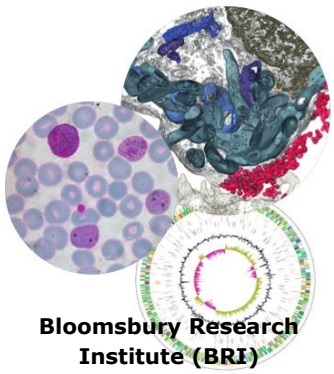

Bloomsbury Research Institute (BRI)

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Department of Pathogen Molecular Biology

Brochure

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Contents

Mission statements

London School of Hygiene and Tropical Medicine

The mission of the LSHTM is to contribute to the improvement of health worldwide through the pursuit of excellence in research, postgraduate teaching and advanced training in national and international public health and tropical medicine, and through informing policy and practice in these areas. The LSHTM was rated second among UK institutions for research excellent in the 2008 Research Assessment Exercise. Leading researchers have backgrounds in public health medicine, epidemiology, clinical medicine, infectious diseases, chemotherapy, biochemistry, immunology, genetics, molecular biology, entomology, statistics, demography, health economics, public health engineering, medical anthropology, health promotion, and health policy.

Faculty of Infectious and Tropical Diseases (ITD)

ITD encompasses all of the laboratory-based research in the School as well as that on the clinical and public health aspects of infectious and tropical diseases. The range of disciplines represented in the Faculty is broad and inter-disciplinary research is a feature of much of our activity. The spectrum of diseases studied is wide and there are major research groups with a focus on malaria, tuberculosis, HIV/AIDS and other sexually transmitted diseases, vaccine development and evaluation, vector biology and disease control. The Faculty is organized into four Departments comprising: Disease Control, Clinical Research, Infections and Immunology and Pathogen Molecular Biology. There is close interaction between scientists in different departments. The Faculty has strong overseas links, which provide a basis for field studies and international collaborations in developed and developing countries.

Department of Pathogen Molecular Biology (PMB)

Research in PMB focuses on the molecular biology and genetics of pathogens and their hosts in the context of improving the understanding and control of infectious diseases. Aspects of pathogen biology of interest include: (i) determining the mechanisms of infection of globally important viral, bacterial and parasitic pathogens, (ii) studying immune evasion mechanisms of particular disease agents, (iii) deciphering the genetic

diversity of pathogens in natural populations, (iv) exploiting parasitic, bacterial and viral pathogens as model biological systems and (v) developing practical applications including improved diagnostics, antimicrobials and vaccines. PMB currently investigates, amongst others, malaria (*Plasmodium* spp), Chagas disease (*Trypanosoma cruzi*), African sleeping sickness (*Trypanosoma brucei*), amoebic dysentery (*Entamoeba*), the *Leishmania* species, bacterial food borne pathogens (*Campylobacter jejuni* and *Yersinia enterocolitica*), gastric ulcers/cancer (*Helicobacter pylori*), pseudomembranous colitis (*Clostridium difficile*), plague (*Yersinia pestis*), paddy field melioidosis (*Burkholderia pseudomallei*), tuberculosis (*Mycobacterium tuberculosis*), pneumonia (*Streptococcus pneumoniae*), bluetongue viral disease of livestock, herpesviridae, and the enteric rotavirus that cause significant diarrhoeal disease in infants developing countries.

The long-term aim of PMB research is to gain a fully rounded understanding of the complex and dynamic ways by which pathogens modulate virulence and interact with the human/animal host. Such a holistic approach will vastly increase the scope for the rational design of long-term intervention strategies to reduce the burden of infectious diseases.

In recent years such a mission has been significantly enhanced by the availability of whole genome sequences. The interpretation and exploitation of this basic information is the platform for numerous new avenues of research on pathogenesis, epidemiology and the evolution of virulence.

The genome sequencing facility, bioinformatic suite and protein expression laboratory have greatly expedited genome data mining, population genetics, mathematical modeling, phylogenetic and transcriptome analyses. One example of the application of this technology has been the development of “comparative phylogenomics” for the whole genome comparison of pathogens coupled with Bayesian-based algorithms to model phylogeny. This method has identified previously hidden population structures and has expedited the identification of novel virulence factors and has now been applied to several pathogens. Other recent research areas include a project to optimize the expression of multiprotein complexes using the baculovirus system. This project will have broad applicability to a range of pathogens, and will support the current

international lead the Department has in the area of safe multiprotein particulate vaccines against viral diseases. In the longer term out research will help to translate the research expertise that we have in pathogen genomics into practical applications and will facilitate research on the structural analysis of virulence determinants and the development of vaccines and antimicrobial agents.

Collaborations

A distinctive feature of PMB is the large number of long term collaborations that we have with scientists from around the globe, particularly in disease endemic countries. Members of the Department frequently visit overseas research sites, including those in Africa, South America and South East Asia. This international dimension allows us to benefit from the wide range of specialist expertise available in these regions and provides ready access to the biological samples that underpin our research effort. Members of the Department in turn, frequently host academics and students on research visits to London as an integral part of these collaborations.

PMB has also played a major role in helping to establish strategic partnerships between LSHTM and other major UK research institutions. This includes a more formal alliance with the Wellcome Trust Sanger Institute, which builds on the large number of joint projects in which we already participate. An important new initiative has been the formation of the Bloomsbury Research Institute (BRI), launched in November 2011. This venture between University College London (Division of Infection and Immunity) and the LSHTM will involve more than 70 principal investigators who between them have attracted research income in excess of £100M over the past four years. The BRI will bring together basic science, translational studies and clinical expertise from across both institutions and their associated hospitals, to provide an optimal environment to develop new drugs, vaccines and diagnostics. Researchers from PMB have a central role in promoting the success of this new initiative.

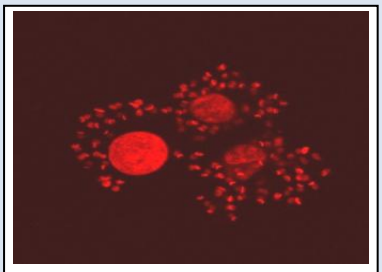
More details of PMB can be found on www.lshtm.ac.uk/itd/pmbd/

Head of Department

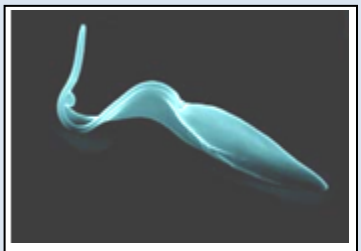
John Kelly

Professor of Molecular Biology

The parasitic protozoa *Trypanosoma cruzi* and *Trypanosoma brucei* are responsible for two major tropical infections, Chagas disease and African trypanosomiasis, respectively. These diseases represent a major public health problem in regions of the world least able to deal with the associated economic burden. Advances by ourselves, and others have led to the development of a wide range of genetic tools that can be used to address fundamental biological questions associated with these important pathogens. In addition, the completion of the trypanosomatid genome projects, together with major advances in imaging technology, is providing a research framework where rapid progress can be expected. We are exploiting these new approaches and opportunities to gain greater understanding of the mechanisms of drug action and resistance, disease pathogenesis and genome inheritance. In collaboration with biologists, biochemists and organic chemists, we have validated a number of parasite drug targets and identified several lead compounds that show promise in terms of therapeutic development. This multidisciplinary approach, which brings together of both academic and industrial partners, is now widely seen as the way ahead to provide better treatments for these previously 'Neglected Diseases'.



