



THE UNIVERSITY
of EDINBURGH



A Strategy for Antimicrobial Resistance Research in Edinburgh:

*Contributing solutions to
a global crisis*

March 2017



NDM-1 and colistin-resistant *Klebsiella pneumoniae*
THAMARAI SCHNEIDERS, UNIVERSITY OF EDINBURGH

“AMR is one of the most important issues currently facing the world, and we recognise that Edinburgh scientists and clinicians have a key role to play in addressing this truly global challenge.”

Professor Ross Fitzgerald,
Director of Edinburgh Infectious Diseases

SUMMARY

- Antimicrobial resistance (AMR) is a huge global challenge with important implications for human and animal health and food production
- The national and global prioritisation of AMR will provide significant opportunities for research funding in Edinburgh
- We have identified four key AMR-related research areas with potential for excellence in Edinburgh including (i) epidemiology of AMR (ii) diagnostics (iii) mechanisms of resistance, and (iv) alternatives to antimicrobials
- We have identified an AMR Champion and theme leaders to promote our AMR science, coordinate activities and lead funding applications
- Edinburgh should build capacity in excellent AMR research through support of early career scientists
- Links with International (particularly in low and middle income countries) and Industrial partners should be enhanced and developed
- A highlighted initiative will promote the profile of Edinburgh as a major centre of excellence for AMR research



Edinburgh Infectious Diseases (EID) is a network of over 800 infectious disease scientists and clinicians in the city of Edinburgh. The role of EID is to provide a strategic overview of infectious disease research and training, maximise synergy in established activities, and promote new avenues for investigation.



Microbiology researcher at The Roslin Institute, University of Edinburgh

BACKGROUND

Antimicrobial resistance (AMR) is one of the most important challenges currently facing humankind. The government-commissioned O'Neill report (Review on Antimicrobial Resistance, 2014-2016) predicted a massive increase in deaths per year by 2050 as a direct result of the acquisition of resistance to antibiotics (from a baseline of 700,000 deaths per year currently). Furthermore, without effective policies to prevent the spread of AMR, it is estimated that the cost to the global economy would be 100 trillion USD. These potentially devastating predictions have led to the prioritisation of AMR research as a major focus for UK research funding by RCUK, and Wellcome Trust, and additional dedicated resources have been provided in the form of the Fleming fund, and Global Innovation fund, etc. The \$1.5 Billion Global Challenges Research Fund will provide further impetus for research on AMR that addresses the specific challenges associated with low and middle income countries.

AMR is inextricably linked to other global challenges such as food security. Despite the European Community (EC) ban on use of antimicrobials as growth promoters, there remains widespread use in non-EC countries and therapeutic and metaphylactic use in support of animal production continues to rise worldwide.

It is clear that there will be considerable and sustained funding opportunities in the area of AMR research over the coming years and it is imperative that Edinburgh researchers are successful in competing for available funding and provide leadership in addressing this global challenge. The current document aims to summarise current strengths in AMR research in Edinburgh, highlighting potential areas for future focus, synergy and enhancement in the context of the current and ongoing national AMR research priority areas.



“The University of Edinburgh excels at interdisciplinary research and the creation of new knowledge. We are committed to playing our part in overcoming antimicrobial resistance.”

Professor Sir Timothy O’Shea,
Principal and Vice-Chancellor, The University of Edinburgh

AMR RESEARCH PRIORITY AREAS SET BY FUNDING BODIES

In 2013, the UK government established its 5 year antimicrobial resistance strategy with its 3 strategic aims of (i) improving the knowledge and understanding of AMR; (ii) conserving and stewarding the effectiveness of existing treatments; and (iii) stimulating the development of new antibiotics, diagnostics, and novel therapies. In that context, **RCUK Cross-council research priorities** for the next years have been established with **4 major themes** in the area of **(i) Understanding resistant bacteria** including studies on evolution and transmission of AMR in human and animal populations, identification of novel therapeutic targets towards alternative therapies; **(ii) Accelerating therapeutic and diagnostics development** including studies focussed on new and old small molecule approaches, alternative approaches such as human and animal vaccines and development of new technologies for better identification of resistant bacteria; **(iii) Understanding real world interactions** including studies aiming to understand how different environments and their uses influence the evolution and spread of resistance; **(iv) Behaviour within and beyond the healthcare setting** including studies to understand motivations for human behaviours relating to AMR and how those behaviours can affect emergence and spread of resistance. Of note, the Wellcome Trust has identified drug-resistant infections and vaccines as major priority areas. In particular, vaccine research is the subject of **Global Challenges Research Fund** calls. The recently launched Industrial Strategy Challenge Fund has highlighted 2 broad areas of relevance to AMR, namely ‘Bioscience & Biotechnology’ and ‘Leading Edge Healthcare & Medicine’ that will involve partnership with Industry.



