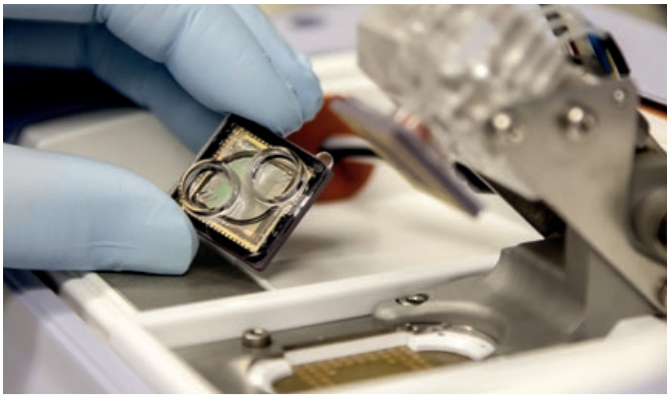
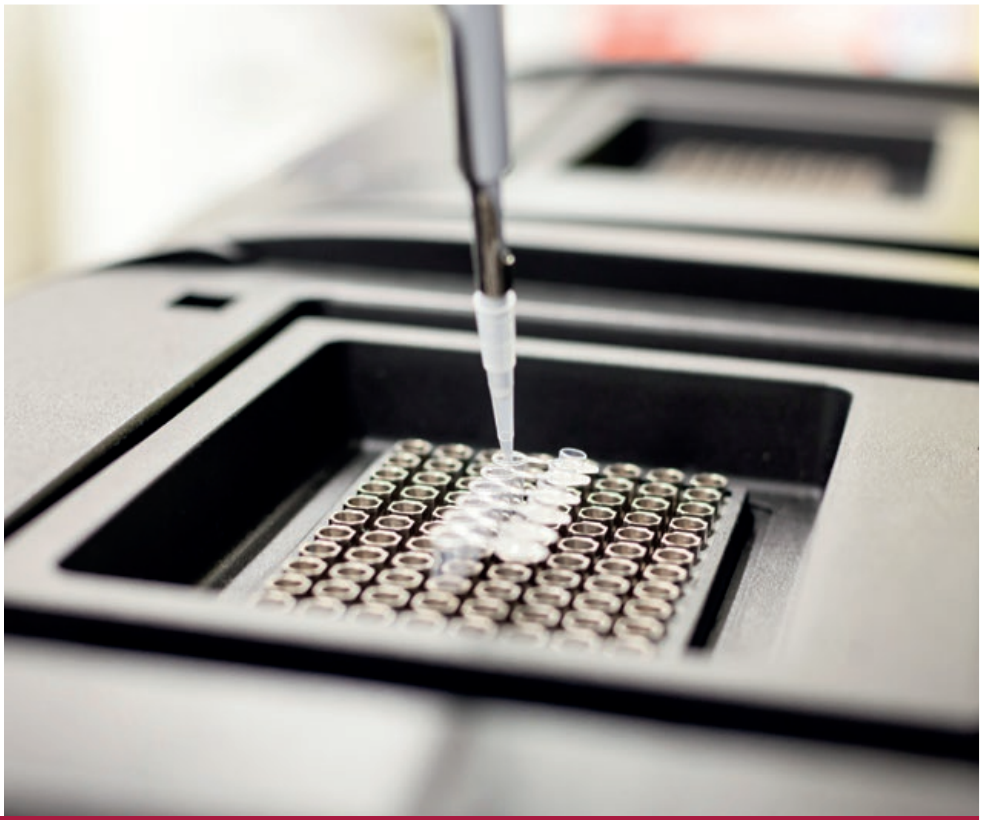
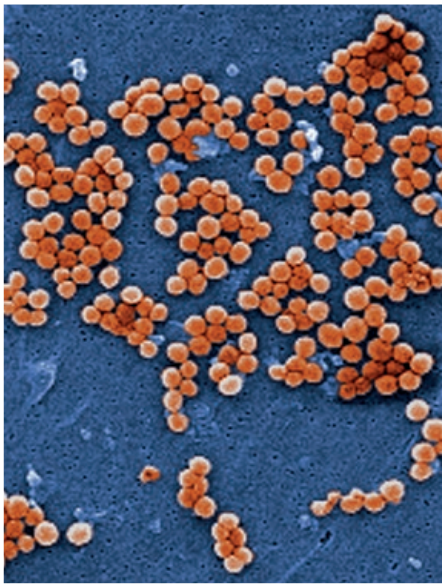
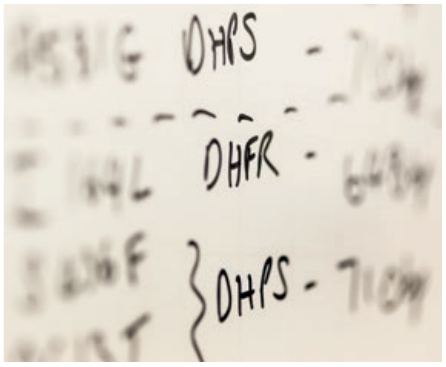


CENTRE FOR DIAGNOSTICS AND ANTIMICROBIAL RESISTANCE (CDAR)







ACCELERATING THE DEVELOPMENT OF NEW TOOLS TO CONTROL INFECTIOUS DISEASE

St George's University of London

INSTITUTE FOR INFECTION & IMMUNITY

CENTRE FOR DIAGNOSTICS AND ANTIMICROBIAL RESISTANCE

Our mission: "*to accelerate development, evaluation and implementation of simple, accessible and affordable diagnostic tests and interventions for infectious disease*"

The Centre for Diagnostics and Antimicrobial Resistance (CDAR), part of the Institute for Infection and Immunity at St George's, University of London (SGUL), focuses on:

- developing, evaluating and implementing new diagnostic devices
- understanding the origins, spread and impact of antimicrobial resistance.

