8th Annual Medawar Day

4th October 2018
Oxford Martin School

Nuffield Department of Medicine ...fostering your career in science

University of Oxford

Medawar pathogen research

Department of Zoology

Medawar Day
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Welcome to the Medawar Day 2018.

Consistent with the focus of the building, this meeting has evolved over the years in response to selective pressure from different forces. The main aim is to have one day where the different labs can share their work and we can all get some sense of what is going on – it is not a huge building but it is still easy to miss out.

One set of selective forces acts to diversify the talks so you get to hear from as many groups as possible, and the other set (I guess purifying selection) serves to trim the whole day down so it is not a rush and something of a blur.

So today's programme represents we hope optimal adaptation with minimal fitness cost. Hopefully this will also spark some conversations and some joint projects so we can all get the best out of the opportunities that come from working in the building, which we hope is a really enthusiastic and welcoming environment for everybody.

Talking of which, one other aim of the day is to introduce the new postgraduate students and other team members, and for them to see what is going on, so if you see a new face, or even one that is not so new, please go and say hello.

Thanks should go to John Frater who has championed the day - and also a new event planned for next term where those finishing their DPhils can present their work to the building and we can all celebrate their success. Also major thanks to Suki and Kate, who are putting in the effort in running the building smoothly through all the recent changes and organised (and paid for) today. Finally, a big hand for Rebecca who is juggling the new liquid nitrogen tanks, new autoclaves and the HSE inspection.

If anybody has any ideas for next year's event, or for other community events at the Medawar please come and find me or one of the other group leaders. (In particular I would like to extend the film poster display, so I need more suggestions).

Meanwhile enjoy the talks - and everybody should feel free – in fact actively encouraged - to ask questions and join in the discussion.

Best wishes

Paul Klenerman

Medawar Day
4 October 2018
Principal Investigators

Proochista Ariana

Ellie Barnes

Susanna Dunachie

Lynn Dustin

Mike English

Nuno Faria

John Frater

Philip Goulder

Sunetra Gupta

Aris Katzourakis

Paul Klenerman

Martin Maiden

Kevin Marsh

Vicki Marsh

Philippa Matthews

Angel McLean

Oliver Pybus

Peter Simmonds

Adrian Smith

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Programme

Main talks: 20 minutes plus 5 minutes for questions
Rapid fire: 5 minutes, 5 slides plus 3 minutes for questions

9.30 – 9.45 Introduction and Overview of the Year – Paul Klenerman

9.45 – 11.00 NDM session

9.45 – 10.10 Peter Simmonds
10.10 – 10.35 Rapid Fire:
Tianqi Leng
Jolynne Mokaya
Lucia Parolini
10.35 – 11.00 Lynn Dustin

11.00 – 11.30 Coffee

11.30 – 12.00 Gavin Screaton; Head, Division of Medicine

12.00 – 1.15 Zoology session

12.00 – 12.25 Nuno Faria
12.25 – 12.50 Rapid Fire:
Bernardo Gutierrez
Emilia Skirmuntt
Marianne Clemence
12.50 – 1.15 Jose Lourenco

1.15 – 2.15 Lunch

2.15 – 2.45 "You couldn't make it up" – When Science meets panel games

2.45 – 4.00 Tropical Medicine session

2.45 – 3.10 Mike English
3.10 – 3.35 Rapid Fire:
Rabbi Chowdhury
Tim Tuti
Christiane Hagel
3.35 – 4.00 Jake McKnight

4.00 Summary and close – Paul Klenerman

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Guest Speaker

Professor Gavin Screaton

Bio: Professor Screaton received his first degree from Cambridge in 1984 before moving to Oxford to complete his medical studies in 1987. He then completed training in general internal medicine and obtained a DPhil from Oxford University in 1998. In 2004, Professor Screaton was appointed to the Chair of Medicine at Hammersmith Hospital, Imperial College and became Dean of the Faculty of Medicine in 2015. He returned to Oxford as Head of the Medical Sciences Division in October 2017.

His research, which has been supported by a series of Fellowships awarded by the MRC and Wellcome Trust, has covered a variety of topics from control of RNA processing and apoptosis to immunology. The current interests of his laboratory revolve around the immunology of infectious diseases with a special interest in dengue haemorrhagic fever and Zika, where his research is currently funded by the Wellcome Trust, with active research collaborations in South-East Asia.

