AMR

Tackling Antimicrobial Resistance

Antimicrobial Resistance:

How Research is Tackling the Challenge

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Foreword

Antimicrobial resistance (AMR) is now recognised as one of the most serious global threats to human health in the 21st century, with the resistance of bacteria to antibiotics increasingly spreading from one country to the next.

Research continues to be crucial to tackling AMR, which arises from a complex interplay between biological, economic, cultural, environmental, and technical factors. By preventing infections, preserving existing antibiotics and promoting the development of new therapies and interventions, we will reduce the development and impact of AMR.

An interdisciplinary approach is crucial for making a step-change in addressing AMR. As Executive Chair of the Medical Research Council (MRC), I am proud of the strategic direction we are providing in this area, establishing the UK AMR Funders Forum (AMRFF) and leading the AMR Cross-Council Initiative, alongside our fellow research councils.

The UK Research and Innovation (UKRI) AMR Cross-Council Initiative has so far invested £85 million in vital projects that are increasing our knowledge and understanding of AMR. Meanwhile, the AMRFF brings together 21 research funders, including UKRI councils, government departments, devolved administrations and charities, to improve co-ordination of research and co-operation between funders. AMRFF members span research disciplines and work with international partners and industry. By sharing information, we reduce duplication of effort and maximise the impact of investments.

The UK is already a global leader in combatting AMR, but we can do more. The key to maintaining the UK research position, and indeed delivering a step-change, is in identifying the relative importance, interactions, health and economic impacts of different sources, drivers and transmission routes of AMR. This will allow government, practitioners and industry partners to identify, prioritise and pilot cost-effective and sustainable interventions.

We must also support co-ordinated AMR related research on priority areas, continue to develop interdisciplinary networks across all sectors, and further develop the scientific capacity needed to support and deliver high-quality research in infectious disease, prevention and microbiology-related disciplines.

Finally, addressing the global nature of AMR goes well beyond the production of new antibiotics and therapies. Reducing inappropriate use of antibiotics in developing and developed countries through public awareness, infection control, and good surveillance in humans, animals and the environment are crucial. Ensuring access to appropriate antibiotics, clean water and improved sanitation will help reduce the spread of infection and generation of AMR in lower income countries. We must continue to influence global research strategies on AMR, ensuring the alignment of UK-funded research, and emphasising the need for research that is useful for front-line teams.

Professor Fiona M. Watt,
MRC Executive Chair

Introduction

The MRC launched the AMR Cross-Council Initiative in 2014 in response to the UK AMR Strategy 2013-2018. It is considered by other funders within Europe, India and China as a model of successful collaboration in addressing major research and societal problems.

With the first phase of research activity now underway, and the launch of the UK 20-year vision and five-year AMR National Action Plan for 2019-2024, this brochure showcases how we have fostered collaboration and information-sharing between diverse stakeholders to build capacity and support interdisciplinary AMR research.

The AMR Cross-Council Initiative is working across four research themes:

- Better understanding resistant bacteria
- Accelerating therapeutic and diagnostic development
- Understanding real-world interactions
- Investigating how behaviour of the public, professionals and organisations impacts AMR

Between 2014 and 2018, the AMR Cross-Council Initiative has supported 78 interdisciplinary projects at a total commitment of £44m, and, in recognition of the global dimension of antibiotic resistance, has committed £41m to support projects in partnership with members of the EU Joint Programme Initiative in AMR (JPIAMR), with emerging economies, and in low- and middle-income countries.

The case studies in this brochure demonstrate the evolving impact of the AMR Cross-Council Initiative, illustrating the interdisciplinary, global “One Health” approach we take to tackling AMR, encompassing people, animals, agriculture and the wider environment, as well as drug development.

University of Edinburgh, Professor David Dockrell

Shield Consortium – Optimising Innate Host Defence to Combat AMR

The SHIELD consortium is an AMR cross-council funded consortium focused on new strategies to combat AMR by enhancing the most effective natural defence systems of the human body. It brings together over 20 researchers from four UK universities, and is led by Professor David Dockrell at the University of Edinburgh.

Not everyone exposed to harmful bacteria develops an illness, because they have an effective natural response to infection, with immune cells (the body's defence cells) 'consuming' and killing harmful bacteria.

The Consortium are developing new methods to identify and understand the key features of normally effective natural host responses, to explore how they might be enhanced in relevant patient groups at risk of infection.