A global challenge

Antimicrobial resistance is widely recognised as an urgent threat to world health. As well as new drugs, there is also a need to make best possible use of existing antimicrobial agents.

We are applying the latest molecular and genetic technologies to generate a better understanding of how antimicrobial use leads to the emergence and spread of resistance.

We have a complementary focus on diagnostics – central to effective antimicrobial management, enabling drugs to be tailored to patients' specific infections.

Integrating research and clinical practice

CDAR brings together basic scientists with clinical academics to form a centre that is highly focused on clinically oriented goals.

Close integration with our adjoining hospital, St George's University Hospitals NHS Foundation Trust, ensures that research is rooted in the realities of clinical practice and addresses clinical priorities, while also providing opportunities for evaluation and implementation within health systems.

A collaborative centre

As well as extensive academic and clinical links, we are also embedded in national and international networks for antimicrobial resistance surveillance and epidemiology, antimicrobial stewardship and healthcare policy.

Development and deployment of medical technologies demands an interdisciplinary approach, and CDAR is committed to working collaboratively with all sectors – academia, industry, clinicians, patients and the public, and health policy-makers – to deliver practical, reliable and clinically useful tools.

A track record in innovation

CDAR researchers have extensive experience in diagnostic development and evaluation, clinical trials and surveillance, across multiple types of pathogen and in both the developed and developing world.

Now, we aim to work with partners to exploit new technological opportunities to develop and deliver much-needed new diagnostics and interventions for key infectious diseases.

NETWORKING FOR SUCCESS

CDAR is committed to working collaboratively, with internal and external partners, with clinical colleagues and policy-makers, and across both academia and industry.

CDAR aims to maximise its impact by forging links with individuals, groups and companies with like-minded interests and complementary expertise. It is well-placed to respond rapidly to emerging threats and opportunities.

There is a strong culture of collaboration and sharing of information and expertise within the Centre, and within the wider SGUL Institute for Infection and Immunity. Our researchers also maintain close ties with collaborators in the UK, Europe and in low- and middle-income countries. These international links provide opportunities for extensive field-based work and evaluation of new diagnostic tools, as well as for clinical trials of new therapies.

Clinical partners…

Our close relationship with St George's Hospital roots our work in the everyday necessities of clinical practice. Our relationships with organisations such as the South London Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and Public Health England reinforce connections to clinical practice.

Policy connections…

CDAR researchers have excellent links with policy-makers and, internationally, to NGOs with an interest in diagnostics development. Our researchers are members of multiple national and international expert advisory groups and UK Department of Health Expert Advisory Committees. We also advise the Foundation for Innovative New Diagnostics (FIND).

Commercial partners…

We have established multiple productive partnerships with biotech companies in product development, and Centre researchers act as advisors for pharmaceutical companies.

