Novel technical solutions to combat antimicrobial resistance: A focus on Europe

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Antimicrobial resistance (AMR) represents a growing global concern that is often referred to as a new pandemic due to its substantial health and economic consequences. The overuse and inappropriate use of antimicrobial agents in human health, animal husbandry and the environment have contributed to the emergence and spread of this hazard, which means potential solutions have to be multifaceted, innovative and technologically sustainable. Regarding the AMR disease burden, two recent publications from the Global Research on Antimicrobial Resistance (GRAM) project have shown that resistant bacteria can be associated with up to 541,000 deaths in Europe and up to 4.95 million deaths on a global level.[1,2]

Consequently, key challenges in addressing AMR as a global health hazard include obtaining accurate and timely data on the prevalence and spread of resistant organisms, as well as having effective antimicrobials at our disposal. Nonetheless, there are many challenges in data collection efforts, while traditional methods of antibiotic discovery are slow, costly, frequently ineffective, and lack adequate incentives for the companies that develop them.[3] Hence, a more pervasive use of innovative technology can actually play a critical role in tracking and monitoring AMR, while examples in the European context show that such technologies can be utilised to tackle this problem.

Pertinent technologies to track resistant microorganisms

One of the most promising technologies for tracking AMR is whole-genome sequencing (WGS), which allows for the identification of specific genetic mutations associated with AMR, thereby providing a more accurate and comprehensive understanding of resistance patterns. By sequencing the entire genome of a bacterial isolate, researchers can identify the specific genes and mutations that contribute to resistance, enabling them to track the spread of resistant organisms more effectively. One specific example is its routine usage in the United Kingdom, which aided in limiting/establishing the extent of the spread of plasmid-encoded resistance to the antimicrobial agent known as colistin.[4]

Another auspicious technology helping with AMR is machine learning. For starters, machine learning algorithms can analyse large datasets of AMR-related information – including genomic data, clinical data, and epidemiological data – to pinpoint patterns and predict the spread of resistant organisms. This information can then be used to inform public health strategies and policies, as well as guide clinical decision-making. And not only that; a study led by a researcher from the European Molecular Biology Laboratory, European Bioinformatics Institute and Wellcome-MRC Cambridge Stem Cell Institute in the United Kingdom applied a machine learning algorithm to characterise AMR associated with the International Space Station surface microbiome, broadening the concept of "One Health" to an unprecedented scale.[5]

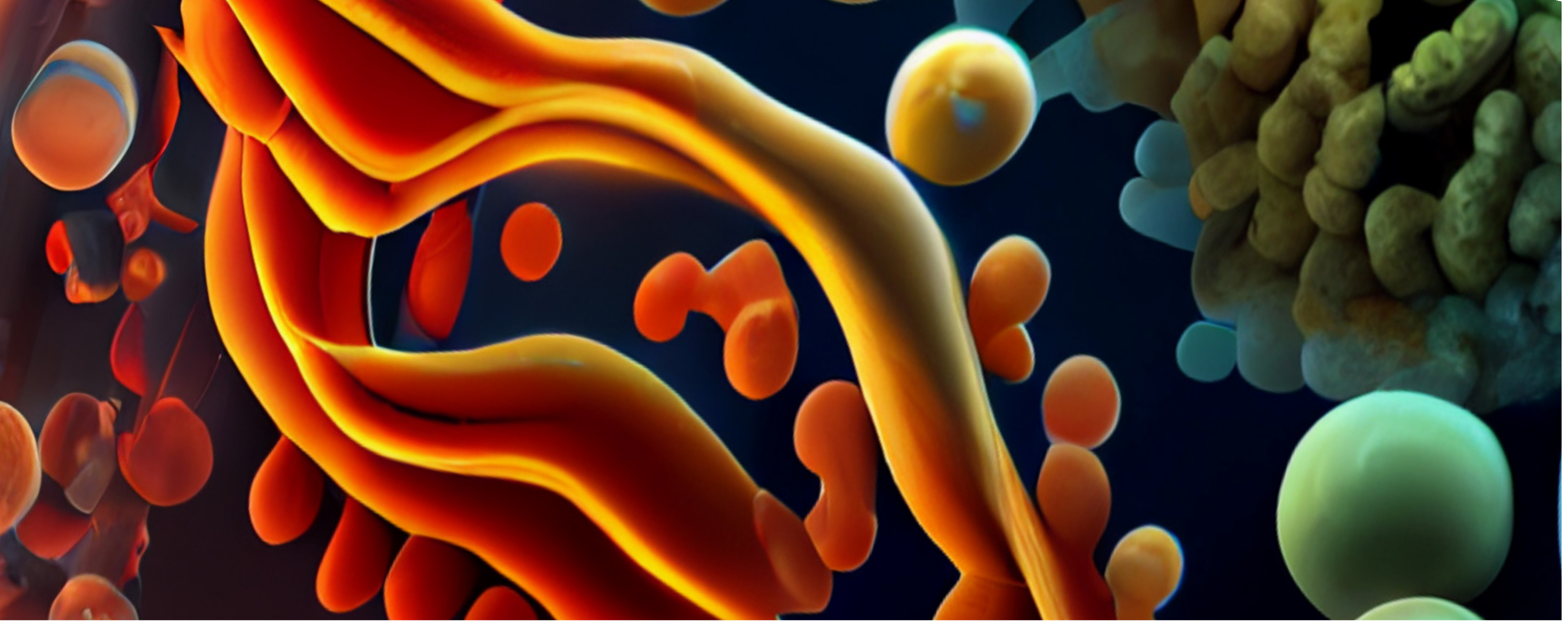
Mobile health (mHealth) technologies, such as smartphone apps and wearable devices, can also play a role in tracking and monitoring AMR. These technologies can be used to gather data on antimicrobial use, resistance patterns, and disease outbreaks, enabling public health officials to quickly identify and respond to emerging threats. A team from France recently presented an artificial intelligence (AI)-based smartphone app with a user-friendly graphical interface that can conduct reproducible and automatic antibiogram analysis.[6]

