A Multidrug-resistant Monophasic *Salmonella* Typhimurium Co-harboring *mcr-1*, *fosA3*, *bla*_{CTX-M-14} in a Transferable IncHI2 Plasmid from a Healthy Catering Worker in China

This article was published in the following Dove Press journal:
Infection and Drug Resistance

Zhenyu Wang^{1-3,*}

Haiyan Xu^{4,*}

Yuan Yue Tang¹⁻³

Qiuchun Li¹⁻³

Xinan Jiao¹⁻³

¹Key Laboratory of Prevention and Control of Biological Hazard Factors (Animal Origin) for Agri-Food Safety and Quality, Ministry of Agriculture of China, Yangzhou University, Yangzhou, People's Republic of China; ²Jiangsu Key Laboratory of Zoonosis/Jiangsu Co-Innovation Center for Prevention and Control of Important Animal Infectious Diseases and Zoonoses, Yangzhou University, Yangzhou, People's Republic of China; ³Joint International Research Laboratory of Agriculture and Agri-Product Safety, Yangzhou University, Yangzhou, People's Republic of China; ⁴Nantong Center for Disease Control and Prevention, Nantong, People's Republic of China

*These authors contributed equally to this work

Background: Polymyxins are currently regarded as a possible last-resort therapy to eradicate multidrug-resistant (MDR) gram-negative bacteria. Meanwhile, the old antimicrobial agent fosfomycin has recently been reintroduced into clinical use for the treatment of extended-spectrum β -lactamase (ESBL)-producing and carbapenem-resistant *Enterobacteriaceae*. This study investigated a multidrug-resistant *Salmonella* 4,[5],12:i:- strain from a food catering handler, which had the potential to act as a vehicle for transmitting MDR foodborne pathogens.

Methods: A *Salmonella* 4,[5],12:i:- YZU1189 strain was isolated from the fecal sample of a food catering worker according to the standard protocol of the *Salmonella* detection method from World Health Organization in 2003. Serotyping of YZU1189 was performed according to the Kauffmann–White scheme. The antimicrobial resistance phenotype of the strain was determined by the agar dilution method according to the instruction from Clinical and Laboratory Standards Institute (CLSI). Plasmid conjugation was performed between the donor strain *Salmonella* 4,[5],12:i:- YZU1189 and the recipient strain *Escherichia coli* C600. The genetic locations of *mcr-1*, *bla*_{CTX-M-14} and *fosA3* genes were determined by the whole genome sequence analysis.

Results: *Salmonella* 4,[5],12:i:- YZU1189 was an ESBL-producing stain isolated from a healthy catering worker. The strain displayed resistance to aminoglycosides, beta-lactams, polymyxins, fosfomycins, phenicols, trimethoprim, sulfonamides, tetracyclines and fluoroquinolones. Whole genome sequence analysis and plasmid conjugation revealed that the strain had a transferable IncHI2 plasmid carrying the *mcr-1*, *bla*_{CTX-M-14} and *fosA3* genes. Sequence homology analysis showed that this plasmid possessed high sequence similarity to previously reported *mcr-1*, *bla*_{CTX-M-14} and *fosA3* positive plasmids in China.

Conclusion: This study reported a the multidrug-resistant *Salmonella* 4,[5],12:i:- isolate harboring *mcr-1*, *bla*_{CTX-M-14} and *fosA3* from human for the first time in China. The occurrence of *mcr-1* and *fosA3* genes in the transferable IncHI2 plasmid pYZU1189 from the ESBL-producing *Salmonella* 4,[5],12:i:- isolate showed a potential threat to public health. Great concern should be taken for the spread of multidrug-resistant ESBL-producing *Salmonella* isolates from food catering workers to consumers.

Keywords: *Salmonella* 4,[5],12:i:-, whole genome sequencing analysis, multidrug resistant, ESBL, colistin resistance, *fosA3*

Correspondence: Qiuchun Li; Xinan Jiao
Jiangsu Key Laboratory of Zoonosis,
Yangzhou University, Yangzhou, Jiangsu
Province, People's Republic of China
Tel +86-514-87971136
Email qcli@yzu.edu.cn; jiao@yzu.edu.cn