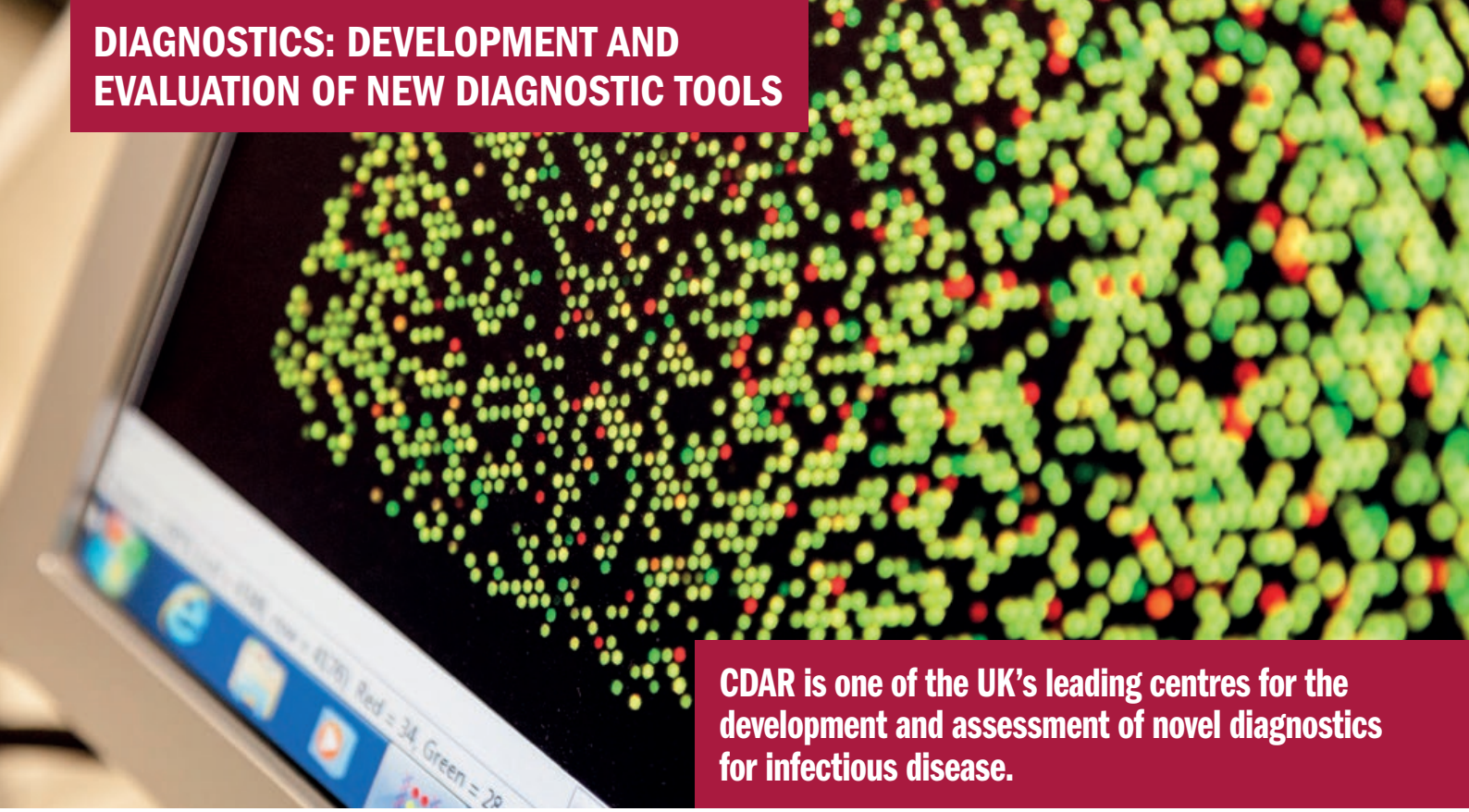
International links…

We have strong international connections, including clinical research partners throughout Europe and the USA and in sub-Saharan Africa, South-East Asia and South America.

Developing new links…

The Centre is keen to develop these relationships further in order to accelerate development and application of new diagnostics. We are committed to establishing laboratory systems compatible with industry standards to promote efficient collaboration, and to strengthening our interactions with clinical colleagues to more fully integrate research and practice. Ultimately, tackling the urgent threat posed by antimicrobial resistance will depend on effectively mobilising these interdisciplinary connections.

DIAGNOSTICS: DEVELOPMENT AND EVALUATION OF NEW DIAGNOSTIC TOOLS



CDAR is one of the UK's leading centres for the development and assessment of novel diagnostics for infectious disease.

The SGUL Institute for Infection and Immunity has a strong focus on the molecular basis of pathogen biology. Within CDAR, an important application of this knowledge is in the development of new diagnostics for some of the most important pathogens affecting the UK and developing countries.

CDAR has an extensive track record in diagnostic development (see Box) and CDAR researchers are currently leading a range of major collaborative initiatives developing new diagnostic tools for use in the UK and internationally. These address major health threats including malaria, TB and sexually transmitted infections. Our research has had important impact on diagnostic practices both within the UK NHS and globally.

Whole life cycle development

Our expertise spans all stages of the development and assessment of diagnostic devices. We have an exceptional **scientific base** for understanding and characterising pathogenic organisms, including the molecular basis of resistance.

We also have strong **clinical links**, enabling us to gain a deeper understanding of how resistance affects clinical practice, and how diagnostics need to be designed to integrate into health systems. These links provide an important platform for evaluating the performance of diagnostics in real-world settings.

CDAR has key input into the South London CLAHRC. It also has strong links to Public Health England. The lead public health microbiologist for London holds an honorary chair and is based at SGUL.

Development of novel diagnostic devices is based on fruitful **collaborations with technology-based companies**, combining our deep understanding of the molecular biology of pathogens and of antimicrobial resistance with novel technological applications.

CDAR scientists have recently established the Applied Diagnostics Research and Evaluation Unit, which provides a platform for evaluation of diagnostics in good clinical practice (GCP)-compliant laboratories and is building on networks of clinics providing access to tens of thousands of patient samples nationally and internationally. Furthermore, our extensive **international connections** provide opportunities for field-testing of devices.

A TRACK RECORD IN DIAGNOSTIC DEVELOPMENT AND EVALUATION

***pfmdr1* and antimalarial drug resistance**: Working in South-East Asia, Professor Sanjeev Krishna showed that amplification of the *Plasmodium falciparum pfmdr1* gene was associated with mefloquine resistance. This test for *pfmdr1* amplification has since been widely used to screen for resistance and incorporated into global monitoring carried out by the Worldwide Antimalarial Resistance Network (WWARN).

***Clostridium difficile* diagnostics**: A two-step testing protocol developed by Dr Tim Planche, validated in a large multicentre trial, overcomes significant shortcomings in *C. difficile* testing methods, and has become standard practice across the UK.

Nanotechnology for diagnosis: CDAR researchers are collaborating with technology companies to develop high-tech, low-cost diagnostic and resistance-profiling devices, for malaria, TB and sexually transmitted infections.

Cryptococcal diagnosis: Professor Tom Harrison has helped to develop and evaluate a novel assay of *Cryptococcus* infection in HIV patients. The diagnostic has been implemented as part of a screening and pre-emptive treatment strategy in South Africa and elsewhere.

*e*STI²: NEW TOOLS FOR SEXUALLY TRANSMITTED INFECTIONS

The *e*STI² consortium, uniting academia, industry and public health, is developing tools to transform care of people with sexually transmitted infections (STIs).

