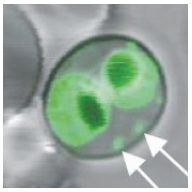
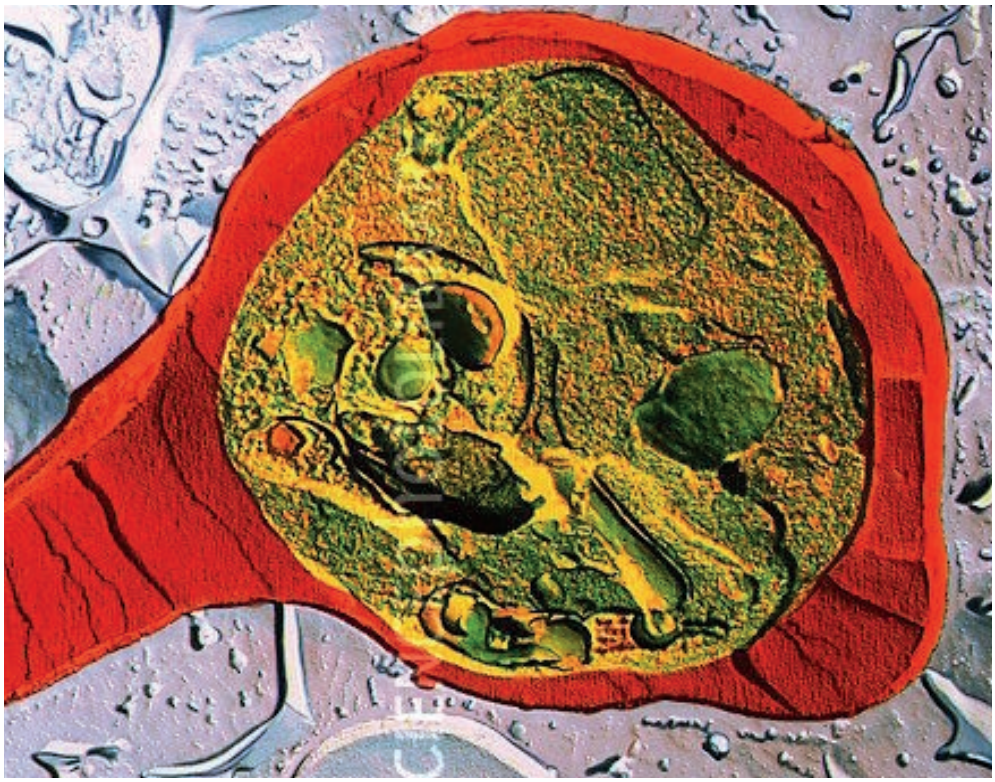
MOLECULAR & MEDICAL PARASITOLOGY GROUP



LABORATORY, CLINICAL AND FIELD STUDIES OF MALARIA AND OTHER TROPICAL INFECTIOUS DISEASES

St George's University of London



BY COMBINING LABORATORY INVESTIGATIONS WITH STUDIES IN THE FIELD, WE AIM TO HAVE A MAJOR IMPACT ON MALARIA AND OTHER TROPICAL DISEASES.

TROPICAL INFECTIOUS DISEASE: THE BIGGER PICTURE

The Molecular and Medical Parasitology Group at St George's University of London, led by Professor Sanjeev Krishna, is notable for the breadth of its research interests. Our ultimate aim is to improve the diagnosis, treatment and control of tropical parasitic diseases, including malaria – responsible for the deaths of nearly a million children a year – and sleeping sickness (African trypanosomiasis).

A core focus of our work are 'transporter proteins' of the malaria parasite, which move key molecules into and out of the cell. These transporters are of fundamental importance to the biology of the parasite, and they may also be important drug targets. We have generated evidence that one transporter, known as PfATP6, is a target of artemisinins – the most widely used class of antimalarial drug. In addition, a glucose transporter, PfHT, could be an important target for drug development.

Our laboratory studies are based on expression of transporters in artificial systems, which enable us to study their function systematically. As well as a conventional frog egg expression system, we have recently introduced a more flexible and powerful yeast platform.

Our laboratory studies are rooted in the realities of malaria treatment and control. We are continuing to characterise PfATP6, to shed light on possible mechanisms of drug resistance (and how they might be overcome). Our previous work also identified an important mechanism responsible for resistance to other commonly used antimalarial drugs – amplification of the *pfmdr1* gene.