The use of electronic health records (EHRs) is another technology that can facilitate AMR surveillance by concentrating on antibiotic utilisation and consultations with infectious disease physicians and clinical microbiologists. These EHRs can also provide real-time data, enabling healthcare providers to make more informed clinical decisions, but also informing further research on the topic. For example, state-of-the-art clinical data integration systems that integrate electronic health records have been described by researchers from Switzerland, and will seemingly play an increasingly important role in our fight against AMR.[7]

Novel solutions for the development of new antimicrobial agents

One promising technology from the drug development side is high-throughput screening (HTS), which allows for the rapid screening of large libraries of compounds for their capacity to kill or inhibit the growth of various microorganisms. HTS can be used to identify novel compounds that have antibiotic activity against a myriad of bacterial agents, including those with resistance to existing antibiotics. By screening thousands or even millions of compounds in a short period, HTS enables researchers to identify potential antibiotic candidates more quickly and efficiently. One recent example from Sweden is an automated live-cell imaging system IncuCyte S3, which can evaluate existing drugs, as well as search for new ones against a causative agent of tuberculosis.[8]

Another promising technology is computational modelling, which can be used to forecast the properties and potential efficacy of new antibiotic compounds before they are synthesised and tested in laboratory conditions. This can reduce the time and cost involved in the drug development process and



increase the success rate of drug candidates. Such approaches are exploited by many groups, as exemplified at the University of Trieste and University of Cagliari (both in Italy), where compounds with antimycobacterial activity are being discovered by using such approaches.[9]

Another technology that can be employed in the development of new antibiotics is CRISPR-Cas9 gene editing. CRISPR-Cas9 can be used to modify bacterial genomes to make them more susceptible to existing antibiotics, or to make them more vulnerable to new antibiotics. This technology has the potential to considerably increase the efficacy of existing antibiotics and facilitate the development of new antibiotics. A research group from the University of Exeter (United Kingdom) are developing various approaches to help achieve its full potential.[10]

Artificial intelligence and machine learning algorithms can also be used to advance the development of new antibiotics. These algorithms can analyse large datasets of chemical and biological data to identify potential drug candidates and predict their efficacy, in turn steering the researchers' focus on the most promising drug candidates and increasing the success rate of drug development programs. This was even a theme of the recent panel of the European Parliamentary Research Service.[11]

Conclusions

Technology has the propensity to play a significant role in tracking and monitoring AMR. Whole-genome sequencing, machine learning, mHealth and EHRs are just a few examples of the technologies that can be utilised to expand our understanding of AMR and inform public health strategies, while many inventive and clever technological solutions are also being embraced to combat this global health threat. However, the success of these technologies will depend on their widespread adoption and integration into existing healthcare systems.

At the moment, Europe is among the continents that lead the race in using technology to improve our battle against AMR. For example, a recent European Cooperation in Science and Technology (COST) initiative known as the European Network for diagnosis and treatment of antibiotic-resistant bacterial infections (EURESTOP) was successfully kicked off. Its aim is to unite European scientists from both academic and industrial backgrounds (who possess a diverse range of skills and expertise) into a collaborative and multidisciplinary network. This initiative will encompass various disciplines, including (but not limited to) chemistry, physics, medicine, genetics, bioinformatics, biology and immunology.

The primary focus of EURESTOP is to explore the genetic and molecular foundations of bacterial AMR, thereby creating innovative diagnostic tools, and generating lead/pre-clinical candidates, antibody-based therapies, and clinical-ready repurposed drugs to provide personalised treatments for drug-resistant bacterial infections. Additionally, this initiative aims to bolster networking among European scientists and increase the competitiveness of European research by promoting the utilisation of translational research outcomes. All interested experts are invited to join this collaborative effort at the website: https://www.cost.eu/actions/CA21145/.

Despite Europe's strong leadership in this area, even among European countries there are stark disparities that need to be addressed (e.g., inter-country variability in political and economic resilience). Furthermore, to better facilitate solutions that target the long-term threat of AMR, we need health technology assessment agencies to expand their philosophical approach and methodological toolkit.[12]

And of course, if we are to have a truly global impact, focusing only on technology will not be enough; instead, policy actions that aim to tackle the larger issues of systemic inequality will be needed.

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