STIs typically occur together and interact with one another to cause particular disease syndromes. Ideally, diagnostic tools therefore need to be able to identify multiple pathogens, and characterise their drug resistance profiles. As well as achieving these aims, the multicentre *e*STI² consortium, led by Dr Tariq Sadiq, aims to use new technologies to fundamentally reshape the STI clinical care pathway.

With £5.7m funding from the UK Clinical Research Collaboration, and partners from academia, industry and Public Health England, the *e*STI² consortium is using 'lab-on-a-chip' technologies to develop rapid point-of-care diagnostics that will identify a suite of STIs and their antibiotic susceptibility. As well as handheld diagnostic 'readers', it is developing smartphone-based devices that will upload results to secure servers, supporting novel 'virtual care pathways'.

Through extensive engagement with public health physicians, clinicians and patients, the *e*STI² consortium is aiming to ensure that devices reflect the needs of both professional groups and patients, to ensure acceptability and promote take up.

The pioneering programme is also playing an important role in developing platform technologies for microbiological diagnosis and resistance profiling, and in building capacity in their evaluation and implementation within health systems.

*e*STI² has facilitated the development of the Applied Diagnostics Research and Evaluation Unit at SGUL, led by Dr Sadiq, which is staffed by clinical scientists, trial managers and clinicians. The Unit conducts diagnostic evaluations of novel diagnostic technologies in collaboration with industrial and academic partners in GCP-compliant laboratories.

NANOMAL: A FIELD-DEPLOYABLE DIAGNOSTIC FOR MALARIA

With €5.2m of EU funding, the public–private Nanomal partnership, led by Professor Sanjeev Krishna, has developed an innovative 'lab-on-a-chip' device to diagnose malaria and characterise its drug resistance profile.

Led from SGUL, the Nanomal Consortium brings together the expertise in malaria of Professor Krishna and academic partners at the Karolinska Institute in Sweden and Tübingen University in Germany and the innovative nanotechnological applications being developed by biotech company QuantuMDx (www.quantumdx.com).

Nanomal has developed prototype devices that can not only reveal the presence of malaria parasites within 15 minutes, but also identify the species of parasite present and its likely susceptibility to antimalarial drugs. The device is simple, robust and affordable enough to be used by healthcare workers in developing countries. Following successful laboratory demonstrations, prototype devices are due to be tested in the field. This platform can readily be adapted to deal with emerging pathogens such as Ebola virus.

The device is a point-of-care diagnostic, providing results while a patient waits. But it will also generate results important to wider surveillance of disease and drug resistance, and data will be transmitted to central repositories for collation and analysis.

www.nanomal.org

TWO-STEP DETECTION OF *C. DIFFICILE*

Irked by the inadequacies of *C. difficile* diagnostics, Dr Tim Planche proposed a novel two-step approach – since validated in a national trial and incorporated into national guidelines.

As St George's Hospital's clinical lead for microbiology, Dr Planche is intimately familiar with key issues in infection control and clinical diagnosis in a large and busy hospital. Splitting his time 50:50 between clinical practice and research, he can therefore ensure that research reflects clinical priorities and that clinical practice is rapidly informed by advances in research.

His work on *C. difficile* emerged from practical difficulties in detection of this important healthcare-associated infection. In a landmark 2008 systematic review, he and Professor Sanjeev Krishna characterised significant drawbacks in currently used laboratory methods. He proposed a two-step approach subsequently validated in a national study carried out with colleagues in Leeds, Oxford and UCLH, assaying more than 12,000 samples.