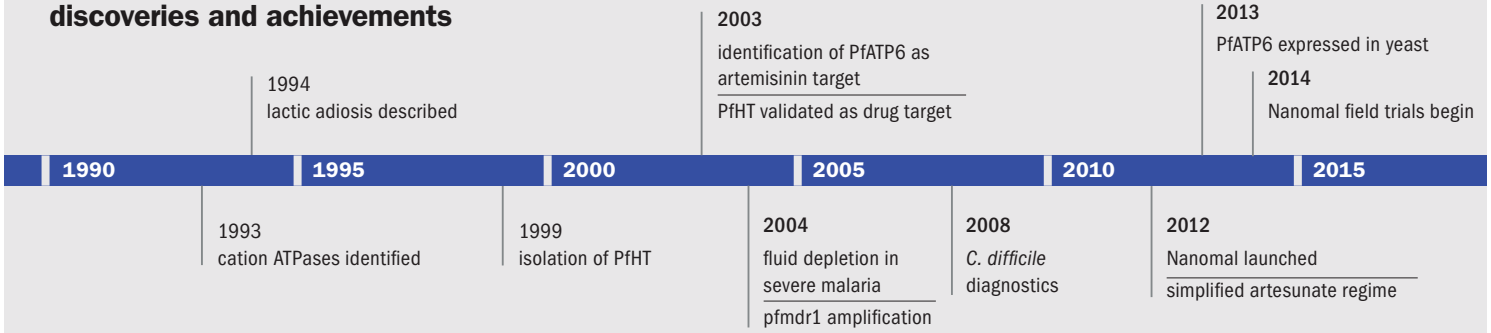
Furthermore, field studies are core to our work. We have been involved in numerous clinical trials of antimalarial treatments, particularly in Africa, helping to establish treatment regimes tailored to local needs. Thanks to our longstanding collaboration with Peter Kremsner in Tübingen, we have particularly strong links with Gabon.

Other clinical studies have focused on the consequences of malaria infection. Our main interests have been around harmful build up of lactate in the bloodstream and fluid balance, providing important evidence to guide treatment.

Left: Malaria parasite within an infected red blood cell.

WE ARE WORKING TO CREATE A DEVICE THAT CAN NOT ONLY DETECT THE MALARIA PARASITE BUT ALSO IDENTIFY ITS DRUG RESISTANCE PROFILE – SO PATIENTS CAN BE GIVEN 'PERSONALISED' DRUG TREATMENTS.

A timeline of the group's major discoveries and achievements



Diagnostics

A third major area of interest is diagnostics. Effective treatment of infectious diseases is often hampered by the lack of diagnostic tools – clinical symptoms are rarely specific enough to permit accurate diagnosis and referral to centralised facilities is slow, inefficient and expensive.

We have worked for several years on new technological approaches to underpin diagnostics for diseases such as tuberculosis and African trypanosomiasis (sleeping sickness). Recently, we were awarded €5.2m/£4m EU funding to lead an international consortium, Nanomal, developing a smartphone-like diagnostic for malaria, drawing on innovative 'lab-on-a-chip' technologies developed by project partners QuantuMDx.

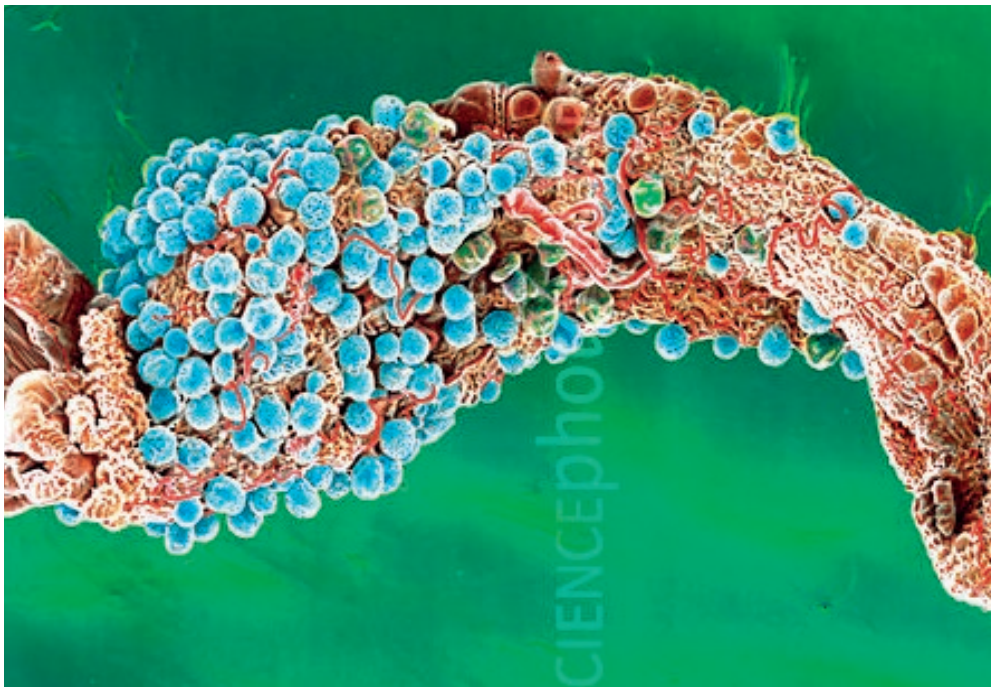
With our understanding of malaria infection and drug resistance, we are working with QuantuMDx and academic partners – Peter Kremsner in Tübingen and Pedro Gil at the Karolinska Institute in Stockholm – to create a device that can not only detect the malaria parasite but also identify its drug resistance profile – so patients can be given the most appropriate 'personalised' drug treatments.

With Professor Phil Butcher at St George's, we are also working with QuantuMDx to adapt the technology for TB, in a £1m project funded by the UK Government's Technology Strategy Board. The technology is also being applied to sexually transmitted infgections, through the MRC-funded eSTI2 consortium, led by Tariz Sadiq.