COMPETITORS & STRENGTHS

Other Universities in the UK have highlighted AMR research as a major priority area. For example, the Institute of Microbiology and Infection at the *University of Birmingham* have identified AMR as their main focus supported by significant financial investment from the University in new appointments and infrastructure. The Birmingham approach to tackling AMR is multifactorial with significant emphasis on understanding the evolution of antibiotic resistance and transmission routes and dynamics of resistance as well as the study of membrane proteins in terms of resistance and the development of novel therapeutics. *Warwick University* has established an Antimicrobial interdisciplinary research centre (WAMIC) with funding from EPSRC with special emphasis on AMR across different scales: from small molecule therapeutics to bacterial targets, from rapid diagnostics to predictive epidemiology. This has supported a new MRC DTG in Quantitative Cell Dynamics and Molecular Microbiology with special emphasis on AMR. *Imperial College London* has established the Antimicrobial Research Collaborative of over 100 academic experts that collectively aim to combine strengths across different areas of AMR research to address the challenge using a ‘One Health’ approach.

CURRENT STATUS OF AMR RESEARCH IN EDINBURGH

We have carried out an evaluation of the current strengths in AMR research in EID and the identification of infrastructure and core research strengths that could be applied to develop major funding initiatives. In the University of Edinburgh and the wider Edinburgh Infectious Diseases network, there are a large number of researchers with a wide array of research activities in AMR.

Several existing key areas of strength have been identified that align with current and future predicted funding opportunities. An AMR Champion (Prof. Mark Woolhouse) and theme leaders (listed below) have been identified to promote the successes of Edinburgh AMR research and to co-ordinate activities within and across disciplines. In the past 18 months grant successes in this area have been worth over £6.5m, and include funding from NERC, The Wellcome Trust, the MRC, the Bill & Melinda Gates Foundation, UK-China Newton fund, and the Joint Programming Initiative on AMR, Horizon2020.

1) Global and local epidemiology of AMR (Theme leader, Prof. Mark Woolhouse)

The University of Edinburgh has a strong track record in the epidemiology of infectious disease, particularly in the Centre for Immunity, Infection and Evolution (CIIE) and The Roslin Institute. The study of the dynamics and spread of AMR in humans and at the veterinary-human interface (One Health) has been a significant focus within these centres for over a decade. Allied to core strengths in computational biology, the University of Edinburgh's existing collaborative links with Scotland's Rural College (SRUC), and synergies between veterinary and medical schools, make epidemiology a significant strength with potential for further consolidation and enhancement.

2) Rapid diagnostics for more effective use of antibiotics (Theme leader, Dr. Till Bachmann)

A major focus for future funding calls will be the development of enhanced diagnostic methods to inform more effective and appropriate use of antibiotics. In Edinburgh there are several researchers working in this area, spanning human and veterinary health. For example, in a truly cross-disciplinary translational collaboration involving chemists, physicists, microbiologists, informaticians, engineers and clinicians, the EPSRC-funded PROTEUS consortium, centred at QMRI is developing bench-side optical imaging technology for rapid diagnostics. Other strengths in diagnostics research exist in Division of Infection and Pathway Medicine (DIPM) in vitro diagnostic platforms for human pathogens, and The Roslin Institute for novel diagnostics for bacterial and parasitic infections of humans and livestock. Edinburgh Genomics and the strong bioinformatics research community place us in a good position for rapid sequence-based diagnostics.