T. cruzi **replicating amastigote forms (red dots) inside infected mammalian cells.**



T. cruzi **insect stage epimastigote form.**

Selected publications

1. **Evidence that transport of iron from the lysosome to the cytosol in African trypanosomes is mediated by a mucolipin orthologue.** Taylor M, *et al. Molecular Microbiology*. 2013.
2. **Benznidazole-resistance in *Trypanosoma cruzi* is a readily acquired trait that can arise independently in a single population.** Mejia A, *et al. J. Infectious Diseases.* 2012.
3. **Centromere-associated repeat arrays on *Trypanosoma brucei* chromosomes are much more extensive than predicted.** Echeverry M, *et al. BMC Genomics* 2012.
4. **Centromere-associated topoisomerase activity in bloodstream form *Trypanosoma brucei*.** Obado S, *et al. Nucleic Acids Res*. 2011.
5. **Novel lipophilic acetohydroxamic acid derivatives based on conformationally constrained spiro carbocyclic 2,6-diketopiperazine scaffolds with potent trypanocidal activity.** Fytas C, *et al. J. Med. Chem.* 2011.

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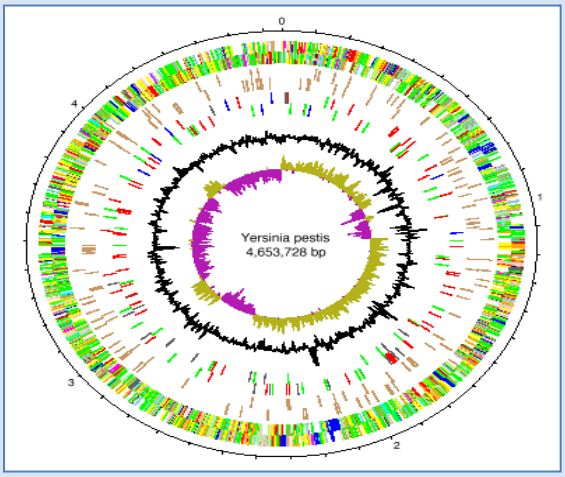
Brendan Wren

Professor of Microbial Pathogenesis

Professor Wren joined the School with his research team in July 1999. His research interests include determining the genetic basis by which bacterial pathogens cause disease. Research on individual pathogens include; *Clostridium difficile*, *Campylobacter jejuni*, *Helicobacter pylori*, *Burkholderia pseudomallei*, *Streptococcus pneumonia* and the enteropathogenic *Yersinia*. The research group currently exploits a range of post genome research strategies to gain a comprehensive understanding of how these pathogens function, how they evolve and how they interact with their respective hosts.

Current research focuses on:

1. Glycosylation in bacterial pathogens and their application in glycoengineering and novel vaccine design
2. Comparative phylogenomics and the evolution of bacterial virulence.
3. Systems biology of host pathogen interactions.



Circular representation of the plague genome

Selected publications

1. **Emergence and global spread of epidemic healthcare-associated *Clostridium difficile*..** He M., *et al. Nat Genet*. 2013.
2. **Exploitation of bacterial *N*-linked glycosylation to develop a novel recombinant glycoconjugate vaccine against *Francisella tularensis*.** Cuccui J, *et al. Open Biol.* 2013.
3. **Comparative genome and phenotypic analysis of *Clostridium difficile* 027 strains provides insight into the evolution of a hypervirulent bacterium.** Stabler R, *et al. Genome Biol.* 2009.
4. **Bacterial pathogenomics.** Pallen M & Wren B. *Nature*. 2007.
5. **Comparative phylogenomics of the food-borne pathogen *Campylobacter jejuni* reveals genetic markers predictive of infection source.** Champion O, *et al. Proc Natl Acad Sci*. 2005.

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Michael Miles

Professor of Medical Protozoology

Professor Miles's research is primarily focused on *Trypanosoma cruzi*, the agent of Chagas disease (South American trypanosomiasis) and on *Leishmania* species, the agents of visceral (VL) and mucocutaneous leishmaniasis (MCL), encompassing fundamental laboratory research and fieldwork in endemic areas. Principal research interests are the presence, importance and mechanisms of genetic exchange in experimental and natural populations of these organisms, and the molecular epidemiology of Chagas disease and the leishmaniases in the context of improvement of control strategies. Other interests are comparative genomics, diagnostics development, the ecology and population genetics of triatomine bugs, the ecology and behaviour of South American mammals, and the control of African trypanosomiasis. Recent achievements of the research group include the first experimental proof of genetic exchange in *T. cruzi*; demonstration that sylvatic *Rhodnius prolixus* does invade houses in Venezuela, and several detailed population genetics studies of natural populations of *T. cruzi* using multilocus sequence typing (MLST) and microsatellite analysis (MLMT). Coordinator, of the European/Latin American FP6 network (LeishEpiNetSA), 12 partners, to 2010 - Coordinator (assisted by Martin Llewellyn), of the European/Latin American FP7 network (ChagasEpiNet), 15 partners, to 2012.

Selected publications

1. **Shotgun sequencing analysis of *Trypanosoma cruzi* I Sylvio X10/1 and comparison with T. cruzi VI CL Brener.** Franzen O, *et al. PLoS Negl Trop Dis* 5. e984. 2011.
2. **Recent, independent and anthropogenic origins of *Trypanosoma cruzi* hybrids.** Lewis MD, *et al. PLoS Negl Trop Dis 5, e1363.* 2011.
3. **Visualisation of *Leishmania donovani* fluorescent hybrids during early stage development in the sand fly vector.** Sadlova J, *et al. PLoS ONE 6, e19851.* 2011.
4. **Multilocus sequence typing (MLST) for lineage assignment and high resolution diversity studies in *Trypanosoma cruzi*.** Yeo M, *et al. PLoS Negl Trop Dis 5, e1049.* 2011.
5. **Analysis of molecular diversity of the *Trypanosoma cruzi* trypomastigote small surface antigen reveals novel epitopes, evidence of positive selection and potential implications for lineage-specific serology.** *Bhattacharyya T. et al. Int J Parasitol 40, 921-928.* 2010.

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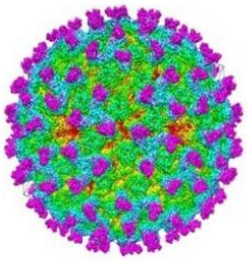
Polly Roy

Professor of Virology

Professor Roy's salient contribution has been the first complete molecular understanding of Orbiviruses, of the *Reoviridae* family, a distinct group of several hundred viruses of serious health and economic impact. Prof Roy used several groundbreaking techniques and multi-disciplinary approaches to provide a detailed understanding of Bluetongue virus (BTV), a major orbivirus pathogen and model for a range of human and animal viruses with similar structure, including human rotavirus. Prof Roy has examined each aspect of the virus, from individual virus proteins to assembly of the complete virus particle and its engagement, at various levels, with the host cell. Her contribution to virology, in particular to virus structure and assembly, has been recognised by her peers worldwide. Indeed BTV is now one of the most well understood viruses and Roy's name is synonymous with it. Her pioneering work on simultaneous expression of several recombinant viral proteins led to the assembly of virus-like particles (VLPs) that have since been applied to many other viruses and vaccine development (e.g. Papillomavirus). The development of a BTV VLP vaccine has been successfully transferred to a vaccine manufacturing company. Other recent ground breaking advances have been the first reverse genetics (RG) system for BTV (the synthesis of infectious virus solely from synthetic genes) and the establishment of an outstanding cell-free system to reconstitute infectious BTV particles, a first in the field. Both technologies have the potential for designing highly efficacious vaccines.