Treatments designed to boost or block aspects of our natural defence system are potentially a viable approach to combatting AMR, and the Consortium are working with industry partners to help identify new drugs that can enhance the natural immune response to target resistant infections.

Ultimately, the aim is to develop a host response-based strategy, which targets an individual's underlying susceptibility to infection, as an approach to limit exclusive reliance on antibiotic therapy.

King's College London, Professor David Demeritt

Animal Husbandry, Prescribing Practices and the Control of Veterinary Medicines and AMR in Colombia's 'Livestock Revolution'

As livestock numbers have risen globally, so too has the use of antibiotics in animal husbandry. Veterinary medicine has played a major role in reducing disease and increasing productivity, but the prevalent use of antibiotics in livestock production strongly favours the emergence of antibiotic-resistant bacteria. This poses serious risks to both human and animal health.

In common with many low- and middle-income countries, livestock production in Colombia has sharply risen in response to a rapidly growing domestic demand. Although this “livestock revolution” promises to enhance food security and improve rural livelihoods, there are also questions about its sustainability and impact on human health.

Researchers from King’s College London are hoping to understand the behavioural factors influencing the control and use of veterinary medicine in Colombia. They are investigating how local animal husbandry methods, regulatory systems and prescribing practices impact on the risk of AMR and intend to build a wider network to support behavioural changes that improve the prescription and regulation of antibiotics across Latin America.

By providing vital evidence about how veterinary medicines are controlled and used, this work will support international efforts to alleviate poverty in low- and middle-income countries and address a major contributing factor in the emergence of AMR.

University of Southampton, Professor Timothy Leighton

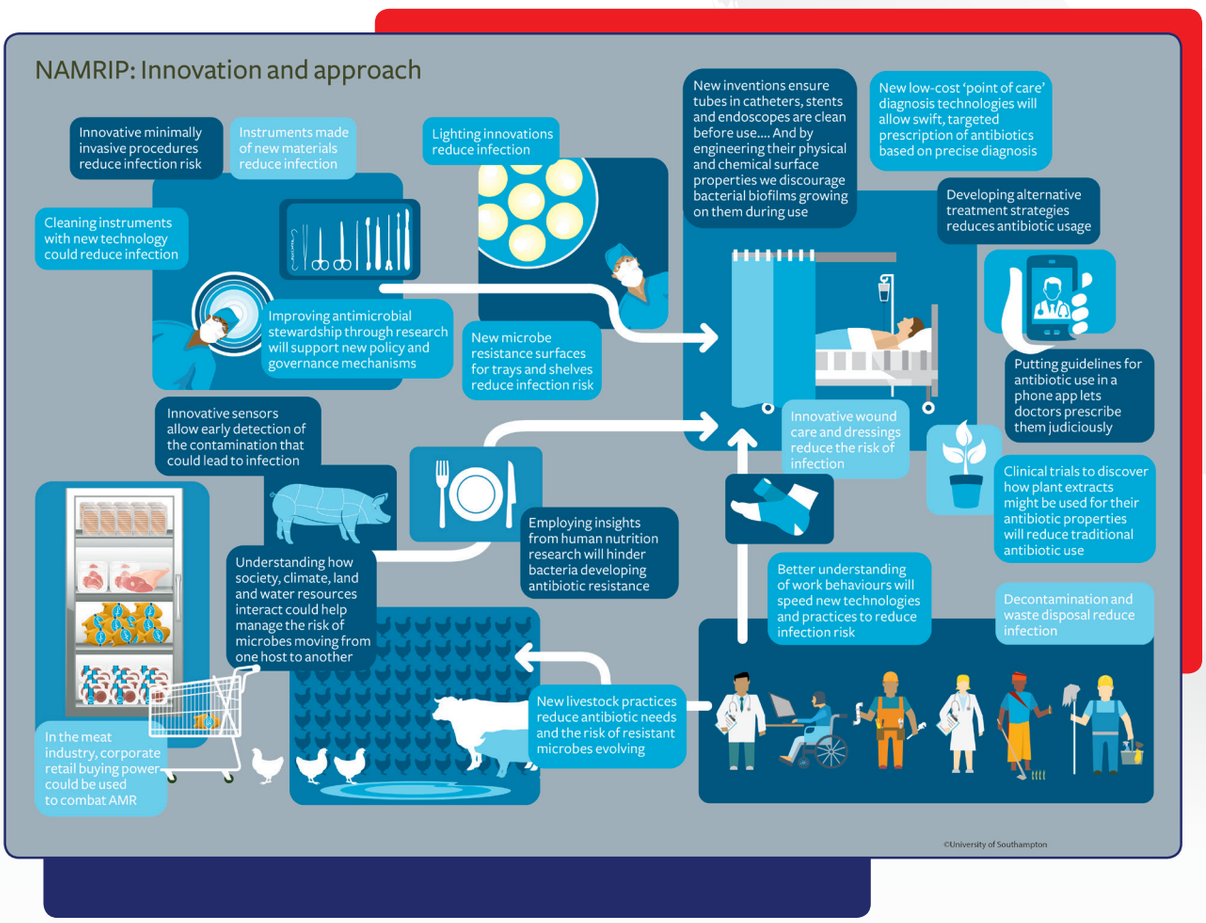
Network for Anti-Microbial Resistance and Infection Prevention