Professor Screaton is a Fellow of the Academy of Medical Sciences, a Fellow of the Royal College of Physicians, and was made a Founder Senior Investigator in the National Institute for Health Research. He is a member of the MRC Strategy Board and is also a Non-Executive Director of Oxford University Hospitals NHS Foundation Trust.

Title: Human antibody responses in dengue and Zika virus infections

Abstract: Dengue is a mosquito borne virus infection occurring in tropical and subtropical countries. There are estimated to be around 400 million infections annually of which approximately one quarter are clinically apparent. The majority of these result in a self-limited, but non the less unpleasant febrile illness, dengue fever. 1-5% of infections lead to a more severe disease, dengue haemorrhagic fever, which is characterized by a severe vascular leak, hypovolaemia and in extreme cases shock and haemorrhage. Dengue exists as four highly divergent serotypes differing in sequence by some 30-35%; infection with one serotype does not provide protection against the other three. In endemic areas serotypes frequently co-circulate and repeat infections are common. Interestingly, severe disease is much more common in secondary as opposed to primary infections, implying a role of the acquired immune system in disease pathogenesis. Understanding this immune enhancement of disease is crucial for the design of safe and effective vaccines. Through clinical collaborations in Thailand and Vietnam we have been studying the immune response to dengue in cohorts of infected children. We will describe the antibody response to the two virion surface glycoproteins prM and E and discuss the E dimer epitope (EDE), a novel site bridging the 90 basic head to tail envelope dimers making up the virion surface and also crossreacts against Zika virus.

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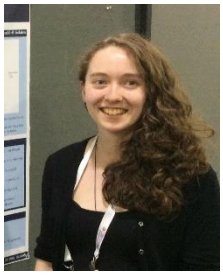
Speakers

Fazle Chowdhury

Bio: Fazle did his MSc. in Tropical and Infectious diseases from the Liverpool School of Tropical Medicine in 2009. He was a Consultant, Internal Medicine in Bangladesh before starting his D.Phil. in Oxford and was recently promoted to Assistant Professor.

Title: Is melioidosis a significant cause of acute febrile illness in Bangladesh?

Abstract: We conducted a prospective clinical study of the aetiology of fever in adult patients admitted with fever to two hospitals in Bangladesh. 210 patients were recruited, and 28 (13%) had positive bacterial cultures. We found melioidosis to be the commonest cause of bacteraemia in Dhaka, with high rates of antimicrobial resistance for other Gram-negative infections.



Marianne Clemence

Bio: Marianne is a final year DPhil student in Martin Maiden's lab. As a student on the Infection, Immunology and Translational Medicine doctoral training programme, Marianne had the opportunity to rotate through three projects in microbiology and molecular immunology before embarking on her DPhil project.

Title: Characterisation of capsule genes in *Neisseria*

Abstract: The variant of capsule – if any – expressed by *Neisseria meningitidis* (the meningococcus) plays a role in determining whether this “accidental” pathogen causes invasive meningococcal disease. In this project, the capsule is characterised in non-pathogenic *Neisseria*, and models of its acquisition in the potentially pathogenic meningococcus are re-examined.

Lynn Dustin

Bio: Lynn, a native of New York City, earned her PhD in Immunology at Harvard Medical School. She was a faculty member at Saint Louis University School of Medicine and then at The Rockefeller University before moving to Oxford in 2013.

Title: Antibodies in infectious and autoimmune diseases

Abstract: We study the roles of antibodies and antibody-producing B cells in infection and autoimmunity, and how responses to pathogens may contribute to autoimmune disease.

Mike English

Bio: Mike trained as a General Paediatrician in the UK but has worked in Kenya for over 20 years supported by a series of Wellcome Trust research fellowships. Mike’s team uses a range of methodologies in research aimed at improving hospital care for children and newborns. A major current project involves a 14 hospital clinical network using detailed information on all paediatric more recently neonatal admissions as part of a formative learning system strategy. Mike also leads the Oxford Health Systems Research Collaboration (OHSCAR) within CTM&GH and in the Medawar Building.