Three-dimensional structure of BTV particle reveals the outer capsid protein VP2 trimers (purple and cyan blue) protrude on the surface to facilitate cell surface receptor binding

Selected publications

1. **Rotavirus mRNAS are released by transcript-specific channels in the double-layered viral capsid.** Periz J, *et al*. *Proc Natl Acad Sci USA*. 2013.
2. ***In vitro* reconstitution of Bluetongue virus Infectious cores.** Lourenco S & Roy P. *Proc Natl Acad Sci USA*. 2011.
3. **Generation of replication-defective virus-based vaccines that confer full protection in sheep against virulent BTV challenge.** Matsuo E, *et al. J Virol*. 2011.
4. **Bluetongue virus coat protein VP2 contains sialic acid-binding domains, and VP5 resembles enveloped virus fusion proteins.** Zhang X, *et al*. *Proc Natl Acad Sci USA*. 2010.
5. **A viral nonstructural protein regulates bluetongue virus trafficking and release.** Celma CC & Roy P. *J Virol*. 2009.

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David Conway

Professor of Biology

Malaria parasites adapt well to diverse and changing environments. Gaining a detailed knowledge of mechanisms of selection operating on parasites in natural populations and in laboratory culture helps guide development of new interventions as well as use of existing ones. For example, extracellular merozoites in the blood use a range of different receptors to invade erythrocytes and present many alternative antigenic phenotypes to the host immune system. Prof Conway's research group wants to understand how enough of them survive and reproduce in the face of acquired immunity, and how future interventions such as blood stage vaccines might impact on them sufficiently to better control malaria. Use of statistical signatures of natural selection from population genetic analyses, now being conducted at the whole genome scale, enables focused investigation on particular genes and their products. The relevance of candidate parasite proteins and their variants as targets of acquired immunity in humans is studied by correlation of invasion phenotypes and immune responses with risk of clinical malaria. The focus is mostly on *Plasmodium falciparum* in several African populations with diverse endemicity and levels of immunity, ranging from dry Sahel areas with limited seasonal transmission through to forested areas with more constant high transmission. This enables comparisons of results across populations in order to test and refine hypotheses, and improve design of experiments to validate molecular targets and mechanisms. For five years until 2010 Prof Conway headed the Malaria Research Programme at the MRC Laboratories in The Gambia, leading a broader programme of work including epidemiology, diagnostics, entomology and immunology. He also continues to collaborate on molecular epidemiology of *Plasmodium knowlesi* in Southeast Asia, and has previously conducted research on trachoma and intestinal nematode infections.

Selected publications

1. ***Plasmodium knowlesi*: reservoir hosts and tracking the emergence in humans and macaques.** Lee K, *et al*. *PLoS Pathog*. 2011
2. **Erythrocyte invasion and merozoite ligand gene expression in severe and mild *Plasmodium falciparum* malaria.** Gomez-Escobar N, *et al*. *J Infect Dis*. 2010.
3. **Allele frequency-based and polymorphism-versus-divergence indices of balancing selection in a new filtered set of polymorphic genes in *Plasmodium falciparum*.** Ochola L, *et al. Mol Biol Evol*. 2010.
4. **Detecting signatures of balancing selection to identify targets of anti-parasite immunity.** Weedall GD & Conway DJ. *Trends in Parasitology*. 2010.
5. **Gene copy number variation throughout the *Plasmodium falciparum* genome.** Cheeseman IH, *et al. BMC Genomics*. 2009.

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Martin Hibberd

Professor of Emerging Infectious Diseases

Since the emerging infectious disease SARS outbreak in 2003, it has become clear that genomic and holistic approaches to infectious diseases can give rapid tools for public health impact. These hypothesis generating, data directed approaches can give novel and sometimes unexpected insights into the disease; that may be turned into diagnostics (my research on SARS lead to the Roche diagnostic kit), prognostics and therapeutic targets. Utilizing human population diversity to understand host-pathogen interactions, such as in Dengue (figure 1) has revealed specific disease control mechanisms. While looking at the host response to infection on a global scale can identify the rapid temporal changes and the critical points in the disease (figure 2). Whole genome pathogen investigations complete this molecular picture and inform on the transmission process. Genomic hypotheses require molecular confirmation; in figure 3, macrophage cells are responding to TB infection with distinct TLR proteins identified from genetically susceptible TB patients. Combining these approaches can lead to strong insights and accurate models of the disease process that can be used to identify novel intervention strategies. Using both pathogen and host diversity is also key to understanding the dynamic process of molecular interaction, that is now known to be modified by other infectious agents, or through an interaction with commensal communities.

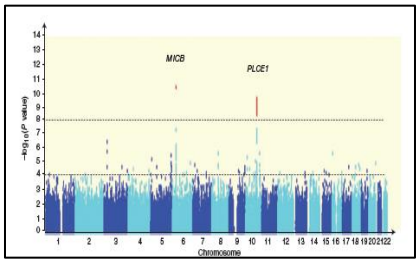

Fig 1. A "Manhattan" plot from a dengue GWAS identifies two novel loci.

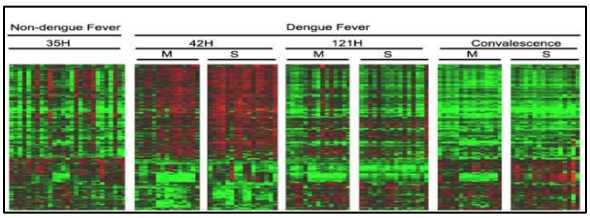

Fig 2. A microarray expression profile of dengue patients identifies novel processes that occur before disease onset.

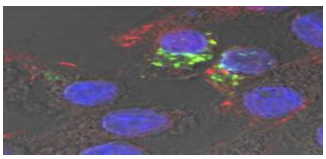

Fig 3. Natural polymorphism in the TLR gene leads to different macrophage trafficking of the protein (red & green).

Selected publications

1. **Reduction of HBV replication prolongs the early immunological response to IFNα therapy.** Tan AT, *et al. J Hepatol.* 2013.
2. **Inhibition of Megakaryocyte Development in the Bone Marrow Underlies Dengue Virus-induced Thrombocytopenia in Humanized Mice.** Sridharan A, *et al. J Virol*. 2013
3. **Exploring the mode of action of bioactive compounds by microfluidic transcriptional profiling in mycobacteria.** Murima P, *et al. PLoS One*. 2013
4. **Microbial genomics: an increasingly revealing interface in human health and disease.** Hibberd ML. *Genome Med*. 2013.
5. **Pathogen chip for respiratory tract infections.** Simões EA, *et al. J Clin Microbiol*. 2013

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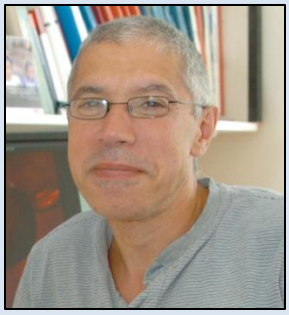
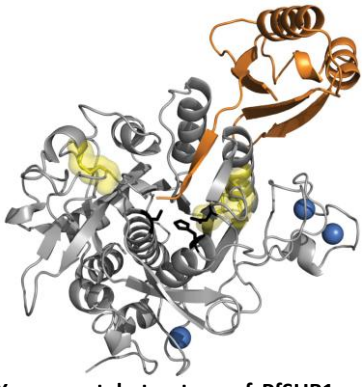
Mike Blackman

Professor of Molecular Parasitology



Malaria is directly responsible for an estimated 2-3 million deaths per annum worldwide, causing terrible suffering and imposing an immense economic burden on the developing world. There is no malaria vaccine, and resistance against antimalarial drugs is widespread. There is a need to find new ways to treat and control this devastating disease. Malaria parasites infect and grow within red blood cells, replicating asexually within a membrane-bound parasitophorous vacuole. During egress, the vacuole and host cell membranes eventually rupture to release merozoites which invade new cells, disseminating the infection and leading to clinical disease. Prof Blackman's research focuses on the molecular mechanisms involved in invasion and egress by *Plasmodium falciparum*, the agent of the most dangerous form of malaria. His work aims to understand the molecular mechanisms by which the parasite enters and exits its host cell, and to dissect the structural changes that occur in the host erythrocyte and at the parasite surface during invasion and egress. A major aim is to translate this information into health benefits by seeking to identify drug-like inhibitors of enzymes and other parasite molecules involved in egress and invasion, and promote their development as potential antimalarial drugs. Prof Blackman's work also provided information on how to improve the design of much-needed malaria vaccines based on merozoite surface proteins.