AMR has become one of the most complex public health threats of our time, involving sectors ranging from health, agriculture and the environment to finance and trade. Addressing the threat of AMR requires a “One Health” approach, with multiple disciplines collaborating at local, national and global levels.

The Network for AMR and Infection Prevention (NAMRIP) at the University of Southampton aims to produce ground-breaking advances in tackling AMR. Research falls into five themes exploring preventing infection, understanding AMR, developing new diagnostics and medicines, improving water quality, and studying human and animal behaviour. Research teams bring together clinicians, engineers and researchers from health, social, biological and physical sciences, as well as experts from industry, charities and policy-making bodies. Dedicated policy and public engagement teams enable NAMRIP to push for impact, and the Global-NAMRIP network aims to tackle AMR in low- and middle-income countries.

Current NAMRIP projects include a new system to more accurately model conditions in tuberculosis patients after taking antibiotics, and a collaboration between two research groups in Medicine and Engineering working alongside the Indian Institute of Technology. Another project is “StarStream”, a device that generates ultrasonic bubbles from water to effectively clean surfaces without requiring heat, now about to be piloted in the NHS.

NAMRIP has enabled academics from across research disciplines to share their knowledge, make new connections and work together to tackle AMR. Future multi-disciplinary collaborative approaches will be necessary to combat this threat to global health.



University of Exeter, Professor William Gaze

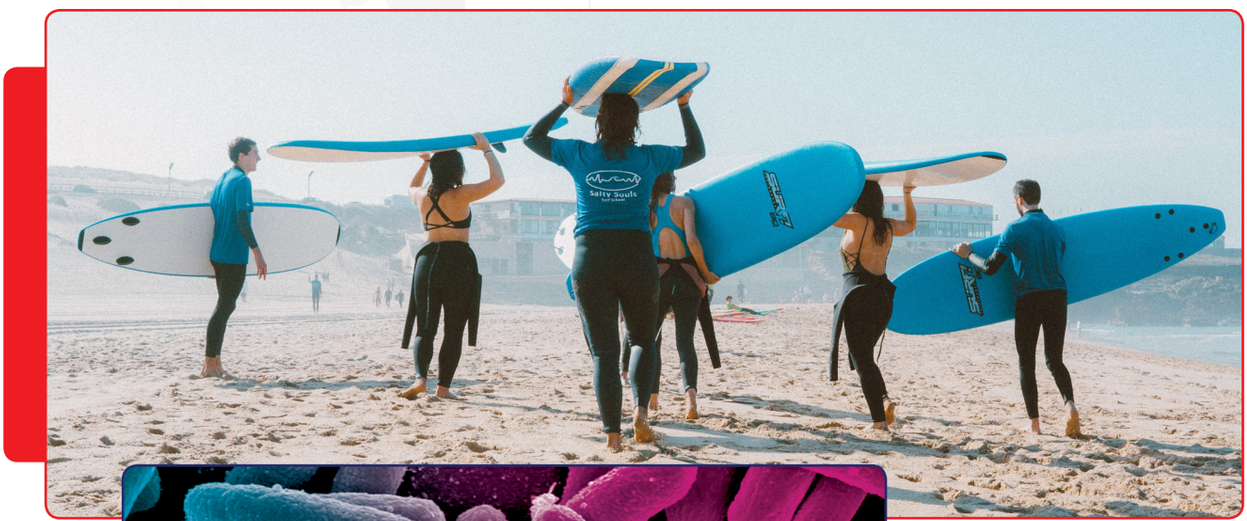
Beach Bums: Examining Antibiotic-Resistant Bacteria in UK Coastal Waters

AMR is most often considered within a healthcare setting, yet exposure to potentially harmful bacteria also occurs through the natural environment. UK coastal locations are visited by millions of people every year, where they come into direct contact with bacteria that have been washed into the sea through sewage and water pollution, such as water run-off from farm crops treated with manure.

