



## **Editorial Editorial for the Special Issue "Antimicrobial Resistance and Genetic Elements in Bacteria"**

Maria Scrascia 🔍, Carla Calia and Carlo Pazzani \*D

Department of Bioscience, Biotechnologies and Environment, University of Bari, Via Orabona 4, 70126 Bari, Italy \* Correspondence: carlo.pazzani@uniba.it

Throughout human history, bacterial infections have been an omnipresent threat, which have, on occasion, resulted in devastating pandemics affecting humanity [1]. We need to consider the fact that before the 1940s, bacterial infections were the most common cause of human death, with an average life expectancy at birth of 47 years [2]. The discovery of penicillin by Sir Alexander Fleming in 1928 led to high expectations and marked the beginning of the antibiotic era. The subsequent finding of new antibiotic molecules between 1950s and 1970s led researchers to believe that antibiotics would bring an end to these infections [3], a hope which was soon to be dashed by the discovery of antibiotic-resistant bacteria (ARB). The emergence and spread of ARB, mainly due to the overuse and inappropriate usage of antibiotics in clinical fields and, above all, in anthropic applications (e.g., zootechny), are now recognised as marking one of the major public health concerns worldwide [4–6]. It is forecasted that by 2050, bacterial infections could become the leading cause of death for human beings, a prediction supported by a recent study covering over 204 countries and territories, published in *The Lancet* journal in 2022 [7].

Antimicrobial resistance is mainly mediated by specific genes that are often harboured by genetic elements such as plasmids, integrons, transposons, insertion sequences, integrative conjugative elements, etc. [8]. Among such elements, plasmids (if conjugative or mobilisable) play key roles in the horizontal transfer of antimicrobial resistance genes (ARG) and in the emergence of new ARB [9,10]. A non-secondary role is also played by insertion sequences (e.g., IS26 and IS257) and transposons (e.g., Tn21), which can shape plasmids by the embedding and/or reassortment of ARG, with the final outcome of expanding the range and enrichment of ARG in plasmids [11–13].

This Special Issue, entitled "Antimicrobial Resistance and Genetic Elements in Bacteria", aimed to collect new data on ARG and their dissemination through mobile or mobilisable genetic elements in both Gram-negative and Gram-positive bacteria. It comprises a review and eleven articles.

In addition to being a public health threat, zoonotic pathogens are responsible for major economic losses. The review published in this Special Issue offers a valuable update on ARG and their co-occurrence and genome localisation (mainly on integrative conjugative and integrative mobile genetic elements) in *Streptococcus suis*, a very important swine pathogen, which is also able to infect humans [14]. Animals, through their commonly harboured bacteria (e.g., intestinal tract), may act as a reservoir for both ARG and mobile genetic elements (MGE) involved in ARG horizontal transfer. The study on multidrug-resistant *Enterococcus faecalis* and *Enterococcus faecium* strains isolated from poultry clearly highlights such a role [15]. In the clinical field, antibiotic resistance is a matter of great relevance, since multidrug-resistant bacteria (MDR) are increasingly isolated from cases of both common and, above all, hospital-acquired infections. Of particular concern is the emerging spread of resistance to carbapenems and cephalosporins (e.g., those of third-generation), which are considered frontline antibiotics. *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are among the antimicrobial-resistant ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* 



Citation: Scrascia, M.; Calia, C.; Pazzani, C. Editorial for the Special Issue "Antimicrobial Resistance and Genetic Elements in Bacteria". *Microorganisms* 2023, 11, 670. https://doi.org/10.3390/ microorganisms11030670

Received: 21 February 2023 Accepted: 3 March 2023 Published: 6 March 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). species) listed by the World Health Organization (WHO) as imminent threats to human health [16]. Two papers report on the characterisation of MDR K. pneumoniae strains isolated in Egypt and harbouring carbapenemase and extended spectrum  $\beta$ -lactamases genes localised on plasmids. These studies highlight the widespread diffusion of similar plasmids and their roles in conferring multidrug resistance [17,18]. Similarly, another study published in this Special Issue provides data on carbapenemase and extended  $\beta$ -lactamase genes harboured by a plasmid conferring MDR in *P. aeruginosa* [19]. From a clinical point of view, the widespread isolation of MDR strains resistant to carbapenems and cephalosporins has greatly limited the range of antibiotics which can be used to effectively treat infectious diseases (caused by Gram-negative bacteria), leaving colistin as an antibiotic last resort. Even the value of colistin has been undermined in the last decade by the discovery of colistin-resistant bacteria caused by the acquisition of plasmid-mediated colistin-resistant (mcr) genes [20–22]. Data on non-conjugative but mobilisable plasmids are constantly expanding, disclosing their important roles in both the horizontal spread of ARG and the insurgence of MDR bacteria. Current knowledge on plasmids shows how complex their world is, and how much remains to be learnt about it. For instance, studies on hybrid or mosaic plasmids are now starting to reveal the means by which plastic plasmids enable the emergence of new plasmids which have the acquired properties of virulence, antibiotic resistance, and/or the ability to be horizontally transferred (e.g., through the acquisition of *mob* genes and/or *oriT* sequences). This Special Issue offers examples of such studies [18,23]. It is worth noting the identification of a mosaic IncR plasmid that has acquired a region harbouring ARG from IncI1 plasmids and, more importantly, oriT and nikAB, enabling its mobilisation in the presence of helper conjugative plasmids [23]. This Special Issue also includes studies on the following topics: the relationship between antibiotic resistance and biofilm-related genes in *Pseudomonas* species isolates, drug resistance detected in *Cedecea* neteri (a clinical opportunistic pathogen), the mobilisation of kanamycin-resistant Col-like plasmids, and the horizontal exchange of a MDR IncFII plasmid between E. coli and K. *quasipneumoniae*, which occurred in the same patient [24–27].