X-ray crystal structure of PfSUB1, a protease with a central role in release of malaria parasites from

Selected publications

1. **Malaria parasite cGMP-dependent protein kinase regulates blood stage merozoite secretory organelle discharge and egress.** Collins CR, *et al. PLoS Pathogens*. 2013.
2. **Adaptation of the genetically tractable malaria pathogen *Plasmodium knowlesi* to continuous culture in human erythrocytes.** Moon RW, *et al. Proc Natl Acad Sci U S A*. 2013.
3. **Juxtamembrane shedding of *Plasmodium falciparum* AMA1 is sequence independent and essential, & helps evade invasion-inhibitory antibodies.** Olivieri A, *et al. PLoS Pathogens*. 2013
4. **Intramembrane cleavage of AMA1 triggers Toxoplasma to switch from an invasive to a replicative mode.** Santos JM, *et al. Science*. 2011.
5. **A multifunctional serine protease primes the malaria parasite for red blood cell invasion.** Koussis K, *et al. EMBO J*. 2009.

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Nick Thomson

Professor of Bacterial Genomics and Evolution

Nick Thomson holds a split academic position between the LSHTM and The Wellcome Trust Sanger Institute. During his career he has transitioned from a classically trained Molecular Biologist to a Genome Scientist using high throughput sequencing technologies. His current work involves the application of phylogeny to understand the contemporary or historical distribution of bacterial pathogens causing diarrheal disease, including *Shigella sonnei*, *Vibrio cholerae* and *Salmonella*. His work on cholera used modern techniques and genomic data to identify a global source for pandemic cholera. In addition his group has contributed to a 'One Health' look at the flow of antimicrobial resistance (AMR) and the zoonotic pathogen *Salmonella* Typhimurium DT104 by considering isolates from both humans and farm animals (Fig 1 & 2). He considers studies of this nature and resolution to be essential if we are to identify the sources and sinks of both food borne pathogens such as DT104 and AMR. AMR being one of the most important threats to public health. His groups work on *Chlamydia* showed that despite the pervasive notion that *Chlamydia* do not recombine, their genomes showed evidence of widespread DNA exchange between isolates affecting different body sites, challenging much of our understanding of *C. trachomatis* evolution and epidemiology. To facilitate this, his group has developed methods to sequence *Chlamydia* directly from uncultured discarded clinical swabs, a methodology with broad applications in clinical microbiology.

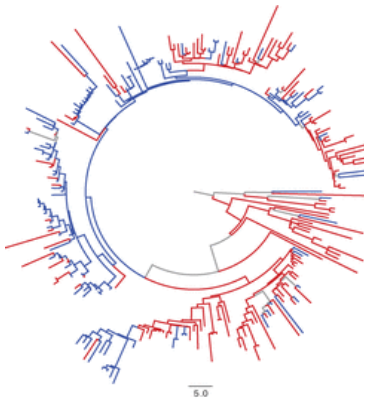

Figure 1. The phylogenetic relationships of DT104 strains found in animals and humans in Scotland over a 22 year period.

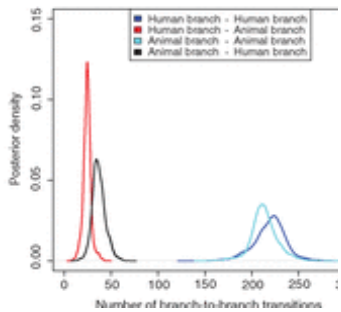

Figure 2. The number of transitions between animals and humans within the phylogeny.

Selected publications

1. **Immuno magnetic separation and multiple displacement amplification to generate whole bacterial genome sequences of low-abundant species directly from complex clinical samples.** Seth-Smith *et al. Nature Protocols*. 2013.
2. **Epidemics of the multidrug-resistant *Salmonella* Typhimurium DT104 in different hosts**. Mather AE, *et al. Science*. 2013.
3. ***Shigella sonnei* genome sequencing and phylogenetic analysis indicate recent global dissemination from Europe.** Holt K, *et al. Nature Genetics* 2012.
4. **Comprehensive whole genome analysis of Chlamydia trachomatis reveals the true underlying relationships masked by current clinical typing.** Harris et al. *Nature Genetics*. 2012.
5. **Evidence for multiple global transmission events within the seventh cholera pandemic.** Mutreja *et al. Nature*. 2011.

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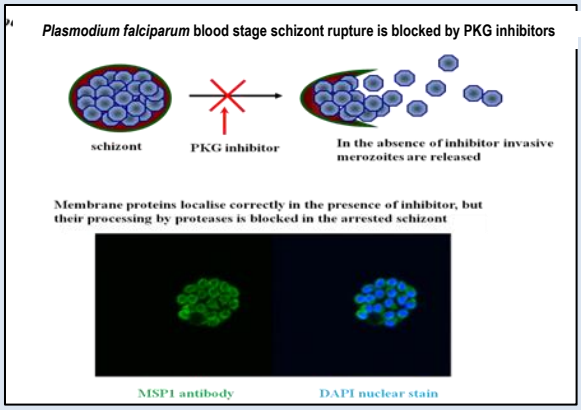
David Baker

Reader in Parasite Molecular Biology

David Baker's research group uses biochemical and genetic approaches to study the cyclic nucleotide signal transduction pathways of malaria parasites. The cyclic nucleotides cAMP and cGMP perform a spectrum of cellular functions in diverse organisms. Earlier work from other laboratories suggested that both of these second messenger molecules may play roles in malaria parasite differentiation. Our studies have focused on the cyclase enzymes that synthesise cyclic nucleotides, the phosphodiesterases that degrade them[1], but also on the protein kinase that is activated by cGMP (PKG). We have found that in the human malaria parasite *Plasmodium falciparum* cGMP and PKG play an essential role in triggering the formation of mature sexual parasite forms (gametogenesis) required to transmit disease to the mosquito vector[2]. We (with others) also showed that this pathway is important for the development of the ookinete form of the rodent malaria parasite *P. berghei* within the mosquito[3]. It is now becoming clear that cGMP signalling and the PKG enzyme are vital for multiple parasite stages, because using specific PKG inhibitors in conjunction with inhibitor-resistant transgenic parasites we have demonstrated that asexual blood stage schizogony cannot progress if this kinase is blocked[4]. Recently, with others we have shown that PKG functions upstream of a protease cascade and a calcium-dependent protein kinase (CDPK5) that are also required for asexual blood stage schizont rupture and merozoite egress[5]. Our current work aims to further understand the function of cyclic nucleotide signalling in malaria parasites, but also to exploit these pathways in the development of novel antimalarial drugs.



Selected publications

1. **Malaria parasite cGMP-dependent protein kinase regulates blood stage merozoite secretory organelle discharge and egress.** Collins C, *et al. PLoS Pathogens*. 2013.
2. **The role of cGMP signalling in regulating life cycle progression of Plasmodium.** Hopp C, Bowyer P, Baker D. *Microbes Infect.* 2012
3. **A plant-like kinase in Plasmodium falciparum regulates parasite egress from erythrocytes.** Dvorin J, *et al*. *Science*. 2010.
4. **A cyclic GMP signalling module that regulates gliding motility in a malaria parasite.** Moon R, *et al. PLoS Pathogens*. 2009.
5. **Gametogenesis in malaria parasites is mediated by the cGMP-dependent protein kinase.** McRobert L, *et al*. *PLoS Biology*. 2008.