The Beach Bums study tested whether surfers were more vulnerable to the bacteria that pollute seawater, and whether these bacteria were resistant to antibiotics. They asked 300 people, half of whom regularly went surfing, to provide rectal swabs, and compared the samples from surfers and non-surfers.

The study, published in January 2018, found that regular surfers and bodyboarders are three times more likely to carry antibiotic-resistant Escherichia coli (E. coli) bacteria in their gut than non-surfers. The E. coli bacteria were resistant to cefotaxime, a commonly used and clinically relevant antibiotic. The study also found that surfers are particularly susceptible to ingesting the bacteria because they swallow up to ten times more seawater than sea swimmers. Regular surfers were also found to carry four times more bacteria containing mobile antibiotic-resistant genes, which can be passed easily between bacteria.

Recognising coastal waters as a pathway for antibiotic resistance is a step towards understanding AMR transmission dynamics. By learning how the natural environment influences this process, we can support future approaches to protect human health.



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Glasgow School of Art, Professor Alastair Macdonald

Vision-On: A Staff Training Tool for the Prevention of Healthcare-Associated Infections

Healthcare-associated infections (HAIs) are a significant problem within the NHS. In addition to causing significant distress to patients, they also lead to increased morbidity, mortality and financial cost due to longer hospital treatment and isolation of infected individuals. With the rise in AMR, preventing the spread of infectious agents has become of increasing importance.

The Vision-On project aimed to develop a tablet-based training tool for healthcare staff to help prevent and control the spread of HAIs. Developed over 12 months with the involvement of GAMA Healthcare Ltd., two NHS Trusts and over 100 healthcare staff, the prototype uses dynamic visualisations of data on pathogens, making it possible to “see” pathogen location, survival and transmission in a virtual ward.

Testing of the prototype found that its interactive and navigable platform offered staff a new perspective on AMR transmission. The tool was also found to be relevant for different staff cohorts with diverse experience levels, providing explanations for infection prevention and control procedures, reinforcing understanding of HAIs, and raising awareness about infectious agents.

New creative platforms such as this, that draw on knowledge from beyond traditional biomedical science, will help to control HAIs and prolong the effectiveness of current antibiotics.

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London School of Hygiene and Tropical Medicine, Professor Clare Chandler

Fresh Approaches to the Study of Antimicrobials in Society (AMIS)

The way in which we use medicines often depends on how our societies, politics and economies work. As a result, we need to understand the context of antimicrobial use and the consequences of AMR to uncover the best approaches to reduce the threat of resistance.

The Antimicrobials in Society (AMIS) Hub is an online resource, curated by the London School of Hygiene and Tropical Medicine, that brings together AMR research across different social science disciplines. The AMIS Hub materials include research summaries, blogs, and reviews of existing and ongoing research and theory. The resource is aimed at funders, life scientists and policy-makers to engage with social science on this issue, promote future collaborations and inspire new approaches to tackle AMR.