Introduction

Salmonella enterica serovar Typhimurium is well known to be associated with foodborne diseases and outbreaks, as well as causing infectious diseases in animals

and humans.¹ In recent year, the *Salmonella* Typhimurium monophasic variant (*Salmonella* 4,[5],12:i:-) was frequently reported from human salmonellosis in both Europe and the US.^{2,3} *Salmonella* 4,[5],12:i:- is described as a variant of *Salmonella* Typhimurium lacking the second phase flagellum, which mostly belonged to the pandemic ST34 clone with an antibiotic resistance pattern of ASSuT (ampicillin, streptomycin, sulphonamides and tetracycline).⁴ In addition, the *mcr-1* gene responsible for the colistin resistance has frequently occurred in ST34 *Salmonella* Typhimurium and *Salmonella* 4,[5],12:i:-.⁴⁻⁷ In China, *Salmonella* 4,[5],12:i:- has increased to being one of the most predominant serovars causing human salmonellosis, while ST34 is the most common ST type of *Salmonella* 4,[5],12:i:-.⁸ ESBL-producing *Salmonella* isolates have raised concern due to their resistance to cephalosporins, which have been widely applied for treating severe salmonellosis.⁹ The ESBL-producing *Salmonella* strains showed a higher prevalence (8.58%) on retail chicken in China than in the US.^{10,11} Meanwhile, fosfomycin has recently been reintroduced into clinical treatment for ESBL-producing *Enterobacteriaceae*. The occurrence of multidrug resistance in *Salmonella* 4,[5],12:i:- isolated from animal origin food products has increased the potential infection risk while treatment options are becoming limited.

In this study, we identified a MDR ST34 *Salmonella* 4,[5],12:i:- isolate carrying an IncHI2 plasmid with *mcr-1*, *fosA3*, *bla*_{CTX-M-14} genes, which was from a healthy catering industry worker in Jiangsu province, China. To our best knowledge, this is the first report of the multidrug-resistant *Salmonella* 4,[5],12:i:- isolate harboring *mcr-1*, *bla*_{CTX-M-14} and *fosA3* from a human in China.

Materials and Methods

Bacterial Isolate

A surveillance study for foodborne pathogens was performed toward food catering workers and diarrheal patients by Nantong CDC, Jiangsu, China.¹² The initial aim of this project was to evaluate the role of food handler as a vehicle for transmitting foodborne pathogens by screening human fecal samples. In order to selectively enrich *Salmonella*, samples were added to the selenite cysteine broth and incubated at 35°C for 24 h. The 10 µL of each incubated sample was inoculated onto xylose lysine deoxycholate (XLD, OXOID, England) and *Salmonella Shigella* (SS) agar plate, and cultured for

24 h at 37°C. Two or more presumptive *Salmonella* colonies were subcultured in the triple sugar-iron-agar medium. The serotyping of *Salmonella* was based on Kauffmann–White (KW) scheme. During the process, we identified *Salmonella* Typhimurium and its monophasic variant by multiplex-PCR for the *fliB-fliA* intergenic region and the *fljB* gene.¹³

Antimicrobial Susceptibility Testing

Minimum inhibitory concentrations (MICs) were determined by the agar dilution method. Antibiotics used in this study were listed in Table 1. MICs were interpreted by CLSI breakpoints,^{14,15} except that florfenicol (>16 mg/L) was interpreted according to EUCAST epidemiological cutoff values (<http://mic.eucast.org/Eucast2>).

Plasmid Conjugation Experiments

Conjugation experiments were performed between donor *Salmonella* 4,[5],12:i:- and recipient streptomycin-resistant *E. coli* C600, and transconjugants were selected on the Luria–Bertani agar plate containing streptomycin (3000 mg/L) and colistin (2 mg/L). The *mcr-1* and *mdh* genes were used to distinguish donor, recipient and transconjugant based on the PCR analysis.^{16,17}

Whole Genome Sequencing Analysis

To understand the genetic background of *Salmonella* 4,[5],12:i:- YZU1189, the strain YZU1189 was sequenced using the Hiseq 2500 platform. Raw sequencing reads were deposited in the European Nucleotide Archive database under the accession number PRJEB38934. The raw reads were trimmed and filtered by NGSQC toolkit (v2.3.3), and subjected to de novo assembly by SPAdes 3.6.¹⁸ The assembled genome was annotated by Prokka version 1.12.¹⁹ The acquired antimicrobial resistance genes and chromosomal mutations was identified by ResFinder 3.2.²⁰ The multilocus sequence type of the strain YZU1189 was obtained by MLST 2.0.²¹ The virulence factors of strain YZU1189 was detected by BLASTn based on seven typical virulence genes in *Salmonella* Typhimurium, of which four genes located on prophages including *gipA* (encoding a Peyer's patch-specific virulence factor), *sspH1* (*Salmonella*-type III effector protein), *sodC1* (putative Cu/Zn superoxide dismutase) and *sopE1* (*Salmonella*-type III effector protein), and three genes (*spvC*, *pefA*, *rck*) in plasmids.²²

Table 1 The Minimum Inhibitory Concentration (MIC) Values of the Donor (*Salmonella* 4,[5],12:i:- YZU1189), Transconjugant (*E. coli* C600-pYZU1189) and Recipient (*E. coli* C600)