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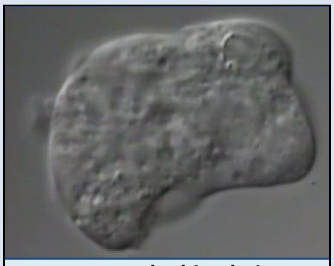
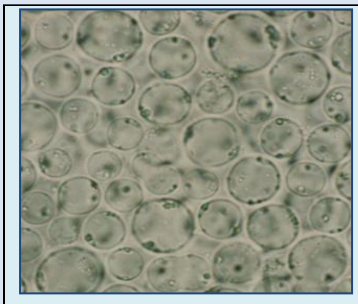
Graham Clark

Reader in Molecular Parasitology

Graham Clark's research is on the genetic diversity and evolution of gut protozoan parasites. The main organisms studied are *Entamoeba histolytica*, the agent of amoebic dysentery and amoebic liver abscesses, and *Blastocystis*, an organism of uncertain pathogenicity. In *Entamoeba*, recent work has focused on genome re-sequencing as a way to build on earlier results that indicated a parasite genetic component linked to the outcome of infection - people who develop disease are infected with a different range of genotypes from those who remain asymptomatic. The work on *Blastocystis* is focused on; 1) investigating whether any of the genetic subtypes detected in the organism are linked to the symptoms found in some individuals, and 2) sequencing its mitochondrial and nuclear genomes in an attempt to understand the function of the mitochondrion-like organelle in this strictly anaerobic organism.



Entamoeba histolytica



***Blastocystis* sp.**

The former study has indicated that in the UK one subtype is much more common in people with symptoms, suggesting that *Blastocystis* may indeed be responsible for disease in at least some cases, but also that there is significant geographic variation in the distribution of subtypes.

The diversity of *Entamoeba* and *Blastocystis* in non-human hosts is also being studied. The results indicate that our understanding of genetic diversity in these organisms is very incomplete.

Selected publications

1. **Recent developments in *Blastocystis* research.** Clark CG, *et al. Adv Parasitol* 2013
2. **Genetic diversity of *Blastocystis* in livestock and zoo animals**. Alfellani MA, *et al. Protist* 2013
3. **Genomic diversity of the human intestinal parasite *Entamoeba histolytica*.** Weedall GD, *et al. Genome Biol* 2012
4. **Levels of genetic diversity vary dramatically between *Blastocystis* subtypes.** Stensvold CR, *et al*. *Infect Genet Evol* 2012
5. **Increased sampling reveals novel lineages of *Entamoeba*: consequences of genetic diversity and host specificity for taxonomy and molecular detection.** Stensvold CR, *et al*. *Protist* 2011

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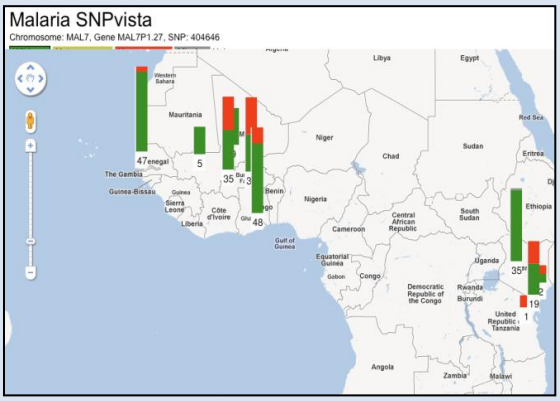
Taane Clark

Reader in Genetic Epidemiology and Statistical Genomics

Taane Clark joined the LSHTM in 2010 after holding senior statistician posts at the Wellcome Trust Centre for Human Genetics (Oxford) and Sanger Institute (WTSI). His research interests include the design and analysis of large-scale association studies of infectious diseases in humans and the investigation of genetic variation in pathogen populations (e.g. *Mycobacterium tuberculosis* (Mtb), *Plasmodium*) using high-throughput sequencing technologies. This research includes developing new tools to integrate genetic and important phenotypic information on maps (see figure), and developing analytical methods to identify loci associated with important disease phenotypes of host and pathogens (e.g. drug resistance). He has initiated global genetic diversity projects of pathogens including Mtb, and provides statistical and epidemiology support and training to research groups at the LSHTM and WTSI. He has established a short course in *Pathogen genomics & genomic epidemiology of infectious disease* (see photo for the inaugural course in 2011). Greater detail of Taane's research, including genomic resources, can be found online at *pathogenseq.lshtm.ac.uk.*



Selected publications

1. **VarB: A visualisation and analysis tool for polymorphisms derived from sequence data.** Preston M, *et al. Bioinformatics* 2012.
2. **ARC3: A genome-wide association study of the genetic basis of delayed parasite clearance following treatment with artemisinins**. Takala-Harrison S, Clark TG *et al. PNAS* 2012.
3. **Next-generation sequencing analysis of *Plasmodium falciparum* diversity within the host and across populations.** Manske M, *et al*. *Nature* 2012.
4. **SpolPred: Rapid and accurate ascertainment of *Mycobacterium tuberculosis* strain types from short genomic sequences.** Coll F, *et al*. *Bioinformatics* 2012.
5. **Targeted restoration of the intestinal microbiota with a simple, defined bacteriotherapy resolves relapsing *Clostridium difficile* in mice.** Lawley T, *et al. PloS Pathogens* 2012

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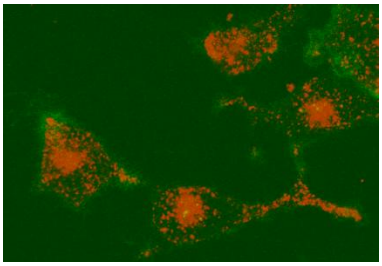
Ursula Gompels

Reader in Molecular Virology

Dr Gompels research is on human herpesviruses, currently focused on the betaherpesvirus subgroup which includes human herpesvirus 6 (variants HHV-6A and HHV-6B) and human cytomegalovirus (HCMV). These viruses can be significant paediatric pathogens and are major opportunistic infections in immunosuppressed populations, as HIV/AIDS and transplantation patients, where they cause both morbidity and mortality. HHV-6, particularly HHV-6A variant, is also an emergent pathogen with links to multiple sclerosis and other neuroinflammatory disease. Betaherpesviruses cause lifelong latent infections adapted to persist in cells of our immune system, and can reactivate to cause disease. These adaptations provide a unique immunological toolbox to devise novel immune-based medicines. Work is multidisciplinary with topics in infection and immune modulation with implications for vaccine studies and paediatric HIV/AIDS: i) genomic variation and viral load in relation to micronutrients and paediatric disease, growth and development in maternally HIV exposed infants, in collaboration with LSHTM EPH and the University Teaching Hospital in Zambia, ii) studies on molecular mechanisms of virus entry and iii) characterisation of virus mimics of inflammatory mediators, chemokine and chemokine receptors, as major components of immune modulation, which can also limit HIV infection.



Herpesirus chemokine arrests HIV CCR5 receptor (green) at the cell surface.