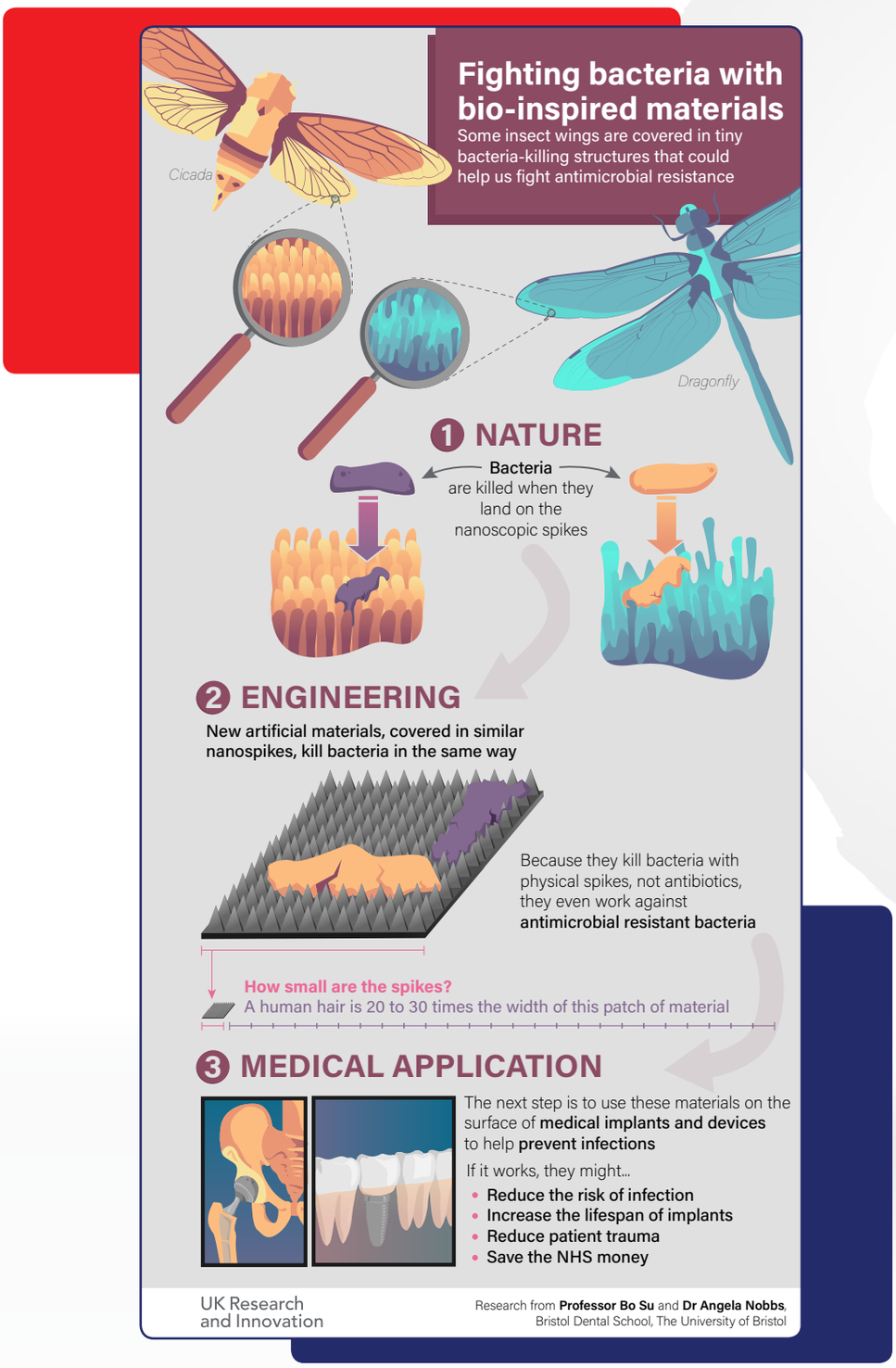
The AMIS programme also includes two research projects in Thailand and Uganda that focus on mapping antibiotic use and the networks that antibiotics travel within, as well as understanding the roles that antimicrobials play in society and everyday life, how they are used and the reasons for reliance on these drugs.

The AMIS programme opens up new avenues in the field of AMR research, drawing on novel research tools from anthropology and collaborating with diverse stakeholders to understand the impact of AMR as a global issue that spans cultural and societal boundaries.

Bristol Dental School, The University of Bristol, Professor Bo Su and Dr Angela Nobbs

Fighting Bacteria with Bio-inspired Materials

A team at Bristol Dental School has been inspired by the antibacterial properties of cicada and dragonfly wings. They're replicating their bacteria-killing nano-spiked surfaces in materials such as titanium and polymers, with the aim of using them for common medical implants. With a rapidly ageing population and nearly a quarter of a million hip replacements already taking place in the UK each year, stopping infection in its tracks in this way would reduce patient trauma and save the NHS millions of pounds.