Above: Professor Sanjeev Krishna (left) and members of the Molecular and Medical Parasitology Group.

Policy and advocacy

As well as these laboratory and clinical studies, we also contribute to policy-making and advocacy for tropical infectious diseases. Professor Krishna has been an advisor to multiple international bodies, including the World Health Organisation. He has sat on advisory committees for the WHO, and major international funders including the US National Institutes of Health, the UK's Wellcome Trust and others. He is an advisor to the Foundation for Innovative New Diagnostics (FIND), a not-for-profit organisation promoting the development of new diagnostic tools for resource-poor countries. He also has strong industrial contacts, and has acted as scientific advisor to several large pharmaceutical companies and biotech firms.



BY UNDERSTANDING THEIR UNIQUE BIOLOGY, WE MAY BE ABLE TO IDENTIFY NEW WAYS TO COMBAT MALARIA PARASITES. OUR RESEARCH FOCUSES ON THEIR DISTINCTIVE TRANSPORTER PROTEINS.

TRANSPORTERS: EXPLOITING PARASITE BIOLOGY

The artemisinin target

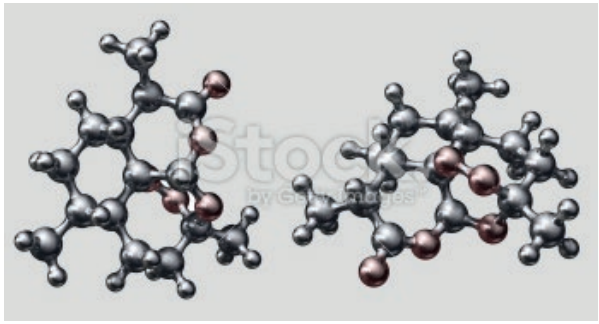
PfATP6 is the likely target of artemisinin antimalarials.

Derived from extracts of the sweet wormwood plant, artemisinin-based antimalarial drugs are recommended for use globally; several hundred million doses are given every year. Yet they were developed without any clear idea of their molecular target. In 2003, we identified PfATP6 as the likely target for artemisinin, and since then have generated more evidence in support of our initial findings.

The unusual chemical structure of artemisinin resembles that of a calcium pump inhibitor, thapsigargin. This led us to suggest that artemisinin might also act on a calcium pump. The malaria parasite genome codes for only one such pump, PfATP6. When expressed in frog eggs, PfATP6 was strongly and specifically inhibited by artemisinin. Furthermore, there was very good agreement between the degree of inhibition of PfATP6 by different artemisinin derivatives and their parasite-killing abilities.

We later showed that a single amino acid change in the likely inhibitor-binding region of PfATP6 could dramatically reduce inhibition by artemisinin.

PfATP6 may not be the only target of artemisinin. Nevertheless, we have recently shown that PfATP6 is essential to parasite survival, and have confirmed our initial findings in studies of PfATP6 expressed in yeast cells. Significantly, variants associated with reduced artemisinin sensitivity in the field were less sensitive to artemisinin inhibition in this assay.



Above: Malaria parasites in the mosquito gut.

Left: Molecular models of artemisinin.

Knowing the identity of the artemisinin target is extremely important. It will provide a way to identify mechanisms of resistance, should they arise, and possibly to monitor for genetic changes associated with resistance. It will also support the development of new therapeutics that bypass these mechanisms of resistance.

Although a spontaneous genetic change in PfATP6 associated with altered sensitivity to artemisinin has been identified, the significance of genetic variation is difficult to assess, as numerous natural variants of PfATP6 exist. The yeast system now provides us with a tool to examine the functional significance of such variants, particularly their susceptibility to artemisinins.

Eckstein-Ludwig U *et al.* Artemisinins target the SERCA of Plasmodium falciparum. *Nature.* 2003;424(6951):957–61.

Uhlemann AC *et al.* A single amino acid residue can determine the sensitivity of SERCAs to artemisinins. *Nat Struct Mol Biol.* 2005;12(7):628–9.

Pulcini S *et al.* Expression in yeast links field polymorphisms in PfATP6 to in vitro artemisinin resistance and identifies new inhibitor classes. *J Infect Dis.* 2013;208(3):468–78.

Blocking glucose uptake

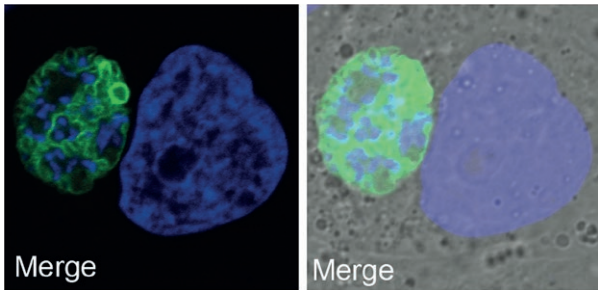
A key parasite sugar transporter could be an important target for new antimalarial drugs.

With resistance always likely to be a problem, new antimalarial drugs are constantly needed. The malaria parasite relies on a key sugar transporter, PfHT, to take up glucose, and selective inhibitors of PfHT are highly effective at killing parasites – pinpointing the transporter as an attractive drug target.