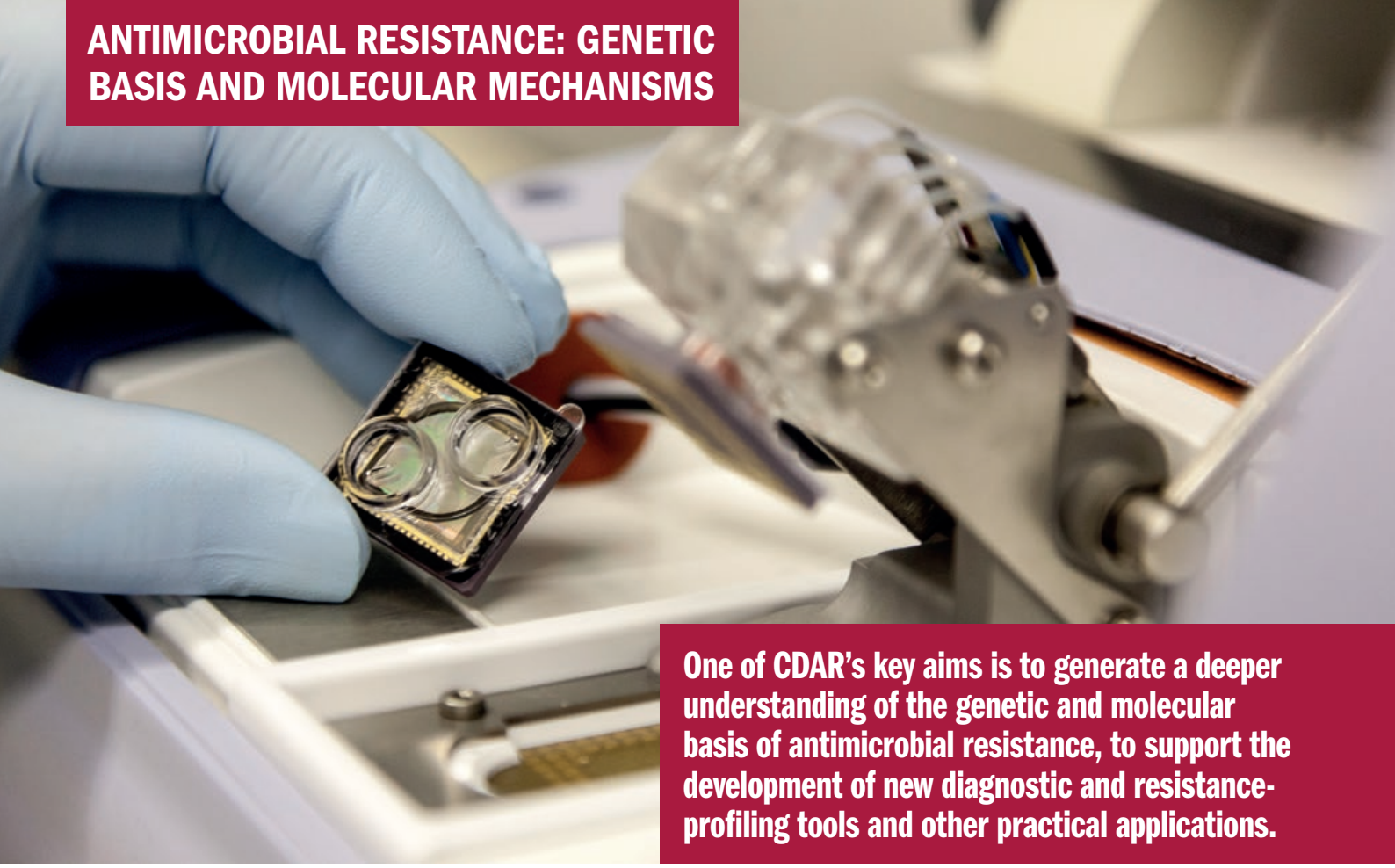
The study also provided important information on the links between the results of different assays and clinical outcomes, leading to improved understanding of disease. The new protocol is highly cost-effective, and has been incorporated into national guidelines for *C. difficile* testing.

Dr Planche and his team support the work of multiple other groups working on hospital infections, and liaise closely with the whole-genome sequencing facility run by Professor Philip Butcher. With St George's Hospital managing clinical microbiology services across South-West London, more than a million samples a year are now processed and potentially available for research.

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

Planche TD *et al*. Differences in outcome according to *Clostridium difficile* testing method: a prospective multicentre diagnostic validation study of *C difficile* infection. *Lancet Infect Dis*. 2013;13(11):936–45.

ANTIMICROBIAL RESISTANCE: GENETIC BASIS AND MOLECULAR MECHANISMS



One of CDAR's key aims is to generate a deeper understanding of the genetic and molecular basis of antimicrobial resistance, to support the development of new diagnostic and resistance-profiling tools and other practical applications.

CDAR is part of one of the UK's leading centres of research into the molecular characterisation of human pathogens. Our researchers are internationally renowned experts in their fields, with particular strengths in TB, malaria, cryptococcal infections and bacterial pathogens such as *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Clostridium difficile*.

Pathogen characterisation

At the heart of the Institute's work is a state-of-the-art microbial genomics facility, founded on the pathogen microarray initiative, **BμG@S**, led by **Professor Philip Butcher**. This facility supported the research of multiple groups in the UK and internationally working on human microbial pathogens. BμG@S has now expanded into whole-genome sequencing of pathogens and supports work across CDAR.

One important goal is to understand the genetic basis for antimicrobial resistance. We carry out functional studies of genes implicated in resistance, to inform drug development and to identify diagnostic markers. We also study the evolution and selection of resistant bacteria in diverse environments, to identify high-risk patient groups and to support antimicrobial stewardship programmes.

Integrating laboratory science and clinical practice

There is a strong translational focus to our work, and we aim to apply our knowledge, expertise and laboratory resources to enhance clinical practice – locally, nationally and internationally.

Our laboratory studies have a strong connection to clinical practice, particularly at St George's Hospital. We study aspects of resistance that are relevant to clinical practice and aim to understand how antimicrobial resistance impacts on the practical delivery of healthcare. This is practically enabled through our close ties and integration with the hospital's medical microbiology services.

Research collaborations

CDAR draws upon the expertise of other groups within the SGUL Institute for Infection and Immunity. Our researchers also maintain extensive networks of national and international collaborations in areas ranging from fundamental research to international phase III clinical trials.

We are a partner in the Wellcome Trust Bloomsbury Centre for Global Health Research, based at the London School of Hygiene and Tropical Medicine, linking the Centre to four of London's leading research institutions. We work closely with the Wellcome Trust Sanger Institute on pathogen genome studies and have strong ties with Public Health England's bacterial reference laboratories.

UNCOVERING MRSA'S SECRETS

Professor Jodi Lindsay's genomic studies are providing novel insights into DNA transfer in MRSA, and how it adapts to hospital environments.

Following a peak in the 2000s, the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in UK hospitals has declined markedly. As well as laboratory studies on plasmid transfer in MRSA, Professor Lindsay has uncovered a likely reason for this decline.