Abstract: Mike will provide an outline of the type of health services work being conducted by the OHSCAR team that is predominantly conducted in collaboration with Kenya and in the fields of neonatal and child health services provided by public hospitals.

Nuno Faria

Bio: Nuno is a Sir Henry Dale Fellow working on the integration of real-time genomic and epidemiological data from viral epidemics. He is particularly interested in understanding what drives the ignition and the sustained spread of emergent infectious diseases, such as Zika, yellow fever, Ebola and HIV/AIDS.

Title: From Zika to yellow fever: towards real-time tracking of virus outbreaks across corridors of mobility and ecological suitability

Abstract: This talk will focus on the integration of epidemiological, spatial and genomic data to monitor transmission of mosquito-borne viruses across corridors of mobility and ecological suitability.

Bernardo Gutierrez

Bio: BSc Biotechnology, USFQ; MSc Evolutionary Genetics, University of Edinburgh. Bernardo is a first year DPhil student at the EvolveZoo group, interested in combining phylogenetic methods with other sources of information to understand zoonotic events in emerging viruses.

Title: The evolution of a neglected Bunyavirus in South America

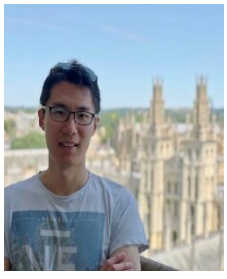
Abstract: Febrile illnesses are common in human populations surrounding the Amazon basin in South America, where the causative agent is never identified in a considerable portion of the cases. We performed a comprehensive analysis of the evolution of Oropouche Virus (OROV), and overlooked Orthobunyavirus responsible for periodic outbreaks in the region in the past 50 years.

Christiane Hagel

Bio: Christiane has recently joined the Oxford Health Systems Collaboration (OHSCAR) team at the Centre for Tropical Medicine and Global Health in the Nuffield Department of Medicine, at the University of Oxford. She holds a Master's degree in Public Health from the Charité – Universitätsmedizin Berlin, Berlin School of Public Health and focussed mainly on infectious diseases and global health. Prior to that she studied Law, specialising in medical criminal law with a particular focus on ethical questions concerning patient consent. During her last position as a scientific consultant at a non-profit health informatics research organisation in Berlin, she advised registries for health services on data quality and how to employ IT solutions adequately. In her spare time, she is actively involved with a fundraising initiative for an orphanage in Bamako, Mali.

Title: Health Information Systems in LMICs

Abstract: District Health Information Software (DHIS2) is an open source health information system used in low- and middle-income countries (LMICs). The system is widely used for collecting aggregated health data but several recent analyses have shown that the quality of data in DHIS2 implementations is reported as being very poor. Kenya was one of the first countries that deployed DHIS2, but in-patient and hospital mortality data are still mostly unreported by Kenyan health facilities. Therefore, our objectives are to assess the current information management process in Kenyan neonatal wards where DHIS2 is used, to find out where the system is currently failing, and to investigate how in-patient data record systems can be developed that can report hospital mortality accurately across the country.



Tianqi Leng

Bio: Tianqi is a final-year DPhil student working with Paul and Chris in the medawar building. He focuses on T cell immunology and inflammatory bowel diseases. In his spare time he enjoys badminton, and maintains strong interest in aviation, classical music, and travelling.

Abstract: Human mucosal associate invariant T (MAIT) cells are a subset of innate-like pro-inflammatory T cells that possess cytotoxic capacity. This talk

discusses differential roles of TCR/MR1-dependent and -independent signals in MAIT cell activation, and how they may integrate and shape specific effector functions of MAIT cells in vitro.

Jose Lourenco

Bio: José is the Research Lecturer in Infectious Disease of the Department of Zoology. He works in the field of Computational Epidemiology (CE) developing dynamic models and bioinformatic tools, which he applies to a variety of pathogens such as FluA, HBV, DENV, ZIKV, HIV and the pneumococcus. José has a BSc in Software Engineering from Instituto Superior Técnico (Portugal) but has always worked in CE, having a DPhil in Zoology (really CE) from the University of Oxford.

Title: The role of HBV vaccination and prevention of mother to child transmission as tools for elimination in the presence of HIV.