**Acknowledgments:** We would like to express our sincere gratitude to the editorial office of *Microorganisms* for their assistance in managing and organizing this Special Issue. We are thankful to all the authors and reviewers who provided contributions. Many thanks to Karen Laxton for the writing assistance.

Conflicts of Interest: The editors declare no conflict of interest.

## References

- 1. Sakai, T.; Morimoto, Y. The History of Infectious Diseases and Medicine. Pathogens 2022, 11, 1147. [CrossRef] [PubMed]
- 2. Adedeji, W.A. The Treasure Called Antibiotics. Ann. Ib. Postgrad. Med. 2016, 14, 56–57. [PubMed]
- Hutchings, M.; Truman, A.; Wilkinson, B. Antibiotics: Past, present and future. *Curr. Opin. Microbiol.* 2019, 51, 72–80. [CrossRef] [PubMed]
- 4. Aljeldah, M.M. Antimicrobial Resistance and Its Spread Is a Global Threat. Antibiotics 2022, 11, 1082. [CrossRef]
- Browne, A.; Chipeta, M.; Haines-Woodhouse, G.; Kumaran, E.; Hamadani, B.; Zaraa, S.; Henry, N.; Deshpande, A.; Reiner, R., Jr.; Day, N.; et al. Global antibiotic consumption and usage in humans, 2000–2018: A spatial modelling study. *Lancet Planet. Health* 2021, 5, e893–e904. [CrossRef]
- 6. Tiseo, K.; Huber, L.; Gilbert, M.; Robinson, T.; Van Boeckel, T. Global Trends in Antimicrobial Use in Food Animals from 2017 to 2030. *Antibiotics* **2020**, *9*, 918. [CrossRef]
- Murray, C.; Ikuta, K.; Sharara, K.; Swetschinski, L.; Gray, A.; Han, C.; Bisignano, C.; Rao, P.; Wool, E.; Johnson, S.; et al. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *Lancet* 2022, 399, 629–655. [CrossRef]
- Partridge, S.; Kwong, S.; Firth, N.; Jensen, S. Mobile Genetic Elements Associated with Antimicrobial Resistance. *Clin. Microbiol. Rev.* 2018, *31*, e00088-17. [CrossRef]
- 9. Meng, M.; Li, Y.; Yao, H. Plasmid-Mediated Transfer of Antibiotic Resistance Genes in Soil. Antibiotics 2022, 11, 525. [CrossRef]
- San Millan, A. Evolution of Plasmid-Mediated Antibiotic Resistance in the Clinical Context. *Trends Microbiol.* 2018, 26, 978–985. [CrossRef]
- Che, Y.; Yang, Y.; Xu, X.; Brinda, K.; Polz, M.; Hanage, W.; Zhang, T. Conjugative plasmids interact with insertion sequences to shape the horizontal transfer of antimicrobial resistance genes. *Proc. Natl. Acad. Sci. USA* 2021, *118*, e2008731118. [CrossRef] [PubMed]

