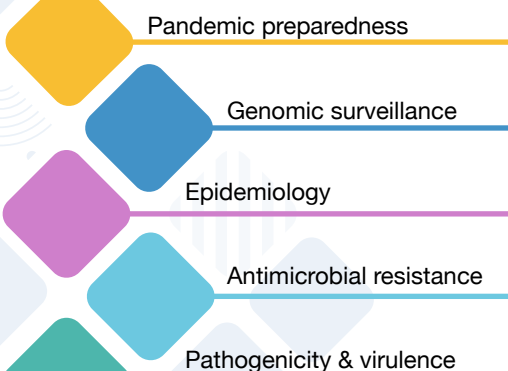
Professor Marc Lipsitch

✉ mlipsitc@hsph.harvard.edu

🐦 @mlipsitch

- Pandemic preparedness
- Genomic surveillance
- Epidemiology
- Antimicrobial resistance
- Pathogenicity & virulence

Research bio

Marc Lipsitch is Professor of Epidemiology and Director of the Center for Communicable Disease Dynamics at the Harvard T.H. Chan School of Public Health. He is an internationally-recognized expert in methods and disease transmission modelling, and has been a leading scientific authority during the COVID-19 pandemic.

Marc has authored more than 300 peer-reviewed publications on anti-microbial resistance, epidemiologic methods, mathematical modelling of infectious disease transmission, bacterial and human population genetics, immunity to *Streptococcus pneumoniae*, and COVID-19 epidemiology. His research informs the use of transmission-dynamic simulations to improve the design of randomized and observational studies of infectious disease interventions, and bioethics related to infectious diseases and clinical trials in emergencies.

His recent COVID-19 research builds on 20 years of work on SARS, pandemic influenza, and other emerging and seasonal infections, including real-time estimation of SARS transmissibility, modelling of control measures, calculating the reproductive number for the 1918 "Spanish flu" and severity of the 2009 H1N1 flu pandemic. This work has contributed to the foundation of modern pandemic responses and informed non-pharmaceutical interventions. During the present pandemic, Marc has been featured in thousands of press articles and media interviews on COVID-19.

In 2014, Marc co-founded the Cambridge Working Group, whose efforts helped to initiate a pause in US government funding for research involving the creation of potential pandemic pathogens, such as transmission-enhanced avian influenza strains. He has written extensively on aspects of science policy in relation to such studies.

Marc was selected to the National Academies of Medicine in 2020, for his pre-COVID-19 scientific accomplishments. In 2015, he was elected a Fellow of the American Academy of Microbiology, and in 2014 he received the Robert Austrian Award for contributions to pneumococcal research. He is or was on the editorial advisory boards/associate editor of eLife, PLOS Medicine, Journal of Infectious Diseases, American Journal of Epidemiology, Epidemiology, and Epidemics. He currently serves on the Massachusetts Governor's Medical Advisory Committee, and both the Massachusetts and WHO COVID-19 Vaccine Working Groups. He has also served on the President's Council of Advisors on Science and Technology Working Group on H1N1 Influenza, as well as CDC's Team B for the 2009 H1N1 pandemic and several advisory groups during the 2014-15 Ebola outbreak in West Africa. He has provided advice to the Food and Drug Administration, Centers for Disease Control, World Health Organization, International Monetary Fund, Congressional Budget Office, Defense Science Board, several pharmaceutical companies and the governments of Canada, Mexico, India, Germany, Austria, and Luxembourg.

Marc joined the faculty of the Harvard School of Public Health in 1999, after completing a postdoctoral fellowship at Emory University with Bruce Levin, and a visiting scientist appointment at CDC. He received a D.Phil. in Zoology as a Rhodes Scholar from the University of Oxford, where he studied with Robert May and Martin Nowak, and a B.A. in Philosophy from Yale University.

Selected publications

Hay *et al*. (2021) Estimating epidemiologic dynamics from cross-sectional viral load distributions. Science. 373 (6552): eabh0635

Kissler *et al*. (2020) Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science. 368 (6493): 860-868

Azarian *et al*. (2020) Frequency-dependent selection can forecast evolution in *Streptococcus pneumoniae*. PLOS Biol. 18 (10): e3000878

Cobey & Lipsitch (2012) Niche and neutral effects of acquired immunity permit coexistence of pneumococcal serotypes. Science. 335 (6074): 1376-80

Mills, Robins & Lipsitch (2004) Transmissibility of 1918 pandemic influenza. Nature; 432 (7019): 904-6

Lipsitch *et al*. (2003) Transmission dynamics and control of severe acute respiratory syndrome. Science. 300 (5627): 1966-70

Professor Christopher Newbold

✉ chris.newbold@imm.ox.ac.uk

Research

Chris Newbold is a molecular parasitologist interested in the basis for adherence related pathogenesis, antigenic variation and immunity in the malaria parasite *Plasmodium falciparum*. The Newbold group focuses on the how *P. falciparum* is able to maintain long term chronic infection and how is causes severe disease. In particular they have focussed on the var multi-gene family, specific to *P. falciparum* among the human malarias, whose protein products that are expressed on the infected red cell surface are thought to be one of the primary mediators of pathogenesis through their ability to cause adhesion of infected cells to host vascular endothelium and to be important targets of the host antibody response. They also undergo transcriptional switching among members as a means of antigenic variation and immune evasion. Using a variety of techniques including functional genomics, transfection, mathematical modelling and whole genome sequencing the Newbold lab study host receptors, pathogenesis, the control of transcriptional switching and sequence evolution. More recently they have become more interested in the more numerous *Plasmodium* Interspersed Repeat (pir) multi-gene family that are common to all sequenced species of *Plasmodium*.