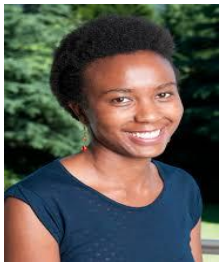
Abstract: Sustainable Development Goals (SDGs) have been set for elimination of HBV as a public health concern by 2030, for which vaccination and prevention of mother to child transmission are the most commonly used interventions (MCUI). There is lack of support for MCUIs in achieving SDGs from modelling studies, in particular in the context of HIV infection. I will present the output of a dynamic model informed by a paediatric cohort in South Africa. Results suggest that while MCUI can have significant positive impact on transmission with little interference from HIV infection, SDGs are very unlikely to be achieved in time due to the particular epidemiology of HBV.

Jake McNight

Bio: Jake has worked with the Oxford Health Systems Collaboration (OHSCAR) team at the Centre for Tropical Medicine and Global Health in the Nuffield Department of Medicine, for 4 years. Prior to that, he was CEO of a company called Altitude Medical which created and manufactured a door handle that cleans hands and records rates of hand sanitisation. His other work concentrates on anti-microbial resistance and neonatal care in Kenyan hospitals.

Title: A TripAdvisor for Kenya's Medical Laboratories.

Abstract: Lab-based diagnosis is an essential part of all effective healthcare systems. Unfortunately, labs in Kenya, particularly those in public hospitals, are beset by a number of issues which limit access to this essential service. Labs suffer from supply chain issues, staffing supply problems, technician 'moonlighting' that undermines effort to improve services, and a general lack of funding and oversight. This results in a high number of errors in existing services but more importantly, means that most Kenyans proceed with medication and even surgery on the basis of a 'working diagnosis'. We are creating a smartphone app that allows Kenyans to find labs that offer high quality, affordable services that deliver dependable results when they need them. We believe that sharing more information about price, quality, availability and Turn Around Time (TAT) will allow patients to make better choices and in so doing, help regulate a dysfunctional market. This Gates funded project now has the backing of major collaborators in Kenya and will shortly enter the trial phase.



Jolynne Mokaya

Bio: Jolynne is a PhD student in a group led by Philippa Matthews. They work with collaborators based in UK, USA, South Africa and Uganda. Their research interest is in chronic hepatitis B virus infection with particular focus on populations in Africa.

Abstract: Hepatitis B virus (HBV) infection is a major public health problem that poses a challenge to the achievement of the 2030 elimination goal. We aim to identify viral and host factors that impact on the outcomes of chronic HBV infection, and explore interventions that improve prevention, diagnosis and treatment. Our goal is to contribute towards understanding the immuno-genetic influences that can inform improved HBV therapy and wider public health strategy for HBV elimination.

Lucia Parolini

Bio: Lucia is an experimental physicist in the field of soft matter physics. She obtained her degree in Physics from the Universita` degli Studi di Milano and her PhD from the University of Cambridge. She is now working as a postdoc in Prof. John Frater group applying microfluidics to the study of HIV infection.

Title: Droplet-based microfluidics for the study of rare cell populations

Abstract: The characterization of rare cell populations can be very challenging especially in the absence of known cell surface biomarkers. Droplet-based microfluidics offers a great platform to tackle this problem and in this talk I am going to present the methods we have developed to identify HIV infected cells with single-cell precision and separate them from the bulk for further analysis.

Peter Simmonds

Bio: Currently, Professor of Virology in the University of Oxford since 2016. Following graduation in Medicine Peter pursued postgraduate medical training (MRCPath 1995) and research in HIV pathogenesis and molecular epidemiology, evolution and variability in HCV. Recent research is focussed on evolutionarily based studies of virus/host interactions at the level of innate cell defences. Research has been funded by grants from the MRC, Wellcome Trust and other grant-giving bodies.

Title: Characterisation of cellular innate immune pathways restricting the replication of RNA viruses with high CpG and UpA dinucleotide frequencies.