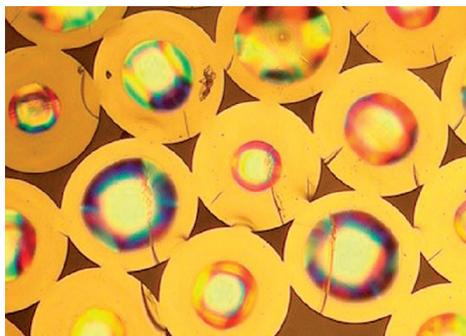
3) Biology, evolution and physics underpinning mechanisms of antibiotic resistance (Theme leader, Dr. Rosalind Allen)

A strong interdisciplinary program of research on AMR involves scientists based in School of Physics (Institute for Condensed Matter and Complex Systems) who are combining experimental microbiology, physics and computational biology to investigate biofilms and the emergence of AMR. Others based at CIIE, Division of Infection and Pathway Medicine (DIPM), and The Roslin Institute are investigating the mechanisms underpinning innate and acquired resistance to antimicrobials. Although the number of individuals working in this area is relatively small, the science is strong and innovative, and benefits from recent major grant funding from the ERC and China-UK Newton fund.

4) Alternatives to antimicrobials for controlling infections (Theme leader, Prof. David Dockrell)

An area of significant research strength in Edinburgh is the development of alternatives to antibiotics for controlling infections and also for growth promotion. Building on core strengths in host-pathogen interactions and immunology, Edinburgh scientists are investigating novel therapeutics based on enhanced understanding of the immune response to infection. Particular interests lie in innate immunology, including antimicrobial peptides and macrophage biology, leading to potential application for novel therapeutic approaches. In addition, science underpinning the design and application of veterinary vaccines is a major focus in The Roslin Institute and Moredun Research Institute. Activity in each of these areas is strengthened by recent major funding awards from MRC and the Wellcome Trust. A potential opportunity is utilising the existing Edinburgh expertise in synthetic biology (Synthsys) for the design of novel vaccines, probiotics or therapeutics for controlling infection. In addition, we will seek to harness activities in the College of Science and Engineering around materials science, sensing and energy delivery as alternative approaches for antimicrobial control in built and hospital environments. Selective breeding and genome editing to improve heritable resistance to diseases that would otherwise require antimicrobials is an important emerging research theme at The Roslin Institute, as is understanding the basis for how antimicrobials enhance growth, and developing alternatives for increasing livestock yields.





Optical fibre bundles KERRIANNE HARRINGTON
AND HARRY WOOD, EPSRC/PROTEUS

“I am delighted to support the launch of Edinburgh Infectious Diseases’ AMR strategy. It is critical that we make the most of the obvious strengths and diversity in AMR research across the city of Edinburgh to help address this urgent problem.”

Professor Lesley Yellowlees,
Head of College of Science and Engineering

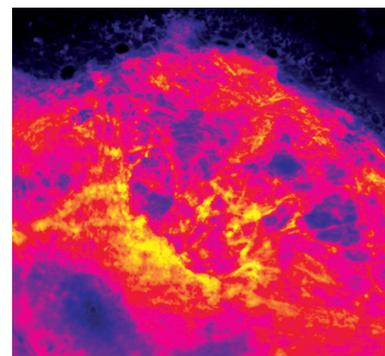
When considering the future development or enhancement of these areas in the future, each must be considered in the context of the overlapping priority area of Official Development Assistance (ODA). We have identified existing links between EID members and low and middle income countries and will seek to increase the number and strength of these to enable GCRF-related bids in the area of AMR. In addition, the recently launch Industrial Strategic Challenge fund provides significant opportunities for new funding based on partnerships with industry.

CURRENT INFRASTRUCTURE & ORGANISATIONAL STRENGTHS

EID provides strong network support for the Infectious Disease community and identifies AMR as a priority area. Within EID we have established the Edinburgh AMR Forum (EAMRF) of over 100 scientists including over 80 PIs in Edinburgh with research interests in the area of AMR which benefitted from a recent grant from the academic networking fund to promote strategic interactions in AMR research. Organisational structures within Edinburgh that have particular current or potential strategic relevance for AMR research include The Roslin Institute, CIIE, the Centre for Inflammation Research, the Division of Infection and Pathway Medicine, the Moredun Research Institute, the Edinburgh Centre for Medical Anthropology, the Global Academies, Edinburgh Genomics, the Innogen Institute, the Usher Institute, NHS Lothian, SRUC and the Scottish Universities Life Sciences Alliance. EID and EAMRF and Edinburgh Research and Innovation provide a framework for co-ordinated and collaborative activities between these different organisation units.