Personal bio

Chris graduated with an MA and PhD from the University of Cambridge in 1978. After a postdoctoral fellowship studying rodent malaria at The National Institute for Medical Research, Mill Hill, he moved to Oxford in 1984. Chris continued to work on rodent malaria with a particular interest in antigenic variation and soon moved to working on the same area in human malaria. He helped to establish the Wellcome Trust unit in Kilifi, Kenya and has worked closely with colleagues there ever since. He became a Professor in 1997 and leads the Molecular Parasitology Group at the Weatherall Institute of Molecular Medicine where he continues to work on mechanisms of disease and immune evasion in malaria. Chris was a key figure in the generation of the *Plasmodium falciparum* reference genome.

Tropical disease

Pathogenicity & virulence

Selected publications

Böhme *et al*. (2019) Progression of the canonical reference malaria parasite genome from 2002-2019. Wellcome Open Res. 4: 58

Otto *et al*. (2018) Genomes of all known members of a *Plasmodium* subgenus reveal paths to virulent human malaria. Nat. Microbiol. 3: 687–697

Rutledge *et al*. (2017) *Plasmodium malariae* and *P. ovale* genomes provide insights into malaria parasite evolution. Nature. 542 (7639): 101-104

Brugat *et al*. (2017) Antibody-independent mechanisms regulate the establishment of chronic *Plasmodium* infection. Nat. Microbiol. 2: 16276

Otto *et al*. (2014) Genome sequencing of chimpanzee malaria parasites reveals possible pathways of adaptation to human hosts. Nat. Commun. 5: 4754

Noble *et al*. (2013) The antigenic switching network of *Plasmodium falciparum* and its implications for the immuno-epidemiology of malaria. Elife. 2: e01074

Lemieux *et al*. (2013) Genome-wide profiling of chromosome interactions in *Plasmodium falciparum* characterizes nuclear architecture and reconfigurations associated with antigenic variation. Mol. Microbiol. 90 (3): 519-37

Recker *et al*. (2011) Antigenic variation in *Plasmodium falciparum* malaria involves a highly structured switching pattern. PLOS Pathog. 7 (3): e1001306

Research support

Team

✉ pam-admin@sanger.ac.uk

The PaM Research Support function comprises a six strong team that provides comprehensive support for the smooth running of the Programme. This includes both operational and strategic support. The team work collaboratively across the Institute with Administrators, Human Resources, Finance and Scientific Administration to facilitate the cutting edge research carried out at the Wellcome Sanger Institute. They are in a unique position to understand the objectives of the programme and are able to act as an interface between the researchers and the other support groups, such as the Legal, Governance and Grants teams, as well as Scientific Operations.

The activities of the team include anything from organising international travel itineraries, servicing multi-million pound collaborative grants and facilitating Faculty management meetings to organising hospitality and fielding day-to-day enquiries relating to specific projects, including sequencing. In addition to this, the team organise recruitment, excel in events management, provide both financial and demand forecasting, as well as pre- and post-award support for third party funding from a wealth of different funding sources.

The team believe in continuous improvement and are active in working groups across the Institute to ensure that any changes are suitable for the PaM Programme. They also seek to ensure that the programme's own processes remain fit for purpose to achieve the best possible outcomes in the most efficient way. Acting as a point of contact for the programme, the wider institute and our external partners, researchers know that if they require information the Research Support team will be able to help.

Laboratory support

Sally Kay

✉ sally@sanger.ac.uk

Liam Prestwood

✉ liam.prestwood@sanger.ac.uk

The PaM laboratories have a dedicated support team to ensure a safe and dynamic environment for flexible research needs within the Programme. Lab operations are co-ordinated by a group of laboratory managers and local co-ordinators, overseeing CL2 and CL3 facilities and maintenance of pathogen vectors (e.g. snails, mice, mosquitoes). The team ensure and expect a high level of health and safety, enabling and supervising research on a broad spectrum of infectious agents. Training, information and support in working in these laboratories is provided for all staff, students and visiting workers from a range of backgrounds and levels of experience.