Abstract: Double-stranded RNA is a potent trigger for innate immune pathways in a wide swathe of eukaryotes ranging from mammals to plants - such recognition pathways induces innate and inflammatory cellular responses that are critical for host defence against viral infections. Our research has discovered that other attributes of viral genomes, such as their dinucleotide composition and degree of RNA secondary structure folding in viral genomes may be similarly exploited by the cell as markers for self/non-self identification. The presentation will summarise current investigations of the role of zinc antiviral protein (ZAP) in RNA recognition and restriction of virus replication and new data on the potential existence of parallel response pathways in plants. Plant viruses show comparable restrictions in CpG and UpA frequencies of mammalian viruses and remarkably, artificially increasing frequencies severely attenuates replication and systemic spread of potato virus Y in tobacco plants.

Emilia Skirmuntt

Bio: Emilia started her DPhil in 2015 with Aris Katzourakis looking at endogenous viruses in bats, genome evolution and host-virus interactions. Their work was mostly bioinformatics based until the last year when they started lab work on bat immune receptors together with Adrian Smith group.

Title: Endogenous viruses of bats and their potential contribution to the immune response

Abstract: Bats can be persistently infected with viruses while not showing any symptoms of disease. It has been suggested that the lack of symptoms of viral infections and low mortality rate in bats, might be caused by their long-term co-evolution with viruses, while some of these might be caused by EVEs (endogenous virus elements) with an EDI (EVE- derived immunity) functions.

Timothy Tuti

Bio: Timothy is an informatics researcher with a focus on health systems research in LMICs. He holds a master's degree in Social Research Methods and Statistics and is currently pursuing doctoral studies in the area of Learning and New Technologies at the University of Oxford. Previously, he held a Wellcome Trust research fellowship with the Health Services Research Group (KEMRI-Wellcome Trust Research Programme), where his work looked into the potential role and acceptability of

performance dashboards as part of clinical quality improvement and audit cycles, with consideration of how they might be designed to meet user needs in the organisational context of clinical practice in Kenyan district hospitals. Currently, his research is exploring the potential for using VR using mobile platforms utilizing serious gaming strategies to provide initial and continuing training to health workers in Sub-Saharan Africa (SSA).

Title: Serious gaming in health: a theory-informed adaptive learning approach to clinical training in the Global South

Abstract: The aim of this research is to explore how data-driven approaches in game-based learning environments might be configured to support and improve personalised scaffolded learning for medical training within low resource settings using self-regulated learning theories. Additionally, by recognising mobile technologies' possible facilitation of medical education, this research seeks to examine how a contextual model of self-regulated mobile learning in healthcare, which is relevant to low-resource settings, might be implemented and scaled up.

About the Peter Medawar Building for Pathogen Research

The PMB is a cross-divisional, multi-disciplinary building focused on research in host-pathogen interactions. Established for nearly 2 decades now it has developed and strengthened over time through a strong sense of combined purpose and a collaborative ethos. There are 3 major strands to the work which are closely integrated:

Pathogen biology. This includes studies of major microbial pathogens with a focus on persistent viruses and invasive bacteria. The work extends from single cell studies to global molecular epidemiology, taking advantage of high throughput sequencing approaches to understand the evolution of pathogens within and between hosts.

Host immune responses. This includes a focus on successful control of pathogens with implications for vaccine development, as well as defining critical mechanisms for pathogen escape. Much of the work has focused on T cell responses and protective memory, including pediatric responses and unconventional T cell populations.

Mathematical biology. This includes development of approaches to understand host-pathogen interactions within host and at the population level. The integration of statistical modelling with sequence evolution and host immunology has been very powerful in shedding light on pathogen history and developing models for future epidemic behaviours, from HIV to Zika.

The shared endeavour across these three strands is to make quantitative descriptions of the processes that generate observed patterns in host-pathogen interactions. Different research groups bring different techniques to that endeavour, but there is a clearly articulated and well-understood shared goal. With an understanding of underlying processes in place it becomes possible to make precise hypotheses about the likely outcome of potential interventions. Close links between theory and observation allow those hypotheses to be tested.

Our aim is to strengthen the interactions in this area which have increasing potential because of the new technologies which allow better insights into host immunity coupled with increasing sequencing power and improved insights through integrative models. On a practical level this is fostered by well-equipped and technically secure category 3 space for pathogen research, shared office space and interaction areas, and core facilities which encourage and sustain group working. It will also benefit from close links with the new Tinbergen replacement and will enhance the ability of all groups in the area to work on major pathogens through improved access.