Selected publications

1. **Human cytomegalovirus infant infection adversely affects growth and development in maternally HIV-exposed and unexposed infants in Zambia.** Gompels U. *et al. Clin. Infect. Dis*. 2011.
2. **Micronutrient fortification to improve growth and health of maternally HIV-unexposed and exposed Zambian infants: a randomised controlled trial.** Filteau S. *et al. PLoS One*. 2010.
3. **High human cytomegalovirus loads and diverse linked variable genotypes in both HIV-1 infected and exposed, but uninfected, children in Africa.** Bates M. *et al. Virology*. 2008.
4. **Immunomodulation by herpesvirus U51A chemokine receptor via CCL5 and FOG-2 down-regulation plus XCR1 and CCR7 mimicry in human leukocytes.** Catusse J. *et al. Eur. J. Immunol*. 2008.
5. **Inhibition of HIV-1 infection by viral chemokine U83A via high-affinity CCR5 interactions that block human chemokine-induced leukocyte chemotaxis and receptor internalization.** Catusse J. *et al. Blood.* 2007.

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Sam Alsford

Senior Lecturer in Molecular Biology

Sam Alsford's early work focused on the development of a range of molecular tools for use in the genetic manipulation of *Trypanosoma brucei*[5], the causative agent of human African trypanosomiasis. This enabled the transition from candidate-based or reverse genetic approaches, to the use of forward genetics in developing our understanding of trypanosome biology[4].

Initial applications of this technology focused on understanding the uptake and intracellular transit of the current anti-HAT drugs, in particular suramin, and identifying potential routes to resistance[2]. It's now being used to define parasite's interaction with its host environment, in particular the role of parasite factors in determining the efficacy of host and parasite-derived molecules.

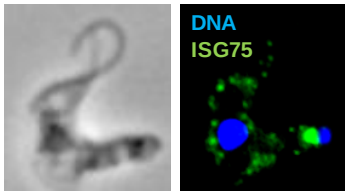

Fig. 1: Distribution of ISG75, a surface protein responsible for suramin uptake.

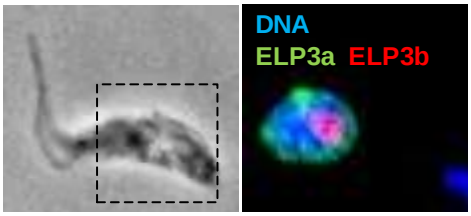

Fig. 2: The nucleolar localization of the *rRNA* transcriptional regulator, ELP3b.

Other interests include the molecular control of antigenic variation, as well as general transcriptional control in *T. brucei*. We have identified a previously unknown role for the elongator protein, ELP3b, in the control of ribosomal RNA transcription[3], and recently characterised the contribution of the histone chaperones, ASF1A and CAF-1b, to the maintenance of repressed chromatin at silent variant surface glycoprotein expression sites[1].

Selected publications

1. **Cell cycle regulated control of VSG expression site silencing by the chromatin chaperones CAF-1b and ASF1A in *T. brucei*.** Alsford S & Horn D. *Nucl Acids Res* 2012
2. **High-throughput decoding of anti-trypanosomal drug efficacy and resistance.** Alsford S, *et al*. *Nature* 2012.
3. **Elongator protein 3b negatively regulates ribosomal DNA transcription in African trypanosomes.** Alsford S & Horn D. *Mol Cell Biol*. 2011.
4. **High-throughput phenotyping using parallel sequencing of RNA interference targets in the African trypanosome.** Alsford S, *et al*. *Genome Research*. 2011.
5. **Single-locus targeting constructs for reliable regulated RNAi and *trans*-gene expression in *Trypanosoma brucei*.** Alsford S & Horn D. *Mol Biochem Parasitol*. 2008.

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Stephen Baker

Senior Lecturer in Emerging Infections

Stephen Baker heads the enteric infections research group at the Wellcome Trust Major overseas programme (WT-MOP) in Ho Chi Minh City, Vietnam. His group studies the microbiology, genetics, epidemiology and treatment of enteric infections caused by members of the Enterobacteriaceae. The Gram-negative Enterobacteriaceae incorporate a number of enteric pathogens, including pathogenic variants of *E. coli* (the most common cause of community-acquired diarrhoea), *Shigella* spp., the cause of shigellosis, and the many serovars of Salmonella enterica, including *S*. Typhi and *S*. Paratyphi A, the causative agents of enteric (typhoid) fever. Transmission of the organisms frequently occurs via faecal contamination of food, water and the environment. Thus, the risk of infection with pathogenic members of the Enterobacteriaceae is higher in areas with poor sanitation and hygiene. This is a significant global problem, as acute infectious diarrhoea is the second biggest killer of children, accounting for 21% (~2.5 million annually) of childhood deaths worldwide and *S*. Typhi and *S*. Paratyphi A are estimated to cause >25,000,000 new infections annually with >200,000 deaths. Our current focus combines microbiological, immunological and geographical information to study how organisms are transmitted in urban environments and how this interplay can be used to design and implement vaccination strategies. Areas of particular interest include: i) Evolutionary adaptation and clonal replacement of gastrointestinal pathogens, ii) Molecular diagnostics of bacterial pathogens, iii) The impact of antimicrobial resistance, iv) Horizontal gene transfer. v) Epidemiological and clinical aspects of gastrointestinal infections. vi) Randomised controlled trials for enteric infections, vii) Serological markers of infection and pathogen exposure, viii) Genome sequencing and pathogen genotyping.

Selected publications

1. **Tracking the establishment of local endemic populations of an emergent enteric pathogen.** Holt KE, *et al. Proc Natl Acad Sci USA*. In press.
2. **Epidemiology and Rising Prevalence of Pediatric Symptomatic and Asymptomatic Norovirus Infections in Ho Chi Minh City, Vietnam.** My PVT, *et al. Emerg Infect Dis.* 2013.
3. **Immune profiling with a Salmonella Typhi antigenmicroarray identifies new diagnostic biomarkers of human typhoid.** Liang L, *et al. Nature Sci Rep*. 2013.
4. **Shigella sonnei genome sequencing and phylogeneticanalysis indicate recent global dissemination from Europe.** Holt KE, *et al*. *Nat Genet*. 2012.
5. **The decline oftyphoid and the rise of non-typhoid salmonellae and fungal infections in achanging HIV landscape: bloodstream infection trends over 15 years in southernVietnam.** Nga TV, *et al. Trans R Soc Trop Med Hyg*. 2012.

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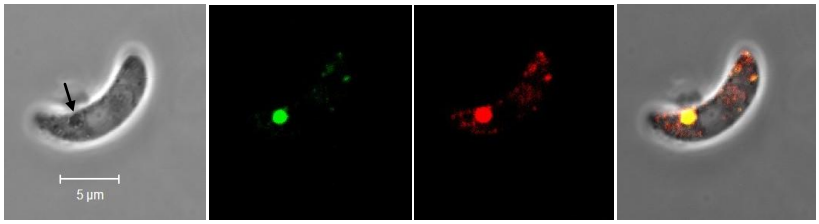
Johannes Dessens

Senior Lecturer in Parasite Cell Biology

Research in the Dessens' lab focuses on the molecular genetics of malaria parasites using the rodent malaria parasite model *Plasmodium berghei.* Central to this work is the generation of genetically modified parasites in which target genes are disrupted, tagged or mutated, providing important information on the expression, subcellular localization, function and redundancy of gene products. The emphasis of the work is on the molecular and cell biological characterisation of new genes, in particular those expressed in the mosquito stages: ookinetes, oocysts and sporozoites, with the aim to discover new ways to reduce parasite transmission. Current successful research projects involve studies of a family of LCCL proteins involved in sporozoite development and infectivity; and a family of cytoskeletal proteins (alveolins) involved in parasite shape, motility and mechanical strength. The team have expertise in parasite genetic manipulation, mosquito infection and parasite transmission, electron and confocal microscopy, and *in vitro* culture of ookinete, oocyst and sporozoite stages. They have also pioneered dual tagging with enhanced green fluorescent protein and mCherry red fluorescent protein (Figure), which has opened the door for the application of fluorescent resonance energy transfer (FRET) to study protein interactions in live parasites.