Although their metabolism is complex and incompletely understood, malaria parasites rely on a continuous supply of glucose from the host. This is taken up by a single sugar transporter, PfHT. In theory, blocking this transporter should therefore starve the parasite of its energy source.

To explore the potential of PfHT as a drug target, we expressed the transporter in our frog egg system. It efficiently transported glucose, and uptake could be readily inhibited by glucose analogues. Importantly, these analogues had no significant effect on host glucose transporters. One of the most potent inhibitors, compound 3361, killed cultured malaria parasites and significantly inhibited the growth of *P. berghei* parasites in a mouse model of malaria.

A further advantage of targeting PfHT is that glucose uptake is vital at multiple stages of the parasite life cycle. Indeed, compound 3361 inhibited liver-stage parasite development, when parasites multiply asexually, and could also block transmission of the parasite to its mosquito vector.



Donec nisl sapien, feugiat vitae dolor Psuscipit, non pretium purus fringilla. Curabitur tristique tincidunt lectus, tincidunt mollis urna viverra vel.

As a further demonstration of the validity of PfHT as a drug target, we were unable to eliminate the *pfht* gene – suggesting that loss of PfHT is incompatible with parasite survival.

Our results indicate that PfHT is a highly attractive drug target for all human malarias. Although compound 3361 is not well suited to drug development, small molecule inhibitors of PfHT could provide valuable tools in the fight to eliminate the malaria parasite.

Joet T *et al.* Validation of the hexose transporter of Plasmodium falciparum as a novel drug target. *Proc Natl Acad Sci USA.* 2003;100(13):7476–9.

Slavic K *et al.* Use of a selective inhibitor to define the chemotherapeutic potential of the plasmodial hexose transporter in different stages of the parasite's life cycle. *Antimicrob Agents Chemother.* 2011;55(6):2824–30.

Slavic K *et al.* Life cycle studies of the hexose transporter of Plasmodium species and genetic validation of their essentiality. *Mol Microbiol.* 2010;75(6):1402–13.

A drug resistance marker

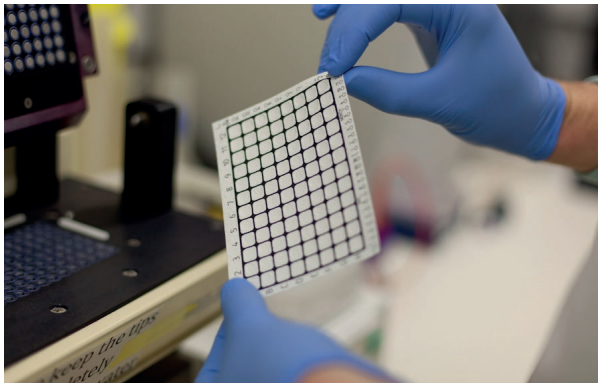
A technological advance helped to identify a critical factor in the development of resistance to commonly used antimalarials.

The antimalarial drug mefloquine was introduced into Thailand in 1984. Within six years, it was rendered near useless by the development of drug resistance. By adapting methods of DNA amplification, we were able to show that drug resistance was caused primarily by duplication of a specific parasite gene, *pfmdr1*, coding for a drug transporter protein. This test has gone on to be used by the Worldwide Antimalarial Resistance Network (WWARN) to monitor for emerging drug resistance.

Initial attempts to identify the causes of mefloquine resistance threw up conflicting results. As well as mutations affecting individual proteins, resistance could reflect duplications of genes such as *pfmdr1*, a relative of which renders some tumours resistant to anticancer drugs. In the early 2000s, however, assaying increases in gene copy number was not straightforward.

We developed a new technique, based on the polymerase chain reaction (PCR), to detect copy number changes in *pfmdr1*. With colleagues in Thailand and elsewhere, we then analysed more than 600 samples from malaria patients, looking for changes to genes associated with drug resistance and *pfmdr1* copy number changes. The latter proved the most common cause of resistance to mefloquine (as well as reduced sensitivity to newly introduced combination treatments of mefloquine and artesunate).

With David Fidock in New York, we also showed that genetically modifying parasites to lower *pfmdr1* copy number increased their sensitivity to mefloquine and a range of other antimalarials.



Molecular methods have provided a way to monitor for resistance to antimalarial drugs.

Our approach has been widely adopted to track the emergence of drug resistance. Globally, it formed part of the WWARN toolkit for monitoring drug resistance. Notably, *pfmdr1* expansion is not yet a major factor in Africa, but this situation could change with increased antimalarial use, emphasising the need for active surveillance.

Price RN *et al.* Mefloquine resistance in Plasmodium falciparum and increased pfmdr1 gene copy number. *Lancet.* 2004;364(9432):438–47.

Sidhu AB *et al.* Decreasing pfmdr1 copy number in plasmodium falciparum malaria heightens susceptibility to mefloquine, lumefantrine, halofantrine, quinine, and artemisinin. *J Infect Dis.* 2006;194(4):528–35.

FIELD STUDIES ARE ESSENTIAL FOR UNDERSTANDING THE IMPACT OF MALARIA PARASITE INFECTION AND THE BEST APPROACHES TO TREATMENT.

CLINICAL MALARIA

A practical guide to antimalarial use

Rigorous clinical trials have helped to establish the most appropriate treatment regimes for children with malaria.

