ARG: Bringing antibiotic research into action

As stated by the World Health Organisation (WHO), "antimicrobial resistance (AMR) is one of the three greatest threats to human health". Antimicrobial resistance, otherwise commonly known as antibiotic resistance, affects us all – no antibiotics, no cure. At the Antimicrobials Research Group (ARG), **Professor Laura Piddock** leads the search to increase understanding of the basic biology of antibacterial drug action and resistance. She recently met with us at *Research Features* to talk about her leadership roles as well as outline the current research carried out to combat AMR.

Antimicrobial resistance (AMR) / antibiotic resistance threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. AMR is a complex problem that affects all of society and is a prominent battle for scientists across the globe. All countries need national action plans on AMR and therefore, greater innovation and investment is required in research and development of new antimicrobial medicines, vaccines, and diagnostic tools. Fortunately, nobody understands how to combat AMR better than Professor Laura Piddock, who leads the Antimicrobials Research Group (ARG) at the University of Birmingham, UK.

In her role, as Professor of Microbiology, Prof Piddock works with her research team to understand how and when bacteria become resistant to antibiotics as well as to identify and design new approaches to prevent and treat bacterial infection. She recently spoke with us at *Research Features* to discuss this, and more, in further detail.

Could you describe your roles as both the Director of Antibiotic Action and leader of the Antimicrobials Research Group (ARG)?

In 2011, The British Society for Antimicrobial Chemotherapy (BSAC) established the global public awareness initiative Antibiotic Action. In 2012, I was appointed the BSAC Chair in Public Engagement and the main activity in this role is as the Director of Antibiotic Action. As Director, this means that I carry out public engagement activities, especially focusing on those activities that increase awareness of the need for new antibiotics and the responsible use of currently available drugs.

At Antibiotic Action, I also lead the secretariat for the All Party Parliamentary Group on Antibiotics (APPG-A; appg-on-antibiotics.com), which exists to raise the profile of antibiotic resistance amongst parliamentarians, the need to preserve antibiotics through education on their appropriate use, including non-human uses, the lack of new treatments for bacterial infections, and to help accelerate efforts to discover, research and develop new treatments.

I am an active science communicator and give talks to groups at local, national and international levels. I have also been interviewed, advised on, and appeared

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in, several documentaries for UK national and international television as well as radio networks.

Finally, in my role at the University of Birmingham, I lead the ARG research team, teach undergraduate and postgraduate students, supervise PhD students and carry out various administrative activities. My research aims to increase understanding of the basic biology of antibacterial drug action and resistance.

You first established the ARG back in 1987. What were the reasons behind this?
It was in 1987 that I became an independent researcher and started my own team. Prior to this, I had previously been a research scientist in a hospital for five years when I carried out the research for my PhD and then spent two years as a post-doctoral researcher.

I established the ARG for various reasons but I particularly wanted a separate identity from my colleagues at the University of Birmingham, in the then Department of Medical Microbiology, so I gave my team a name, the Antimicrobials Research Group (ARG). ARG's primary purpose and research focuses on how antibiotic resistance arises, and also defining and characterising mechanisms of resistance that have a clinical relevance.

What kind of impact have you seen since the ARG was first established? Are there any personal highlights you have had along the way?
Since the ARG was first established, the personal highlights for me have been seeing graduates from my research team become professors at leading institutions. This is an undoubtedly rewarding experience. Furthermore, in 2001, I was awarded the prestigious Bristol-Myers Squibb Unrestricted Infectious Diseases Research Grant. This gave scientists the freedom to pursue uncharted paths. This led to me being able to carry out research that would not otherwise have been funded, and allowed me to investigate the link between multidrug resistance efflux pumps (proteins that vacuum antibiotics out of bacteria) and pathogenicity i.e., the ability of the bacterium to cause infection. With this funding, I focused my research into that topic on Salmonella.

Alongside your role as Director of Antibiotic Action for ARG, you are also Chair in Public Engagement at the British Society for Antimicrobial Chemotherapy (BSAC) and a Professor of Microbiology at the University of Birmingham. Is it ever difficult finding time to balance between these roles?
Having multiple leadership roles is manageable to lots of people's surprise, so long as one is prepared to work long hours and weekends! Being the Director of Antibiotic Action and BSAC Chair in Public Engagement takes up approximately 20% of my time, enabling me to successfully commit to the different responsibilities that accompany these roles. However, when I first took on this role as Chair at BSAC, we had no idea that global interest and activities to address antibiotic resistance would increase so much. Therefore, from interacting on a national level, our activities quickly became international and so I have spent a lot of my personal time carrying out my role as Chair in addition to working as a university professor for 80% of my 'work' time.