Key roles

- PaM representation on Health and Safety Committee and Sulston Building Group

- Main co-ordinators between Sanger Institute teams – safety, facilities, security, engineering

- Facilities maintenance and refurbishment – co-ordination and safe supervision of Sanger Projects, Building and Facilities Management teams, embedded and external contractors

- Equipment – purchasing of new equipment, maintenance and training, sharing of new technology

- Procurement – purchasing and sourcing of consumables, equipment, PPE

- Training, induction and supervision – CL3, CL2, equipment use, new techniques

- Health and Safety – training in safe methods and equipment use, inductions, inspections

- Regulatory compliance – HSE and other Government permits (eg. Home Office), development of laboratory Codes of Practices, tracking, use and storage of human relevant material

- International and national shipping – includes import and export of infectious samples, biological/GM, chemicals, consumables and associated administration, paperwork, permits and licences.

- Secure sample storage – safe storage of samples at required conditions (eg. liquid nitrogen, -80°C), including tracking systems.

The laboratory support team are well equipped to enable new research aims and processes, and continually drive Programme improvements including renewal and reallocation of lab and office spaces, uptake of new technology/equipment and health and safety.

Pathogen informatics

**Group Lead
Christoph Puethe**

✉ christoph.puethe@sanger.ac.uk

Team

✉ path-help@sanger.ac.uk

The Pathogen Informatics team support the research activities of the PaM programme by providing informatics services and developing targeted software applications. The team consists of 12 bioinformaticians and software developers with a range of backgrounds, united by their passion for genomics. Led by Christoph Puethe, they work in a collaborative manner to tackle the challenges posed by the ever-increasing amount of genomic data.

The team currently focus on:

- Development and maintenance of automated pipelines for the analysis of high-throughput sequencing data

- Development of interactive web platforms for sharing genomic data and research findings with collaborators and the community

- Packaging of bioinformatics software and deployment on internal computational platforms

- Development of databases and services that enable scientists to track their genomic data

- Provisioning of informatics and bioinformatics training via an internal web platform

- Ad-hoc informatics support to members of the programme via a helpdesk

Pathogen Informatics collaborate closely with all scientific groups in PaM, with a particular focus on supporting the large-scale surveillance activities for infectious diseases, such as malaria or pneumonia. They also constitute the link between the programme and Sanger's core IT services. The team embrace agile methods and promote open source software development. Their technical stack relies on Python, JavaScript, Docker and NextFlow.

Automated analysis pipelines

Pathogen Informatics provide a number of automated bioinformatics analysis pipelines that are run on demand for scientists in PaM.

These pipelines include:

- Quality control

- Sequence alignment and variant calling

- De-novo assembly and automated annotation

- RNA-Seq expression analysis

More sophisticated, organism-specific pipelines for the programme's surveillance activities are in active development.

Imaging

David Goulding
✉ dag@sanger.ac.uk

With a unique repertoire of modern high-end instrumentation, the imaging facility within PaM works collaboratively with researchers on a range of projects relating genotype to phenotype, exploring functional genomics and analysing dynamic events at sub-cellular resolution. The facility also pioneers advances in imaging and analysis approaches, enables digital cataloguing of samples, and provides training and advice.

Imaging in PaM is run by David Goulding, a microscopist with 35 years' experience in both advanced light and electron microscopy (EM) who previously designed and managed microscope suites at EMBL Heidelberg and Imperial College London and has been at the Wellcome Sanger Institute for the last 16 years. David's expertise lies in ultrastructure techniques, including fine structure immunocytochemistry, to study interactions between host cells and microorganisms.

The facility contributes across many PaM research areas including host-pathogen interactions, disease transmission, vaccinology, organoid modelling, cell signalling and, more broadly across campus, supporting work in other programmes, utilising transmission EM, immunoEM, scanning EM, confocal microscopy, immunofluorescence, RNAscope, immunohistochemistry and histology.

Electron microscopy

EM is in high demand for collaborative research on campus. Chemical fixation and state-of-the-art cryopreservation techniques developed in house, applied to a wide range of sample types, provide excellent conservation of native tissue architecture. Even the subtlest differences in sub-cellular fine structure can be detected, for example relating genotype to phenotype, visualizing the physical interactions between pathogen and host, validating sub-cellular alterations in early tumours and the effects of genetic abnormalities on embryo development.

Advanced light microscopy

The Advanced Light microscope capabilities, including immunofluorescence and FISH, are wide-ranging for both fixed and live cell analysis by confocal, fluorescence and wide field microscopy, providing high content platforms with high resolution for publication. Recent developments in generating cell and organoid cultures and robust imaging techniques developed in house allow these models to be explored by live cell microscopy at super-resolution.

Selected publications

Autheman *et al*. (2021) An invariant *Trypanosoma vivax* vaccine antigen inducing protective immunity. Nature 595: 96–100

Bayés *et al*. (2018) Evolution of complexity in the zebrafish synapse proteome. Nat. Commun. 2: 16276

Yeung *et al*. (2017) Exploiting induced pluripotent stem cell-derived macrophages to unravel host factors influencing *Chlamydia trachomatis* pathogenesis. Nat. Commun. 8: 15013

Browne *et al*. (2016) Culturing of 'unculturable' human microbiota reveals novel taxa and extensive sporulation. Nature 533: 543-546

Klemm *et al*. (2016) Emergence of host-adapted *Salmonella* Enteritidis through rapid evolution in an immunocompromised host. Nat. Microbiol. 1: 15023