The development of artemisinin-based drugs provided a much-needed boost to the antimalarial armamentarium. Drug treatment has the twin aims not just of treating individuals but also of preventing the spread of parasites, calling for careful design of drug regimes, routes of drug delivery and an awareness of how drugs are metabolised in the body. We have been involved in numerous international clinical trials that have shaped global antimalarial policy and national practice.

Children are at particular risk of malaria. Severely ill children may be unable to take antimalarial drugs by mouth and, in areas of poor health infrastructure, injection of drugs may not be practical. In Ghana, we showed that that intrarectal administration of artesunate was a suitable alternative, and later contributed to a landmark international trial showing that intrarectal artesunate was safe and effective in severe malaria.

We have also led other studies in Ghana and Gabon examining different treatment regimes for children. Following work establishing the feasibility of intramuscular injection of quinine for severe malaria, we went on to show that this route of administration was also suitable for artesunate, and also that amodiaquine–artesunate combination treatment was effective for uncomplicated malaria.

With Peter Kremsner and colleagues in the Severe Malaria In African Children network, we also recently showed that a simplified artesunate regime – three doses instead of five, while still delivering the same quantity of drug – was no worse than the standard five-dose regime. A simplified regime would be more convenient for patients and offer significant cost savings.

Above and left: Young children are at particular risk from malaria

Krishna S *et al.* Bioavailability and preliminary clinical efficacy of intrarectal artesunate in Ghanaian children with moderate malaria. *Antimicrob Agents Chemother.* 2001;45(2):509–16.

Gomes MF *et al.* Pre-referral rectal artesunate to prevent death and disability in severe malaria: a placebo-controlled trial. *Lancet.* 2009;373(9663):557–66.

Nealon C *et al.* Intramuscular bioavailability and clinical efficacy of artesunate in Gabonese children with severe malaria. *Antimicrob Agents Chemother.* 2002;46(12):3933–9.

Adjuik M *et al.* Amodiaquine-artesunate versus amodiaquine for uncomplicated Plasmodium falciparum malaria in African children: a randomised, multicentre trial. *Lancet.* 2002;359(9315):1365–72.

Kremsner PG *et al.* A simplified intravenous artesunate regimen for severe malaria. *J Infect Dis.* 2012;205(2):312–9.

Treating dehydration in malaria

Although mild dehydration is sometimes seen in childhood malaria, it does not appear to be a major factor in disease, arguing against use of rapid rehydration.

Most childhood deaths from malaria occur within the first 24 hours of hospitalisation. One factor suggested to be a risk factor for severe malaria is excessive fluid loss, leading some to propose rapid rehydration for severely ill infants. Our studies in Gabon, however, found no evidence that severe malaria was associated with excessive fluid loss.

Determining body fluid levels experimentally is difficult, and many studies have assessed dehydration through clinical proxy measures. We used careful experimental methods to measure body fluids in children with severe and moderate malaria, and also validated a relatively simple method of determining fluid levels by measuring the flow of small electrical currents between hands and feet.

We found that severe malaria was typically associated with mild dehydration, but found no evidence that the severity of symptoms was linked to the degree of dehydration. Hence our results suggested it was unlikely that fluid loss was contributing significantly to disease processes. Gradual fluid replacement was sufficient to normalise patients within 12 hours. We could also find no evidence that body fluid volumes were associated with high blood lactate levels, a known risk factor for severe disease.

Given the potential dangers of rapid rehydration, we therefore argued that it was not warranted in treatment of severely ill children with malaria. Unfortunately, the FEAST clinical trial run to assess rapid rehydration had to be terminated early when it was found to be increasing the risk of death.

Rehydration may be necessary in malaria treatment.

More work is needed to fully understand the impact of malaria parasite infection on the body. In particular, there remains an urgent need to understand the basis of lactic acidosis and how it can best be addressed.

Planche T *et al.* Assessment of volume depletion in children with malaria. *PLoS Med.* 2004;1(1):e18.

Jarvis JN *et al.* Lactic acidosis in Gabonese children with severe malaria is unrelated to dehydration. *Clin Infect Dis.* 2006;42(12):1719–25.

P. knowlesi: an emerging threat

The 'fifth malaria parasite', *Plasmodium knowlesi* may become more significant as control of other species improves.

Plasmodium knowlesi is principally a parasite of macaques, but since the early 2000s it has become clear that it can also naturally infect humans. With colleagues in Malaysia, we have been uncovering more about the disease caused by this parasite and how it can best be treated.

P. knowlesi has emerged as a significant threat in Malaysia and in other parts of South-East Asia – in some locations accounting for the majority of malaria cases. About one in ten patients experience severe, potentially fatal disease. Worryingly, there are signs that *P. knowlesi* infections are rising in areas where human malaria is being brought under control.

Working with Dr Balbir Singh, Dr Janet Cox-Singh and colleagues at the University Malaysia Sarawak, we have been characterising this emerging infection and comparing it with 'conventional' human malarias. As well as carrying out the first post-mortem of a knowlesi malaria patient, we have shown that parasite and platelet counts are a convenient and reasonably accurate way to identify patients at risk of severe disease. We have also found that the inflammatory immune response to *P. knowlesi* parasites differs significantly from that seen in *P. falciparum* infections – comparisons that may reveal factors linked to disease severity.