Demuris Limited

Kanglemycin A: A Naturally-occurring Antibiotic Active Against Drug-Resistant Tuberculosis

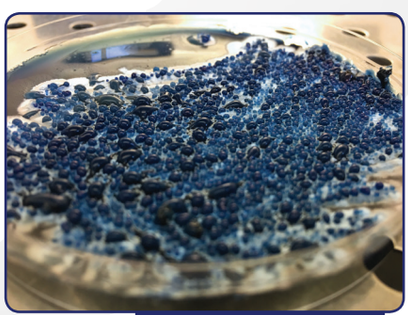
Every year, approximately 10 million people fall ill with tuberculosis (TB), leading to an estimated 1.7 million deaths worldwide. One of the main antibiotics used to treat TB is rifampicin, but many strains of the TB-causing bacterium, Mycobacterium tuberculosis, have developed resistance to it. Approximately 600,000 people every year are diagnosed with rifampicin-resistant tuberculosis, but the treatment success rate is only 54 per cent.

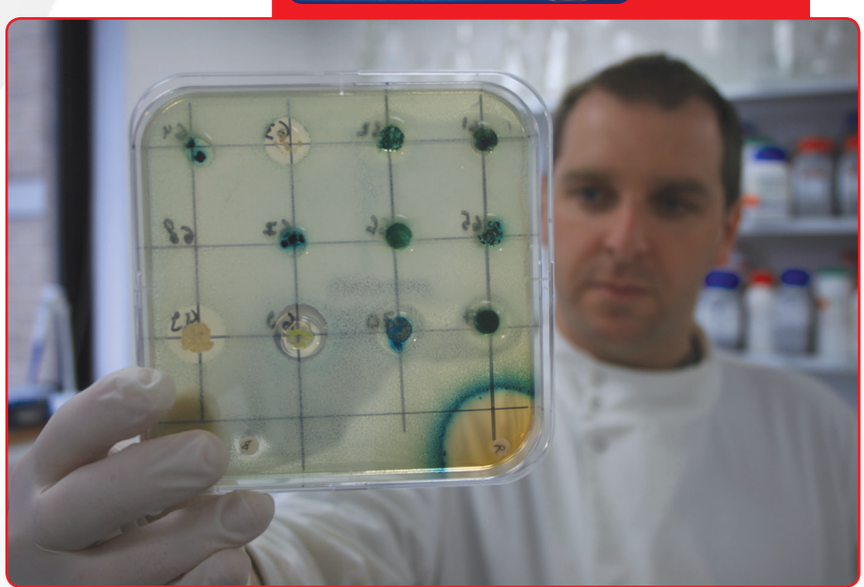
Researchers from Demuris Ltd and Newcastle University have identified a naturally-occurring antibiotic, kanglemycin A, that is active against Mycobacterium tuberculosis. The compound was found through a screen of more than 2,000 extracts from a collection of actinomycete bacteria provided by Demuris. The Actinomycetes are a group of soil-dwelling bacteria that specialise in making natural-product compounds to kill or manipulate the behaviour of surrounding organisms, including bacteria, fungi, plants and animals.

Further testing showed that kanglemycin A works by binding to an essential bacterial enzyme called RNA polymerase, but crucially not the human version. In addition, the compound was shown to be related to rifampicin but had greater antimicrobial activity.

These findings are the first step towards developing a new, effective drug treatment for patients with rifampicin-resistant TB. By supporting research in drug discovery, we can accelerate the development of new therapies to combat drug-resistant infections.

Demuris





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University of Warwick, Professor Christopher Dowson

Accelerate CHNUK: Establishing joint UK-China Training and Research Platforms for Drug Discovery

AMR is a growing threat to global public health worldwide. In China, the high prevalence of resistance to the antibiotic carbapenem is responsible for many life-threatening infections in hospitals, and resistance has recently emerged in E. coli to the drug of last resort, colistin.

In 2015, Professor Dowson and collaborators were awarded £3.19m from the AMR Cross-Council Initiative and £1m from the Newton Fund to investigate a vital link in the chain of antimicrobial resistance – the bacterial cell wall. This landmark project pulls together a unique group of world leaders in bacterial chemistry, genetics, physics and physiology in the area of peptidoglycan metabolism, structure and architecture. Academia, the pharmaceutical industry and charities are working hand in hand, on a global scale with national synchrotron facilities at Harwell, UK and Shanghai, China, in the hope of unlocking new types of antibiotics.