Having helped to sequence the first MRSA genome, she has gone on to identify a critical mechanism limiting the spread of antibiotic resistance genes via plasmids and other genetic elements. While plasmids containing resistance genes are readily shared within an MRSA clonal group, they are rarely transmitted between them. The reason, Professor Lindsay discovered, is the strain specificity of the Sau1 system, part of MRSA's defence against phage, which targets 'foreign' plasmids for destruction.

Were it not for this mechanism, multidrug-resistant MRSA might be an even bigger healthcare problem. However, some plasmids lack Sau1 target sites, enabling them to be shared more widely, and plasmid exchange may be more common than previously thought. Strains that have acquired plasmids tend not to persist, probably because they are out-competed by existing strains – emphasising the importance of selective pressures in microbial survival.

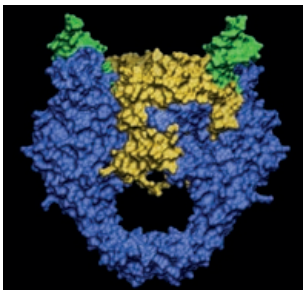
These findings are supported by Professor Lindsay's clinically orientated research. An analysis of ten years' MRSA data from St George's Hospital pointed to changing prescription practice, rather than screening or better infection control, as the key factor behind the drop in MRSA. Reduced use of fluoroquinolones, to minimise *Clostridium difficile* infections, may also have removed a selective pressure that previously favoured the growth of fluoroquinolone-resistant MRSA.

Roberts GA *et al*. Impact of target site distribution for Type I restriction enzymes on the evolution of methicillin-resistant *Staphylococcus aureus* (MRSA) populations. *Nucleic Acids Res*. 2013;41(15):7472–84.

Knight GM *et al*. Shift in dominant hospital-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) clones over time. *J Antimicrob Chemother*. 2012;67(10):2514–22.

TARGETING DNA TOPOISOMERASES

Professor Mark Fisher and colleagues have identified key mechanisms in the inhibition of DNA topoisomerases by fluoroquinolones.



DNA topoisomerases are critical to cell division, ensuring that DNA duplexes do not become entangled as chromosomes are duplicated and separated. They work by temporarily creating stable double-strand breaks, or 'gates', in DNA through which a DNA duplex can be passed. In collaboration with Dr Mark Sanderson at King's College London, Professor Fisher has not only revealed key molecular details of this fundamental process, but also shown how it is affected by antibiotic inhibitors.

In bacteria, the key DNA topoisomerase in cell division is topoisomerase IV (topo IV). Crucially, this enzyme is the target of fluoroquinolone antibiotics such as moxifloxacin and clinafloxacin. Over the past decade, Professor Fisher and Dr Sanderson have generated increasingly detailed structures of enzyme–DNA cleavage complexes interacting with fluoroquinolone molecules. These studies have provided key insight into the mechanisms of inhibition.

In addition, Professor Fisher has examined another notable feature of topo IV activity, its DNA site specificity. Using mutant forms of cleavage sites and a novel competition assay, he has been able to probe the sequence characteristics of sites preferentially targeted by fluoroquinolones.

These studies have provided important clues to the mechanism of action of an important class of antibiotic. They are suggesting new ways a critical bacterial target, topo IV, could be targeted, and are shedding light on mechanisms of resistance and how they might be overcome.

Laponogov I *et al*. Structural insight into the quinolone-DNA cleavage complex of type IIA topoisomerases. *Nat Struct Mol Biol*. 2009;16(6):667–9.

Laponogov I *et al*. Structural basis of gate-DNA breakage and resealing by type II topoisomerases. *PLoS One*. 2010;5(6):e11338.

Arnoldi E, Pan XS, Fisher LM. Functional determinants of gate-DNA selection and cleavage by bacterial type II topoisomerases. *Nucleic Acids Res*. 2013;41(20):9411–23.

Laponogov I *et al*. Structure of an 'open' clamp type II topoisomerase-DNA complex provides a mechanism for DNA capture and transport. *Nucleic Acids Res*. 2013;41(21):9911–23.

UNDERSTANDING RESISTANCE IN *CRYPTOCOCCUS*

Dr Tihana Bicanic and colleagues are generating much-needed information on the emergence of drug resistance in the opportunistic fungal pathogen *Cryptococcus*.

Cryptococcal meningitis is responsible for a high proportion of AIDS-related deaths in Africa. Although it has drawbacks, fluconazole is often used to treat *Cryptococcus* infections, but treatment is often hampered by the development of resistance.

Dr Bicanic's team is tracking the emergence of fluconazole resistance over time in a cohort of Tanzanian patients. Laboratory findings are being compared with the results of treatment, to explore associations between levels of resistance seen *in vitro* and treatment effectiveness.

This provides valuable information to clinicians, revealing clinically relevant levels of *in vitro* resistance liable to lead to treatment failure.

Such work has to be carried out in the field as, unusually, fluconazole-resistance mechanisms in *Cryptococcus* are deactivated in the absence of the drug. The field samples will also be used to explore genomic changes that have been associated with gain and loss of resistance in mouse models of cryptococcal infection, such as amplification of certain regions of the *Cryptococcus* genome.

Sabiiti W *et al*. Efficient phagocytosis and laccase activity affect the outcome of HIV-associated cryptococcosis. *J Clin Invest*. 2014;124(5):2000–8.

TRANSLATIONAL OPPORTUNITIES: EXPLOITING NEW KNOWLEDGE OF ANTIMICROBIAL RESISTANCE

CDAR's expertise in molecular microbiology and antimicrobial resistance is underpinning multiple translational initiatives.