Plasmodium knowlesi is emerging as an important human pathogen in parts of South-East Asia.

With little known about treatment, we have also explored the sensitivity of *P. knowlesi* to currently used antimalarial drugs. While the parasite is highly sensitive to artemisinins, it is surprisingly insensitive to mefloquine – arguing against its use in *P. knowlesi* infections.

Willmann M *et al.* Laboratory markers of disease severity in Plasmodium knowlesi infection: a case control study. *Malar J.* 2012;11:363.

Cox-Singh J *et al.* Anti-inflammatory cytokines predominate in acute human Plasmodium knowlesi infections. *PLoS One.* 2011;6(6):e20541.

Fatih FA *et al.* Susceptibility of human Plasmodium knowlesi infections to anti-malarials. *Malar J.* 2013;12(1):425.

ACCURATE AND AFFORDABLE DIAGNOSTICS WILL BE CRITICAL TO EFFECTIVE HEALTHCARE IN THE DEVELOPING WORLD.

RAPID DETECTION OF PARASITE INFECTIONS

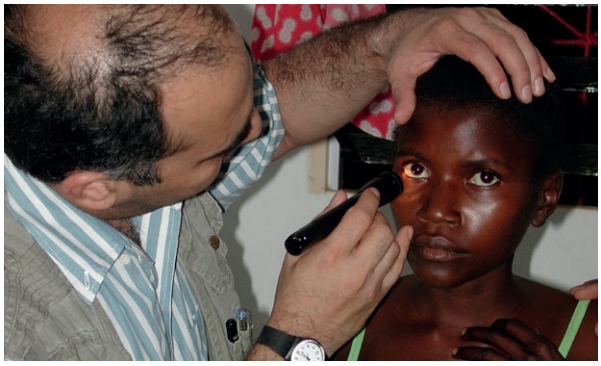
Towards practical diagnostics

It remains technically challenging to develop accurate and affordable diagnostics suitable for use in the developing world.

Accurate diagnosis of infectious disease is important both for treatment of individual patients but also, more generally, for monitoring the prevalence and spread of disease. Unfortunately, clinical symptoms alone are rarely sufficient to allow unambiguous identification of a causative organism, while culture-based or other methods of identification usually require referral to central facilities – which is slow, inefficient and expensive. We have a long-standing interest in diagnostics, for diseases such as African trypanosomiasis (sleeping sickness), tuberculosis and malaria.

To be of practical value, diagnostics must be both highly sensitive (detecting an infectious agent whenever it is present) and specific (not generating 'false positives' – positive results when an organism is not actually present). These can be highly challenging criteria to fulfill. Furthermore, for use in the developing world, an additional set of criteria are important, such as ease of use, reliability, affordability, robustness and the practicalities of use in resource-poor settings.

In the past we have explored the potential of proteomics-based approaches – analysis of characteristic peptide fragments – for trypanosomiasis and TB. Recently, DNA-based methods combined with nanotechnology sensors have emerged as a highly promising approach, as in our Nanomal consortium (see right). With Professor Phil Butcher at St George's, we are also working with Nanomal's technology partners, QuantuMDx, to develop an affordable DNA-based diagnostic for TB.



Above: A prototype malaria handheld diagnostic.

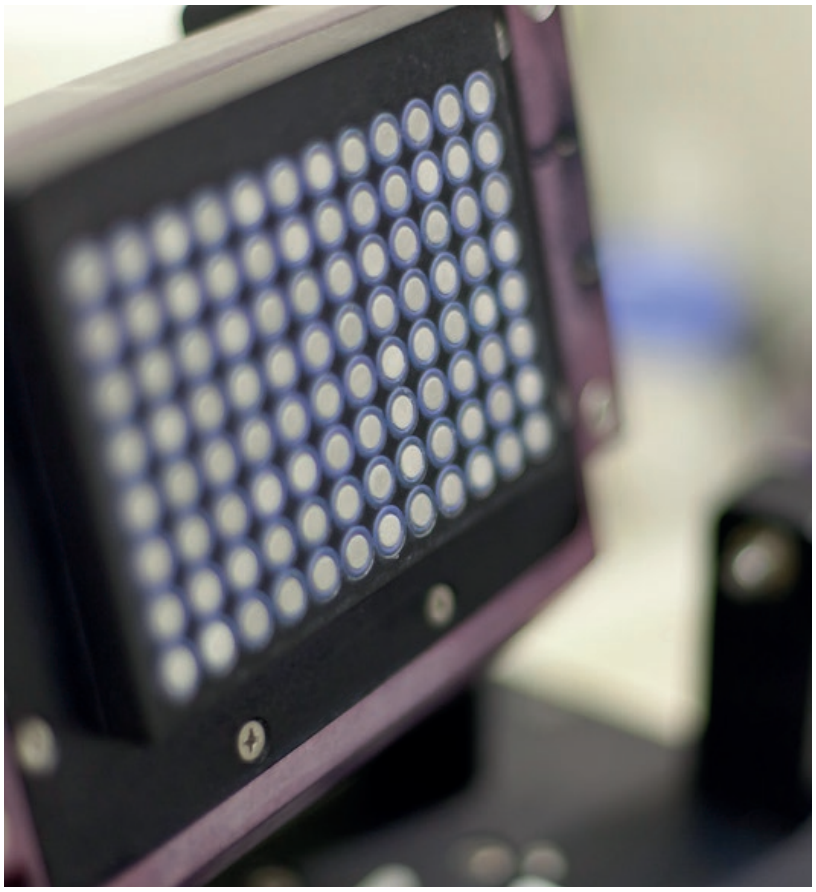
Left: Clinical assessment of a young girl with sleeping sickness.