You state on your website that ARG's research is presented at several major international meetings, including the ASM Microbe, ECCMID and GRC conferences. Why is attending these events so important?
Of course, it is extremely important to share research findings with peers at international meetings. It is far better to discuss research in person then just by publishing papers in journals for others to read. By meeting and interacting with people, new avenues that address research questions can be explored and facilities and technologies not available at Birmingham can be accessed. It is also fun being part of multi-disciplinary teams as you get to work with a wide variety of people.

The ARG are frequently active in the media, appearing on several TV and radio shows in the past, and actively using social media. What influence do these streams of communication have on promoting ARG's work?
Our use of social media and mainstream media, such as TV and radio to carry out many of the Antibiotic Action activities naturally helps promote the research into antibiotic resistance at ARG but it also sometimes offers great opportunities to share information about my latest research. As my research is funded by the public sector, I believe it is important that we share our findings with the general public. I also believe that increasing public understanding of science, especially about antibiotic resistance, is extremely important, as it is imperative that everyone helps to address the global crisis and concern of AMR, and one cannot do that without knowledge.

The threat of antibiotic resistance is an area of widespread concern within science. How is the ARG looking at this, and can you give some examples of research you are currently working on?
My team has investigated resistance in bacteria isolated from animals and humans (*Escherichia coli*, *Salmonella*, *Campylobacter*) and those that infect the respiratory tract (*Pseudomonas aeruginosa* and *Streptococcus pneumoniae*). A particular research focus of my team has been on those bacteria transmitted through the food chain and the ARG showed that the mechanism of resistance to fluoroquinolone antibiotics is the same in bacteria irrespective of whether from either humans or animals. We showed that clinically relevant multi-drug resistance (MDR) in bacteria isolated from people that failed antibiotic treatment, was mediated by proteins that efflux (export) antibiotics from bacterial cells. Following on from this, my team later showed that RND type MDR efflux pumps are required for *Salmonella* to infect its host; subsequently others found the same to be true for related species in the same family (*Enterobacteriaceae*).

My main research interests coincide with my current research which focuses on the following: firstly, regulation and expression of bacterial efflux pumps and impact upon the ability of the bacterium to infect the host; secondly, early drug discovery to identify inhibitors of efflux pumps and plasmid transmission; and thirdly, using genomics to identify mechanisms of antibiotic resistance in bacteria from animals and the environment.

Professor Laura Piddock

Within the ARG, there are researchers who work all around the world. How important is it within science to have this worldwide reach?
It is very important to have a research team that comprises individuals with different social and cultural backgrounds, and scientific expertise. In this way, we can address our scientific questions with a broader understanding of the problems. Hosting researchers from other countries also allows skills, techniques and approaches to research to be shared. Individuals who have trained in my laboratory have then taken and applied their skills back to their own countries and vice versa. It is very important that I have a team that is a 'broad church' as otherwise we are in danger of becoming so focused on the science that we lose an understanding of context.

Which direction would you like to see antibiotic research going over the next ten years and how will ARG's research strategy play into this?
My strategy for the next ten years is to complete our understanding of the regulation of production of multi-drug efflux pumps so that we can find ways to turn them off (i.e., identify new targets for drug discovery). This would make resistant bacteria sensitive to many antibiotics. Likewise, understanding how drug resistance genes are shared between bacteria on small pieces of DNA called plasmids is also very important. Essentially, preventing this transmission will reduce the prevalence of AMR. We are currently in the process of developing tools to monitor plasmid transmission of drug resistance so that we can provide new tools for the community for early drug discovery. I hope that my work and that of the ARG will contribute to the discovery of at least one new drug that will be used in patients in the future.

• For more information on Professor Laura Piddock's work at the ARG, please visit their website: antimicrobialagentsresearchgroup.com/index.html and www.birmingham.ac.uk/laura-piddock. If you would also like to find out more about antibiotic resistance or the group, Antibiotic Action, please visit the following website: www.antibiotic-action.com/

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