Building on the exceptionally close integration between clinical practice and laboratory research, our partnerships with industry, and our national and international connections, there are numerous routes through which our work has practical impact.

Drug development…

A greater understanding of pathogen biology is underpinning the development of new antimicrobial agents. In addition, our work on the mechanisms of resistance is providing insight to guide the development of new compounds to overcome resistance.

Professor Anthony Coates, for example, has pioneered a new approach to antibiotic development, targeting 'quiescent' non-multiplying cells. Compounds being commercialised through a spinout company, Helperby Therapeutics Ltd, are showing great promise as 'antibiotic resistance breakers' – rescuing antibiotics rendered ineffective by the development of resistance.

More generally, our researchers have extensive experience of clinical trials assessing new therapies and refined treatment protocols, in the UK and internationally.

Infection control and treatment…

A further important application has been efforts to characterise outbreaks of healthcare-associated infections. Molecular characterisation of isolates can shed light on transmission pathways and inform infection control. We have made important contributions to understanding *Pseudomonas aeruginosa* and *Enterobacter* outbreaks at St George's Hospital, and the spread of *Pseudomonas* across London.

Increasingly, characterisation of antibiotic resistance profiles in diseases such as TB is helping to guide treatment of individual patients at St George's Hospital. We have used whole-genome sequencing to characterise extremely drug-resistant (XDR) TB in clinically relevant timeframes, to guide clinical decision-making and shed light on possible routes of transmission.

Tracking resistance…

Molecular characterisation can provide important information on the make up of bacterial populations in natural environments, and how they are affected by interventions such as antibiotic use or new vaccine programmes.

To achieve this molecular surveillance, the '**BUGS Bioscience**' spinout company has developed molecular serotyping tools, initially for *Streptococcus pneumoniae*. These tools have been validated and are being used to monitor the impact of several international pneumococcal vaccination programmes.

Antibiotic stewardship and policy-making…

CDAR includes researchers who are national and international leaders in the field of antimicrobial resistance in paediatric infectious disease. **Professor Mike Sharland** and **Professor Paul Heath** are involved in numerous initiatives documenting the changing nature of infections affecting infants and children, mapping the spread of antimicrobial resistance, and identifying the most effective treatments. Both have made many important contributions to the development of recommended clinical practice and health policy, to optimise antimicrobial use and minimise the development of resistance.

RAPID GENOMIC ANALYSIS SUPPORTING CLINICAL MANAGEMENT

Professor Philip Butcher and colleagues are harnessing the power of genomics to guide treatment and support hospital infection control.

Close integration of research and clinical practice is enabling the latest genome sequencing tools to be applied to real clinical problems, over clinically relevant timescales. As well as supporting research across the Centre, a state-of-the-art bacterial genome sequencing facility, led by Professor Butcher, can respond rapidly to clinical priorities at St George's Hospital.

Sequencing of *M. tuberculosis* clinical isolates, for example, identified mutations affecting drug sensitivity within a matter of days, enabling clinicians to choose the most appropriate drug regime for patients.

Whole-genome sequencing also has an important role in outbreak control. The facility characterised a series of cases of *Pseudomonas aeruginosa* infection, tracking drug-resistant organisms across the hospital and identifying possible sources of infection. This experience also enabled Professor Butcher's colleague, Dr Adam Witney, to contribute to a Public Health England investigation of *P. aeruginosa* infection across London.

By contrast, analysis of a series of *Enterobacter* infections suggested they were not related and did not represent an outbreak – avoiding the disruption and financial cost of unnecessary ward closure.

Professor Butcher and his team are working with clinicians to integrate genomic analysis tools more fully into routine hospital practice and infection control.

Witney AA *et al*. Genome sequencing and characterization of an extensively drug-resistant sequence type 111 serotype O12 hospital outbreak strain of *Pseudomonas aeruginosa*. *Clin Microbiol Infect*. 2014;20(10):O609–18.

Witney AA *et al*. Clinical application of whole-genome sequencing to inform treatment for multidrug-resistant tuberculosis cases. *J Clin Microbiol*. 2015;53(5):1473–83.

MOLECULAR SURVEILLANCE OF INFECTIOUS DISEASES

A new spinout company, led by Dr Jason Hinds, is harnessing the power of microbial genomics to assess the impact of international vaccine campaigns.

Streptococcus pneumoniae is responsible for 1.6 million deaths a year. Current pneumococcal vaccines are effective against only a subset of strains, or serotypes, and identifying which serotypes are circulating in a population and causing disease is important when assessing the effectiveness of vaccine programmes.

The Institute's BμG@S team has world-leading expertise in microbial genomics, and has developed a microarray-based molecular serotyping tool for *S. pneumoniae*. In an international methods evaluation, the molecular serotyping tool was the leading method, and proved highly effective at detecting multiple pneumococcal serotypes in clinical samples. This approach has been used globally, to support major vaccine development and surveillance programmes, with academic collaborators and commercial partners.
The method is being rolled out to two satellite centres, in Melbourne and Johannesburg, to further evaluate and extend its use.