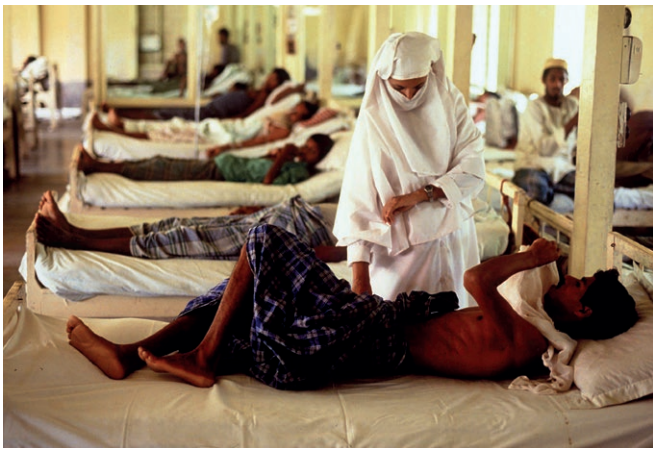
We have also used our diagnostics expertise closer to home. Our evaluation of diagnostic tests for the important microbial pathogen *Clostridium difficile*, for example, revealed significant issues in the way the results of commercially available diagnostic tools were being interpreted, and recommended a screening approach overcoming these drawbacks.

Papadopoulos MC *et al.* A novel and accurate diagnostic test for human African trypanosomiasis. *Lancet.* 2004;363(9418):1358–63.

Agranoff D *et al.* Identification of diagnostic markers for tuberculosis by proteomic fingerprinting of serum. *Lancet.* 2006;368(9540):1012–21.

Planche T *et al.* Diagnosis of Clostridium difficile infection by toxin detection kits: a systematic review. *Lancet Infect Dis.* 2008;8(12):777–84.





THE CHALLENGE IS TO DEVELOP A SIMPLE DEVICE THAT HEALTHCARE WORKERS IN DEVELOPING COUNTRIES CAN USE TO IDENTIFY THE PRESENCE OF MALARIA PARASITES WITHIN 15 MINUTES.

Diagnosing malaria

A 'lab-on-a-chip' device could revolutionise the diagnosis of malaria and the assessment of drug resistance.

Malaria is difficult to diagnose from symptoms alone, and identifying malaria parasites in blood samples is a specialist and time-consuming task. Hence patients may not get antimalarial drugs when they need them, or are given them when they do not actually have the disease. Furthermore, even if they do have malaria, there is currently no way of knowing which drugs patients are likely to respond to. This may all change through the work of the Nanomal consortium.

Led from St George's University of London, the Nanomal consortium has received €5.2m/£4m EU funding to develop a simple, affordable point-of-care diagnostic for malaria. The consortium combines the expertise in malaria treatment and diagnosis in St George's and in the laboratories of our collaborators – Peter Kremsner at Tübingen University and Pedro Gil at the Karolinska Institute – with the innovative nanotechnological applications being developed at QuantuMDx, a biotech company based in Newcastle upon Tyne.

The challenge is to develop a simple device that healthcare workers in developing countries can use to identify the presence of malaria parasites within 15 minutes. In addition, the device needs to identify the species of parasite present and its likely responsiveness to different antimalarial drugs – so patients can be given the most appropriate treatment.

QuantuMDx has developed miniaturised technology that enables complex genetic manipulations to be carried out on devices the size of smartphones. From a blood sample, specific parasite DNA sequences are amplified. These amplified sequences are detected by nanowire sensors, which relay a simple reading to the user indicating the presence of malaria parasites. In addition, the device also incorporates DNA sequencing capacity, which can be used to probe for changes in DNA sequences associated with resistance to antimalarial drugs.

The device is designed to be a point-of-care diagnostic, providing results while a patient waits for treatment. But it will also generate results important to wider surveillance of disease and drug resistance. Potentially, digital data generated by the device could be transmitted to central data stores for collation and analysis.

EU Framework Programme 7 (FP7) funding for Nanomal was awarded in 2012. We hope to begin the first field tests of prototype devices in 2014.

www.nanomal.org

Above: DNA-based methods may allow rapid identification of infections in developing world settings.

OUR FUTURE AIMS ARE TO CONTINUE WORKING ON MULTIPLE FRONTS TO TACKLE THE SCOURGE OF MALARIA AND OTHER TROPICAL PARASITIC DISEASES, ROOTED IN THE REALITIES OF DISEASE AS IT IS ACTUALLY EXPERIENCED.