Targeting of the LCCL protein family member PbSR, which has been tagged with red fluorescent protein at the N-terminus and green fluorescent protein at the C-terminus, to the crystalloid organelle (arrow) of a genetically modified *P. berghei* mature ookinete.

Selected publications

1. **Malaria IMC1 membrane skeleton proteins operate autonomously and participate in motility independently of cell shape.** Tremp AZ and Dessens JT. *J Biol Chem* 2011.
2. ***Plasmodium berghei* crystalloids contain multiple LCCL proteins.** Saeed S, Carter V, Tremp AZ & Dessens JT, *Mol Biochem Parasitol* 2010.
3. **IMC1b is a membrane skeleton protein involved in cell shape, mechanical strength, motility and infectivity of malaria ookinetes.** Tremp AZ, Khater EI & Dessens JT. *J Biol Chem* 2008.
4. **PbSR is synthesized in macrogametocytes and involved in formation of the malaria crystalloids.** Carter V, Shimizu S, Arai M & Dessens JT. *Mol Microbiol* 2008.
5. **A malaria membrane skeletal protein is essential for normal morphogenesis, motility and infectivity of sporozoites.** Khater EI, Sinden RE & Dessens JT. *J Cell Biol* 2004.

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Nick Dorrell

Senior Lecturer in Bacterial Pathogenesis

Nick Dorrell joined the LSHTM in July 1999 and is continuing with his long-standing research interest in bacterial pathogenicity. His current research interests cover four main areas of bacterial pathogenesis relating to the human pathogen *Campylobacter jejuni*. Studies into the regulation of *C. jejuni* gene expression have identified OsrA (Cj1546) and OsrB (Cj1556) as transcriptional regulatory proteins with a role in controlling oxidative and aerobic stress responses. An investigation into the role of bacterial outer membrane vesicles (OMVs) in *C. jejuni* pathogenesis has identified 151 *C. jejuni* proteins associated with OMVs and shown that *C. jejuni* OMVs alone are capable of inducing a host innate immune response. Ongoing studies into the development of models of infection have lead to the use of a Vertical Diffusion Chamber (VDC) to study *C. jejuni* interactions with and invasion of intestinal epithelial cells (IECs) under microaerobic conditions at the apical surface and aerobic conditions at the baso-lateral surface. Using this VDC system, levels of *C. jejuni* interactions with and invasion of IECs are dramatically enhanced as well as an increase in the host innate immune response. This VDC system is currently being used to investigate the mechanisms and outcomes of *C. jejuni* invasion of IECs. Also investigations into the innate immune response to *C. jejuni* infection in collaboration with Mona Bajaj-Elliott (UCL Institute of Child Health) have identified novel bacterial interactions with the host immune system.

Selected publications

1. ***Campylobacter jejuni*** **lipooligosaccharide sialylation, phosphorylation, and amide/ester linkage modifications fine-tune human Toll-like receptor 4 activation.** Stephenson HN, *et al. J. Biol. Chem*. 2013.
2. ***Campylobacter jejuni*** **outer membrane vesicles play an important role in bacterial interactions with human intestinal epithelial cells.** Elmi A, *et al. Infect. Immun*. 2012.
3. **Increase in *Campylobacter jejuni* invasion of intestinal epithelial cells under low-oxygen coculture conditions that reflect the in vivo environment.** Mills D, *et al. Infect. Immun*. 2012.
4. **The *Campylobacter jejuni* transcriptional regulator Cj1556 plays a role in the oxidative and aerobic (O2) stress response and is important for bacterial survival in vivo.** Gundogdu O, *et al. J. Bacteriol*. 2011.
5. **Genomic variations define divergence of water/wildlife-associated *Campylobacter jejuni* niche specialists from common clonal complexes.** Hepworth PJ, *et al. Environ. Microbiol*. 2011.

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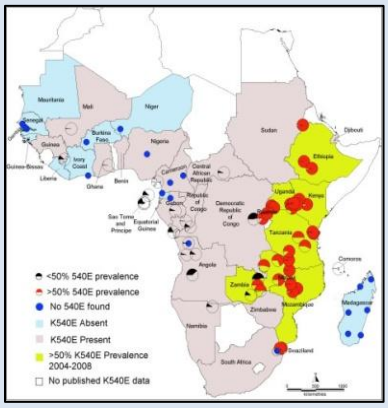
Cally Roper

Senior Lecturer in Malaria Genetics

The evolution of drug resistance is a significant obstacle in the treatment and prevention of malaria. Global patterns of drug resistance are continually changing as resistant parasites spread to new areas and as new drugs are introduced. Using molecular population genetics we described how resistance mutations in the *dhfr* and *dhps* genes emerged and spread globally. Genomic research allowed us to identify regions of the chromosome around drug resistance mutations affected by selective sweeps and we used these linked regions to describe lineages of resistance and to map their dispersal across Africa[5]. By collating and georeferencing all published *dhfr* and *dhps* mutation reports, we have mapped the progress of antifolate resistance in Africa. All this data is compiled in a publically available web-based resource www.drugresistancemaps.org. Our maps of mutation distribution in Africa also feature on the Worldwide Antimalarial Resistance Network (WWARN) website. Our research was used guide WHO policy recommendations on use of sulphadoxine/ pyrimethamine for intermittent preventive treatment of infants (SP-IPTi). The map below reveals that although drug resistance precludes the use of SP-IPTi in eight countries in East Africa, the drug is still suitable for use in 14 countries in Central and West Africa. Importantly there are 7 African countries where there is insufficient data to guide drug policy.



Selected publications

1. **Association between intermittent preventive therapy for malaria during pregnancy using 2 doses vs 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight among African newborns: A systematic review and meta-analysis.** Kassoum Kayentao, *et al. JAMA* 2013.
2. **A community-randomised evaluation of the effect of Intermittent Preventive Treatment in Infants on anti-malarial drug resistance in southern Tanzania.** Pearce RJ, *et al. J Infect Dis*. 2013.
3. **Mapping 'partially resistant', fully resistant' and 'super resistant' malaria.** Naidoo I & Roper C. *Trends Parasitol*. 2013.
4. **Mitigating the threat of artemisinin resistance in Africa: improvement of drug-resistance surveillance and response systems.** Talisuna AO, *et al. Lancet Infect Dis*. 2012.
5. **The Transit Phase of Migration: Circulation of Malaria and Its Multidrug-Resistant Forms in Africa.** Lynch C & Roper C. *PLoS Medicine*. 2011.

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Michael Gaunt

Lecturer in Genome Parasitology

The work focused on using evolutionary models to understand the molecular epidemiology or "microevolution" and "macroevolution" of the parasite *Trypanosoma cruzi* the causative agent of South American trypanosomiasis and its insect vector triatomine bugs.

Microevolution: *T. cruzi* is a zoonose and the genetic relationship, or "population structure", between sylvatic mammals and human reservoir hosts could have important public health implications. The team have developed a population genomics method using "microsatellite" genetic markers that provide the most accurate typing tool available for *T. cruzi*. The application of this tool to field isolates demonstrates *T. cruzi* has a complex epidemiology. For example, some ecotopes show a close genetic association between sylvatic hosts (rodents) and humans but other ecotopes (opossums) show a mixture of close and distant genetic associations. The microsatellites panel identified multiclonal infections as being much more important than previously thought.