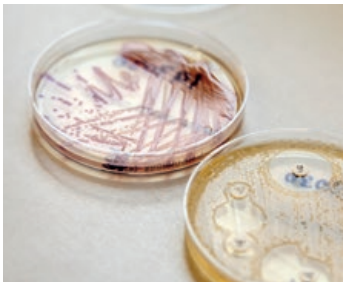
BUGS Bioscience

To meet increasing demand, secure further investment and develop novel applications, a new spin-out company has been established, led by Dr Jason Hinds. Set up with the support of SGUL's Enterprise Office, BUGS Bioscience is a collaborative, not-for-profit enterprise, working with international pharmaceutical companies and NGOs. Its initial focus is on molecular serotyping services but will further apply genomics technologies and integrated software solutions to support molecular surveillance of infectious diseases, addressing global health issues such as vaccine impact and antimicrobial resistance.

http://bugsbio.org/

ANTIMICROBIAL RESISTANCE IN CHILDREN

Through the EU ARPEC programme, Professor Mike Sharland has led research shedding important light on antibiotic-prescribing practice and antibiotic resistance across Europe.



Bringing together 15 partners in 11 EU countries, ARPEC (Antibiotic Resistance and Prescribing in European Children) identified examples of both extensive overuse of antibiotics and under-dosing. It also uncovered a highly variable picture of antibiotic resistance across Europe, geographically and across age groups. Multidrug-resistant Gram-negative infections were identified as a particular issue.

As well as informing new antibiotic stewardship programmes, the project has also developed new training materials for paediatricians to promote good antibiotic use, and fed into multiple international initiatives collecting information on antibiotic use and resistance in children.

Professor Sharland has also led and been part of many other European collaborations aiming to optimise antibiotic treatments and monitoring antibiotic resistance. He is highly active in policy circles, particularly as Chair of the UK Department of Health Expert Advisory Committee on Antimicrobial Resistance, Prescribing and Healthcare-Associated Infection. He has also been an advisor to the European Centre for Disease Control and Prevention and, locally, chairs the infection theme of the South London CLAHRC.

http://arpecproject.eu

CDAR PEOPLE

CDAR is founded on the expertise of 14 leading SGUL researchers with research interests in diagnosis and treatment of infectious disease, and in understanding mechanisms of antimicrobial resistance.

= Bacteria = Virus

= Fungus = Parasite

Centre Lead
Professor Sanjeev Krishna

Additional Centre Contact
Professor Jodi Lindsay

Sanjeev Krishna
Treatment of malaria, mechanisms of antimalarial drug resistance and malaria diagnostic development, sleeping sickness, TB.

Jodi Lindsay
Staphylococcus aureus genetics and resistance.

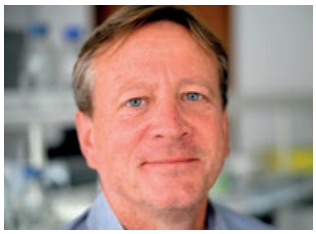
Tihana Bicanic
Fungal pathogens and invasive fungal infections, in particular *Cryptococcus neoformans* and cryptococcal meningitis.

Philip Butcher
Genomic analysis of *M. tuberculosis* and molecular diagnostics.

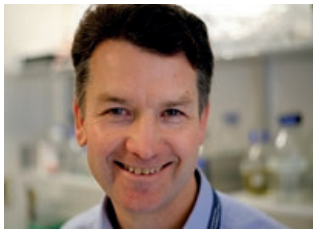
Anthony Coates
Antibiotic discovery and development; tuberculosis; founder of Helperby Therapeutic Group Ltd.

Phil Cooper
Allergy epidemiology and helminth parasites – diagnosis, host response and treatment.

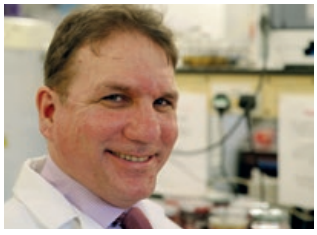
Mark Fisher
DNA topoisomerases, catalytic mechanisms and potential as antimicrobial drug targets.



Tom Harrison
Cryptococcus pathophysiology, management and prevention, and TB chemotherapy.

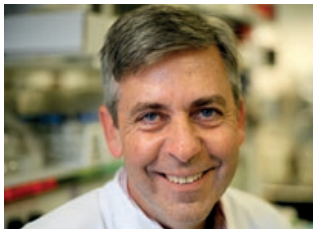


Paul Heath
The epidemiology of paediatric vaccine-preventable diseases, clinical vaccine trials, and perinatal infections.



Tim Planche
Healthcare-associated infections, antimicrobial resistance and diagnostics.

Tariq Sadiq
STI pathogenesis, diagnostics for point-of-care antimicrobial profiling, e-health and personalised medicine.



Mike Sharland
Antimicrobial use and resistance in children.

Henry Staines
Drug development, resistance mechanisms and diagnostics for malaria and other neglected pathogens.

Irina Chis Ster
Statistical and mathematical methodologies applied to epidemiological and clinical infectious diseases data.

WORK WITH US...

We are open to collaborative ventures of all kinds, and we welcome opportunities to work with other organisations, including academic and commercial partners, that share our aims. We have expertise across all types of pathogen.

Viruses: HIV, Ebola, in Europe and Africa.

Bacteria: Multiple Gram-negative and Gram-positive pathogens, particularly *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Clostridium difficile* and bacterial sexually transmitted infections.

Fungi: *Cryptococcus* in the UK and Africa.

Protozoan parasites: Malaria in South-East Asia and Africa, human African trypanosomiasis.

Multicellular parasites: Helminth worm infections in Ecuador.

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