The Diamond Light Source at Harwell

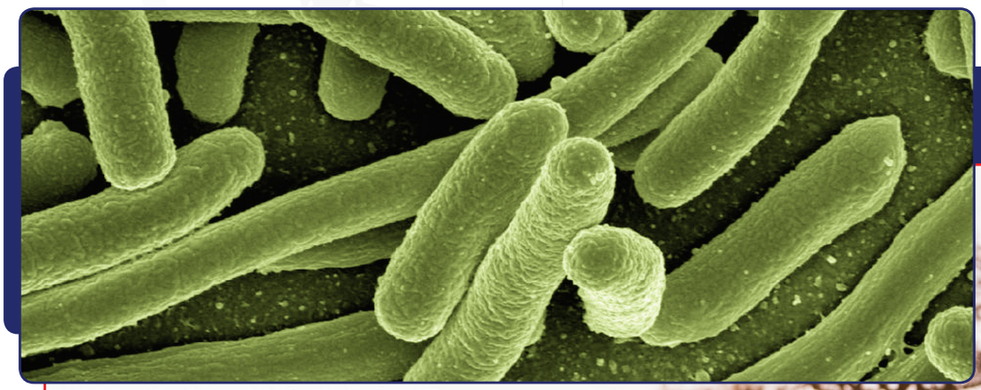
Cardiff University, Professor Timothy Walsh

Determining the Clinical and Environmental Impact, Burden and Cost of Extensively Drug Resistant Enterobacteriaceae in China

Professor Tim Walsh at the University of Cardiff worked with the Chinese Government to help implement a ban on using the last-resort antibiotic colistin in animal feed. Professor Walsh and his team had previously identified in China a new gene called MCR-1 that gave bacteria resistance to colistin. China was one of the world's biggest users of colistin in agriculture, primarily in animals feed as a growth-pro moter. It is likely that colistin resistance evolved in this context. The ban has resulted in the withdrawal of more than 8,000 tonnes of colistin.

Following on from this discovery and using the same network of Chinese colleagues, hospitals and faming sectors, Professor Walsh and his team are using MCR-1 (MCRPE) and carbapenem-resistant Enterobacteriaceae (E. coli and E. coli-like bacteria) (CRE) as markers to understand how colistin resistance has spread throughout the Chinese animal population.

Unlike previous studies, this study is deliberately holistic in its approach, in order to understand the dynamics and transmission of AMR across a broad range of environmental and human sectors. This study is increasing our understanding of the impact of CRE and MCRPE on human populations, and the burden and cost to the Chinese health system. It will also help us understand the impact of AMR on the chicken and pig trade by using mathematical models. The study has the potential to have a significant influence on practices in the animal, human and economic sectors in China.



Newton Fund

University of Edinburgh, Dr Till Bachmann

AMR-RDT – AMR Rapid Diagnostic Tests

Antimicrobial Resistance (AMR) has become a global threat and rapid diagnostics are urgently needed to tackle this challenge. Dr Till Bachmann from the University of Edinburgh leads a multi-sectoral, multi-stakeholder international working group to identify barriers to the development, implementation and use of rapid diagnostics. It brings together over 50 key individuals and organisations from 15 countries worldwide that are active in the field of diagnostics and antimicrobial resistance. The network, funded by the AMR Cross-Council Initiative as part of cross-council activities with the Joint Programming Initiative on AMR, was set up in January 2017 and has recently published a roadmap for antimicrobial susceptibility testing.

jpiamr

Van Belkum et al, Developmental Roadmap for antimicrobial susceptibility testing, Nature Reviews Microbiology, volume 17, pages51–62 (2019)

University of Bristol, Professor Matthew Avison, Academic lead for the PhD Training Programme in AMR

Medical Research Foundation National PhD Training Programme for AMR

The Medical Research Foundation has so far invested £2.85m to create a national PhD Training Programme that will train new scientists to explore ways to tackle AMR.

The Foundation spotted a gap in funding for PhD studentships in AMR – right now there are few emerging researchers trained in the multidisciplinary approach required to tackle the AMR problem. The Medical Research Foundation's PhD Training Programme is designed to help build a strong, active network of new researchers to approach this global challenge in innovative ways.

The National Training Programme is supporting 18 fully funded, multidisciplinary PhD studentships, hosted across the UK. It is also providing a number of training and network-building activities and events, including online training resources, summer residential training weeks, annual AMR conferences and tailored meetings responsive to developments and opportunities relevant to the AMR field. These training and network-building activities will reach a further 150 UK PhD students training in AMR-related research.

The Medical Research Foundation will continue to raise money with the aim of funding two further cohorts of antimicrobial resistance PhD students in the future.

For more information about the Training Programme in AMR, please contact:
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Medical Research Foundation

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