- Oliva, M.; Monno, R.; Addabbo, P.; Pesole, G.; Scrascia, M.; Calia, C.; Dionisi, A.; Chiara, M.; Horner, D.; Manzari, C.; et al. IS26 mediated antimicrobial resistance gene shuffling from the chromosome to a mosaic conjugative FII plasmid. *Plasmid* 2018, 100, 22–30. [CrossRef] [PubMed]
- 13. Varani, A.; He, S.; Siguier, P.; Ross, K.; Chandler, M. The IS6 family, a clinically important group of insertion sequences including IS26. *Mob. DNA* **2021**, *12*, 11. [CrossRef] [PubMed]
- Dechene-Tempier, M.; Marois-Crehan, C.; Libante, V.; Jouy, E.; Leblond-Bourget, N.; Payot, S. Update on the Mechanisms of Antibiotic Resistance and the Mobile Resistome in the Emerging Zoonotic Pathogen Streptococcus suis. *Microorganisms* 2021, 9, 1765. [CrossRef] [PubMed]
- Cho, S.; McMillan, E.; Barrett, J.; Hiott, L.; Woodley, T.; House, S.; Frye, J.; Jackson, C. Distribution and Transfer of Plasmid Replicon Families among Multidrug-Resistant Enterococcus faecalis and Enterococcus faecium from Poultry. *Microorganisms* 2022, 10, 1244. [CrossRef]
- 16. De Oliveira, D.; Forde, B.; Kidd, T.; Harris, P.; Schembri, M.; Beatson, S.; Paterson, D.; Walker, M. Antimicrobial Resistance in ESKAPE Pathogens. *Clin. Microbiol. Rev.* **2020**, *33*, e00181-19. [CrossRef]
- Abdelwahab, R.; Alhammadi, M.; Hassan, E.; Ahmed, E.; Abu-Faddan, N.; Daef, E.; Busby, S.; Browning, D. Antimicrobial Resistance and Comparative Genome Analysis of Klebsiella pneumoniae Strains Isolated in Egypt. *Microorganisms* 2021, *9*, 1880. [CrossRef]
- Edward, E.; Mohamed, N.; Zakaria, A. Whole Genome Characterization of the High-Risk Clone ST383 Klebsiella pneumoniae with a Simultaneous Carriage of bla(CTX-M-14) on IncL/M Plasmid and bla(CTX-M-15) on Convergent IncHI1B/IncFIB Plasmid from Egypt. *Microorganisms* 2022, 10, 1097. [CrossRef]
- Gomez-Martinez, J.; Rocha-Gracia, R.; Bello-Lopez, E.; Cevallos, M.; Castaneda-Lucio, M.; Lopez-Garcia, A.; Saenz, Y.; Jimenez-Flores, G.; Cortes-Cortes, G.; Lozano-Zarain, P. A Plasmid Carrying bla(IMP-56) in Pseudomonas aeruginosa Belonging to a Novel Resistance Plasmid Family. *Microorganisms* 2022, 10, 1863. [CrossRef]
- Dadashi, M.; Sameni, F.; Bostanshirin, N.; Yaslianifard, S.; Khosravi-Dehaghi, N.; Nasiri, M.; Goudarzi, M.; Hashemi, A.; Hajikhani, B. Global prevalence and molecular epidemiology of mcr-mediated colistin resistance in Escherichia coli clinical isolates: A systematic review. J. Glob. Antimicrob. Resist. 2022, 29, 444–461. [CrossRef]
- Hernandez-Mendoza, A.; Salgado-Morales, R.; Moran-Vazquez, A.; Lopez-Torres, D.; Garcia-Gomez, B.; Dantan-Gonzalez, E. Molecular Characterization of pBOq-IncQ and pBOq-95LK Plasmids of Escherichia coli BOq 01, a New Isolated Strain from Poultry Farming, Involved in Antibiotic Resistance. *Microorganisms* 2022, 10, 1509. [CrossRef]
- Zakaria, A.; Edward, E.; Mohamed, N. Genomic Insights into a Colistin-Resistant Uropathogenic Escherichia coli Strain of O23:H4-ST641 Lineage Harboring mcr-1.1 on a Conjugative IncHI2 Plasmid from Egypt. *Microorganisms* 2021, *9*, 799. [PubMed]
- Calia, C.; Oliva, M.; Ferrara, M.; Minervini, C.; Scrascia, M.; Monno, R.; Mule, G.; Cumbo, C.; Marzella, A.; Pazzani, C. Identification and Characterisation of pST1023 A Mosaic, Multidrug-Resistant and Mobilisable IncR Plasmid. *Microorganisms* 2022, 10, 1592. [CrossRef] [PubMed]
- McMillan, E.; Nguyen, L.; Hiott, L.; Sharma, P.; Jackson, C.; Frye, J.; Chen, C. Genomic Comparison of Conjugative Plasmids from Salmonella enterica and Escherichia coli Encoding Beta-Lactamases and Capable of Mobilizing Kanamycin Resistance Col-like Plasmids. *Microorganisms* 2021, 9, 2205. [CrossRef] [PubMed]
- 25. Mohamed, H.; Alnasser, S.; Abd-Elhafeez, H.; Alotaibi, M.; Batiha, G.; Younis, W. Detection of beta-Lactamase Resistance and Biofilm Genes in Pseudomonas Species Isolated from Chickens. *Microorganisms* **2022**, *10*, 1975. [CrossRef] [PubMed]
- Thompson, D.K.; Sharkady, S.M. Genomic Insights into Drug Resistance Determinants in Cedecea neteri, A Rare Opportunistic Pathogen. *Microorganisms* 2021, 9, 1741. [CrossRef]
- van Almsick, V.; Schuler, F.; Mellmann, A.; Schwierzeck, V. The Use of Long-Read Sequencing Technologies in Infection Control: Horizontal Transfer of a bla(CTX-M-27) Containing IncFII Plasmid in a Patient Screening Sample. *Microorganisms* 2022, 10, 491. [CrossRef]

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.