EDINBURGH OPPORTUNITIES

We have identified *One Health* as an area in which Edinburgh has a particular potential to be a leading force within the UK and internationally. AMR is an archetypal One Health issue, where solutions must include medical, veterinary and environmental considerations. In Edinburgh, we are well placed to utilise the strong links between our veterinary and medical schools, and the new Global Academy of Agriculture and Food Security, to lead the UK in driving forward truly collaborative research programmes addressing AMR. There is also significant potential for social scientists in Edinburgh to engage with basic scientists across the 4 major themes, through contribution to multidisciplinary projects based on their existing research interests, activities and partnerships with low or middle income countries.



Imaging human lung tissue
TUSHAR CHOUDHARY, EPSRC/PROTEUS

WHAT WE AIM TO DO

Build on the identified areas of strength in AMR research.

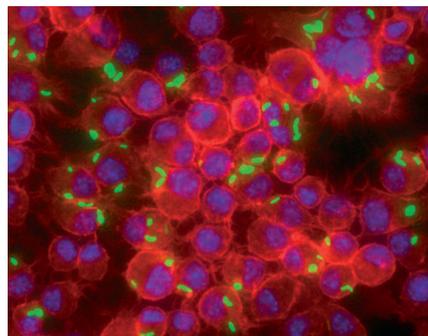
We have identified key individuals in each theme who are international leaders in their field to drive the research program and lead major grant-funding initiatives. In addition, considering the likely future funding priority areas, strategic recruitment in each of the 4 identified areas of strength would significantly enhance our capacity to build on recent grant funding successes and compete successfully for those funding streams. This should include a mixture of senior and early career posts.

Bring through the next generation of AMR scientists.

Successfully addressing the AMR challenge requires a long-term sustained approach that invests in future capacity in AMR research. We will target capacity-building in AMR research by supporting post-graduate training in relevant technologies, including workshops for existing PhD students working in AMR-related research, and applying for doctoral training programmes in AMR-related areas. We will also target fellowship applications from outstanding early career scientists with research interests in AMR to build on the identified research themes.

Engage with Industry. We recognise that collaboration with industry is essential to support commercially-relevant AMR research and to ensure effective translation of research to address AMR. In partnership with Edinburgh Research and Innovation, EID will promote engagement between Edinburgh scientists and clinicians and industrial partners to extend current partnerships and to build new collaborative projects benefitting from public and industrial funding. These projects will likely focus on the development of novel therapeutics, vaccines, and diagnostic approaches towards addressing AMR.

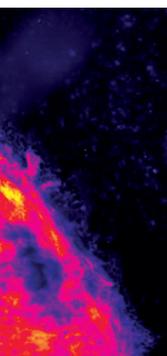
Raise the profile of AMR research in Edinburgh. Clearly there are considerable strengths in AMR research in Edinburgh, and recent and on-going major grant awards highlight our capacity to compete for funding. To help establish Edinburgh as a major centre of excellence for AMR research, we must actively promote our AMR profile to the outside world. We need to ensure we engage other academics, both in the UK and worldwide, and more broadly involve funders, policy makers, and the general public. This will be achieved by developing web resources, policy briefings and public engagement activities, along with social media outputs that emphasise our expertise, strengths, and successes, highlighting key individuals and their achievements. In addition we will highlight the roles of Edinburgh scientists currently involved with national and international strategy groups who are addressing the worldwide challenge of AMR, and encourage all our members to continue building connections with key global policy makers.



Klebsiella pneumoniae (green) interacting with murine macrophages
THAMARAI SCHNEIDERS, UNIVERSITY OF EDINBURGH

“There is no magic bullet for solving the AMR crisis, no single measure will be sufficient. What is needed is an integrated, multi-disciplinary, science-led approach that addresses issues ranging from diagnostics to drug development to global governance. This is also a One Health problem, requiring coordination across the human, animal and environmental sectors. The University of Edinburgh is exceptionally well placed to meet this challenge; we have world class researchers covering many of the disciplines relevant to AMR. Working together, we believe we can make a real difference in this hugely important area.”

Professor Mark Woolhouse,
EID AMR Champion,
Centre for Immunity, Infection & Evolution
& Usher Institute of Population Health
Sciences & Informatics



Edinburgh Infectious Diseases

Leading infectious disease research and training

Edinburgh Infectious Diseases

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Ross Fitzgerald, Hilary Snaith, Till Bachmann, Mark Woolhouse
& Edinburgh Infectious Diseases Executive Committee



Testing antibiotic sensitivity of
Pseudomonas aeruginosa
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