FORWARD LOOK

Tropical parasitic diseases remain a major source of ill-health and death in developing countries. Nearly a million children still die of malaria every year, and diseases such as sleeping sickness remain difficult to diagnose and treat, affecting the lives of millions of the poorest people on the planet. Even when effective therapies are available, the emergence of drug resistance ensures that there is always a need for new medicines. Recent signs that malaria parasites may have reduced sensitivity to artemisinins, for example, are a cause for genuine concern.

Parasite transporters remain at the core of our laboratory studies. Our new yeast expression system provides us with a powerful platform for analysing the properties of transporters such as PfATP6. This will enable us to find out more about its interactions with artemisinins, and about the functional consequences of naturally occurring genetic variations and new mutations that may affect these interactions. These studies could provide important clues to the development of resistance to artemisinins and how they might be overcome, or how PfATP6 could be targeted in other ways.

Similarly, we plan to continue our work on PfHT, a potentially important new target for antimalarial development. One advantage of our new yeast expression platform is the ability to conduct high-throughput screens to identify potential inhibitors, and hence new leads for drug development.

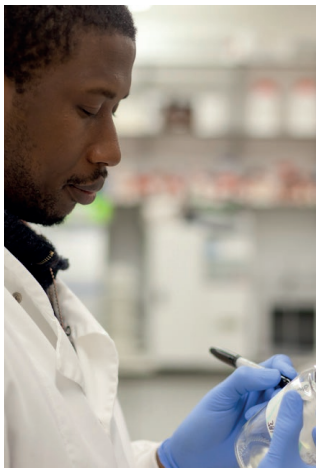
Our clinical studies will continue in Gabon, where we are aim to minimise the burden of disease through a multifaceted approach encompassing policy advice as well as clinical studies to test new classes of antimalarial drugs. Such work would also benefit from the introduction of new diagnostic tools.

Indeed, diagnostic development will remain a key focus. Field trials will be used to test prototype devices developed through the Nanomal consortium. If successful, we will work to refine the technology and identify ways in which they can be deployed in the field to support treatment, control programmes and surveillance for drug resistance. We will also be working with our St George's colleagues on similar diagnostic tools for TB.

Through these and other routes we hope to have a major impact on the diagnosis, treatment and control of malaria and other major parasitic diseases of the tropics.

Above: Dr Henry Staines.

NEARLY A MILLION CHILDREN STILL DIE OF MALARIA EVERY YEAR, AND TROPICAL DISEASES REMAIN DIFFICULT TO DIAGNOSE AND TREAT, AFFECTING THE LIVES OF MILLIONS OF THE POOREST PEOPLE ON THE PLANET.



From malaria to cancer

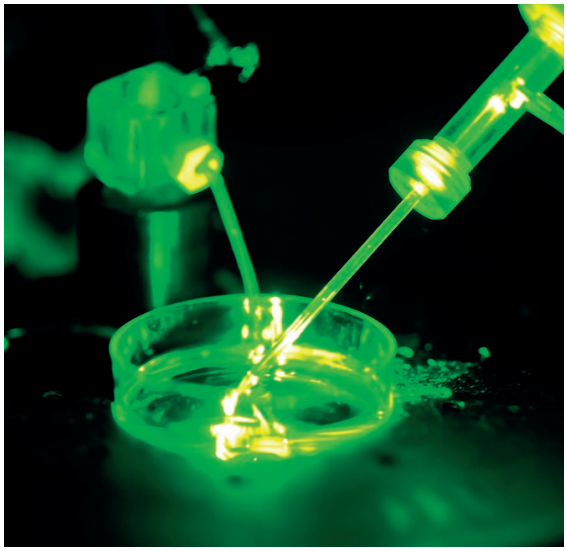
Artemisinins may have multiple medical benefits – including in cancer.

Artemisinins were originally isolated from the sweet wormwood plant, long used in the Chinese herbal remedy Qinghaosu. As well as their antimalarial properties, they have been shown to have multiple other potentially beneficial activities – leading to some suggestions they could become the 'new aspirin', another plant-derived product with a host of beneficial effects.

One possible application of artemisinins is in treatment of cancer. Many groups have established that artemisinins have activity on cancer cells. We have contributed to one study on a synthetic derivate of artemisin, artemisone, finding significant activity on a range of cancer cells lines. Artemisone was also able to enhance the anticancer effects of other commonly used anticancer agents.

These and other results argue that further clinical studies of artemisinins in cancer are justified.

Gravett AM *et al*. In vitro study of the anti-cancer effects of artemisone alone or in combination with other chemotherapeutic agents. *Cancer Chemother Pharmacol*. 2011;67(3):569–77.



Above: Professor Sanjeev Krishna and members of the Molecular and Medical Parasitology Group.

Molecular and Medical Parasitology Group
St George's, University of London
Cranmer Terrace
London SW17 0RE, UK

T: +44 (0)208 725 5836
E: s.krishna@sgul.ac.uk
W: www.tropmed.ac.uk

Main funders:
Wellcome Trust, Medical Research Council, European Union, National Institutes of Health, Medicines for Malaria Venture.

Acknowledgements:
Photography: Gary Knight, Noel Murphy.
Text: Ian Jones (Jinja Publishing Ltd)
Design: Jag Matharu (Thin Air Productions Ltd)

TAP2116/13-02-14/V2A