Macroevolution: Evolutionary studies on triatomine bugs revealed the insect evolved blood-feeding behaviour once and this occurred exactly at the same time as the formation of South America. Finally, theoretical work on evolutionary models reveals that several commonly used assumptions (mutation matrices) may result in erroneous epidemiological inferences. Refining these models provides new epidemiological insights.

Selected publications

1. **Mechanism of genetic exchange in American trypanosomes**. Gaunt M *et al. Nature.* 2003.
2. **Phylogenetic multilocus codon models and molecular clocks reveal the monophyly of haematophagous reduviid bugs and their evolution at the formation of South America.** Patterson P and Gaunt M. *Mol Phyl Evol*. 2010.
3. **Genome-scale multilocus microsatellite typing of *Trypanosoma cruzi* discrete typing unit I reveals phylogeographic structure and specific genotypes linked to human infection.** Llewellyn M *et al. PLoS Pathog.* 2009.
4. **Trypanosoma cruzi IIc: phylogenetic and phylogeographic insights from sequence and microsatellite analysis and potential impact on emergent Chagas disease.** Llewellyn M *et al. PLoS Negl Trop Dis.* 2009.
5. **Comparative phylogenomics of the food-borne pathogen *Campylobacter jejuni* reveals genetic markers predictive of infection source.** Champion O *et al. Proc Natl Acad Sci USA.* 2005.

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Richard Stabler

Lecturer of Molecular Bacteriology

Richard Stablers' main focus has been the genomic analysis of the important nosocomial infection *Clostridium difficile*. Initially he used a whole genome microarray in combination with Bayesian statistics (comparative phylogenomics) to analyse a diverse collection of animal and clinical isolates. This identified for the first time that isolates from diverse geographical locations were due to the spread of hypervirulent clones. The team were able to use this information to select two examples, one historic and one modern, of the PCR-ribotype 027 hypervirulent lineage for whole genome sequencing. This gave an insight into the genetics behind the rapid evolution and emergence of this clone. To further dissect the genetics, high throughput sequencing technology (HTST) was used. Dr Stabler is currently investigating the diversity of *C. difficile* using both Multilocus Sequence Typing (MLST) and next generation genome sequencing (NGS).

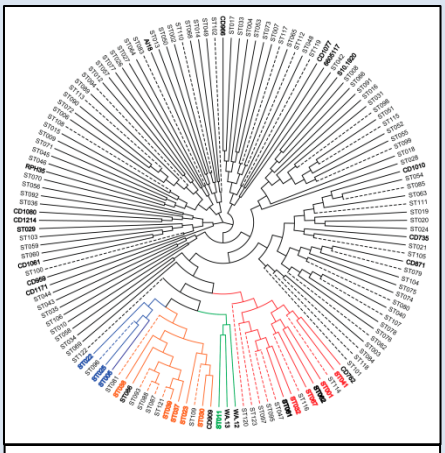

Fig 1. *C. difficile* population structure based on MLST.

Dr Stabler designed an Active Surveillance of Pathogens (ASP) microarray. The microarray was designed to monitor gene flux with particular interest in emerging infectious diseases.

Dr Stabler is also using HTST to investigate the genetic diversity and spread of MRSA in South London, a novel capsule depolymerase present in soil bacteria and the dissemination of drug resistance genotypes with hospital environments. He is also involved in a number projects looking at virulence factors from *Acinetobacter baumannii*, *Streptococcus pneumoniae*, *Shigella sonnei* and *Campylobacter jejuni.*

Selected publications

1. **Draft Genome Sequences of Pseudomonas fluorescens BS2 and Pusillimonas noertemannii BS8, Soil Bacteria That Cooperate To Degrade the Poly-γ-d-Glutamic Acid Anthrax Capsule.** Stabler RA, *et al. Genome Announc.* 2013
2. **Characterization of water and wildlife strains as a subgroup of Campylobacter jejuni using DNA microarrays.** Stabler RA, *et al. Environ Microbiol*. 2013
3. **Macro and micro diversity of Clostridium difficile isolates from diverse sources and geographical locations.** Stabler RA, *et al PLoS One*. 2012
4. **In-depth genetic analysis of *Clostridium difficile* PCR-ribotype 027 strains reveals high genome fluidity including point mutations and inversions.** Stabler RA, *et al. Gut Microbes.* 2010.
5. **Evolutionary dynamics of *Clostridium difficile* over short and long time scales.** He M, *et al*. Proc Natl Acad Sci. 2010.

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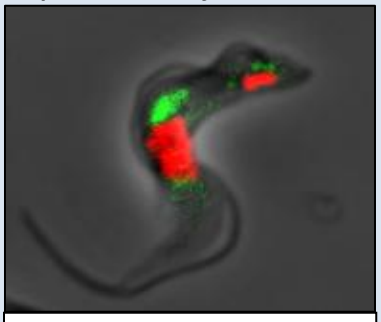
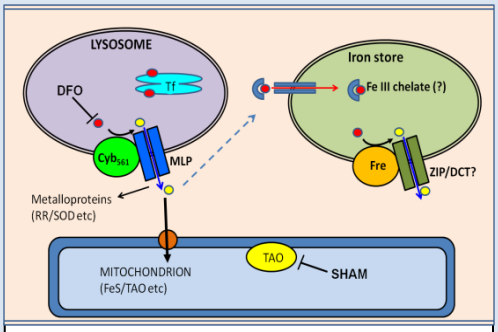
Martin Taylor

Lecturer in Molecular Biology

Dr. Taylor is primarily interested in nutrient uptake and utilisation in Kinetoplastids. His recent work has focused principally on iron and ascorbate (vitamin C). Iron is a crucial nutrient for a variety of pathogenic organisms and can be sequestered by the innate immune system. Dr. Taylor's work is centred on the mechanisms used by kinetoplastid parasites to obtain iron in their mammalian host. His primary interest is in the African and American trypanosomes, *T. brucei* and *T. cruzi*. *T. brucei* being extracellular in the mammal obtains non-heme iron from transferrin by endocytosis. The roles of various proteins in this uptake are currently being analysed using a variety of techniques including RNA interference, conditional null mutants, drug assays and fluorescence based assays for intracellular iron levels. Dr. Taylor has created a conditional expression system for the American trypanosome which will be used to characterise iron uptake pathways in this intracellular parasite. Dr. Taylor is also involved in developing highly sensitive *in vivo* imaging models for drug discovery programmes for Human African Trypanosomiasis (Sleeping Sickness), Chagas disease and visceral leishmaniasis.



Expression of TbMLP1 (green) in the endocytic pathway, The large green organelle next to the nucleus (large red) is the lysosome.



Our current model of iron trafficking in the blodstream form trypanosome. Incoming ferric iron is reduced by Cyb_{561} to ferrous iron. This is transported across the membrane by MLP.

Selected publications

1. **In Vivo Imaging of Trypanosome-Brain Interactions and Development of a Rapid Screening Test for Drugs against CNS Stage Trypanosomiasis**. Myburgh E *et al. PLoS Negl Trop Dis*. 2013.
2. **Evidence that transport of iron from the lysosome to the cytosol in African trypanosomes is mediated by a mucolipin orthologue.** Taylor MC *et al. Mol Microbiol*. 2013.
3. **Benznidazole-Resistance in Trypanosoma cruzi Is a Readily Acquired Trait That Can Arise Independently in a Single Population.** Mejia AM *et al. J Infect Dis*. 2012.
4. **Iron metabolism in trypanosomatids, and its crucial role in infection.** Taylor MC & Kelly JM. *Parasitology,* 2010.
5. **Validation of spermidine synthase as a drug target in African trypanosomes** Taylor MC *et al. Biochem J.* 2008.

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