Classes	Antibiotics	MIC (mg/L)			Antibiotic Resistance Genes (YZU1189)
		YZU1189 (<i>S. 4,[5],12:i:-</i>)	C600 (<i>E. coli</i>)	C600-pYZU1189 (<i>E. coli</i>)	
Aminoglycosides	Gentamicin	16 (R)	0.25 (S)	64 (R)	<i>aac(3)-IV</i> , <i>aph(4)-Ia</i> , <i>aph(3')-Ia</i> , <i>aac(6')-Iaa</i>
	Streptomycin	4 (S)	>256 (R)	>256 (R)	
	Amikacin	0.5 (S)	1 (S)	2 (S)	
Beta-lactams	Ampicillin	>128 (R)	2 (S)	>128 (R)	<i>bla_{CTX-M-14}</i>
	Cefazolin	>128 (R)	2 (S)	>128 (R)	
	Cefotaxime	32 (R)	0.06 (S)	4 (R)	
Carbapenems	Meropenem	0.015 (S)	0.03 (S)	0.03 (S)	
Polymyxins	Colistin	8 (R)	0.25 (S)	8 (R)	<i>mcr-I</i>
Fosfomycins	Fosfomycin	>512 (R)	32 (S)	>512 (R)	<i>fosA3</i>
Phenicol	Chloramphenicol	128 (R)	2 (S)	64 (R)	<i>floR</i>
	Florfenicol	>128 (R)	4 (S)	128 (R)	
Trimethoprim/ sulfonamides	Trimethoprim/ sulfamethoxazole	64 (R)	1 (S)	64 (R)	<i>sul2</i> , <i>sul3</i> , <i>drfA12</i>
Tetracyclines	Tetracycline	128 (R)	2 (S)	2 (S)	<i>tet(B)</i>
Fluoroquinolones	Ciprofloxacin	1 (S)	0.015 (S)	0.015 (S)	<i>gyrA(D87N)</i>
	Nalidixic acid	>256 (R)	4 (S)	4 (S)	

Abbreviations: MIC, minimum inhibitory concentration; R, resistant; S, susceptible.

Ethical Approval

The study protocol was performed following the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the Ethics Committee of the Chinese Centers for Disease Control and Prevention (CDC). Fresh feces of all healthy catering workers were sampled after obtaining written informed consents.

Results and Discussion

In the surveillance study, we observed a *Salmonella* 4,[5],12:i:- strain YZU1189 harboring *mcr-I*, *fosA3* and *bla_{CTX-M-14}* from a healthy female catering worker. This MDR isolate was defined using the criteria established by Magiorakos et al.²³ MICs of 15 antibiotics for the strain YZU1189 showed that YZU1189 was resistant to antibiotics including aminoglycosides, beta-lactams, polymyxins, fosfomycins, phenicols, trimethoprim, sulfonamides, tetracyclines and fluoroquinolones (Table 1). Compared to the typical ASSuT resistance pattern in most of *Salmonella* 4,[5],12:i:- isolates, this strain lacked the phenotypic streptomycin resistance, while showed resistance to colistin and fosfomycin.

According to the MLST analysis, *Salmonella* 4,[5],12:i:- strain YZU1189 belonged to sequence type (ST) 34. Virulence factors analysis of seven genes showed that this isolate carried virulence factors *gipA* and *sodCI*, which were prevalent in *Salmonella* 4,[5],12:i:- isolates from foods in China.⁸ Strain YZU1189 contained several antimicrobial resistance (AMR) genes including aminoglycosides (*aac(3)-IV*, *aph(4)-Ia*, *aph(3')-Ia*, *aac(6')-Iaa*), β -lactamase (*bla_{CTX-M-14}*), polymyxins (*mcr-I*), fosfomycins (*fosA3*), phenicols (*floR*), sulphonamides (*sul2* and *sul3*), tetracycline (*tet(B)*), and trimethoprim (*drfA12*). In addition, the mutation of codon 87 (D87N) in the GyrA protein causing the quinolone resistance was also detected in this strain. The *mcr-I* gene was previously observed in ST34 *Salmonella* Typhimurium from pigs in China, which located mainly on IncHI2-like plasmids.⁵ The PCR analysis showed that the transconjugant was positive for the *mcr-I* gene and negative for the *Salmonella* Typhimurium specific *mdh* gene, indicating the successful transmission of *mcr-I* positive plasmid into the recipient strain *E. coli* C600. The plasmid conjugation experiment

showed that the *mcr-1* gene in YZU1189 could be co-transferred with *bla*_{CTX-M-14} and *fosA3* genes (Table 1).

By whole genome sequencing analysis, we confirmed several antimicrobial resistance genes located on an IncHI2 plasmid (246Kb), named pYZU1189 (accession number ERS4951189), which harbored *mcr-1*, *fosA3*, *floR*, *sul2*, *sul3*, *drfA12*, *aac(3)-IV*, *aph(4)-Ia*, *aph(3')-Ia*, *bla*_{CTX-M-14} genes (Figure 1). The *mcr-1* gene was located in the common genetic background of IS*Apl1*-*mcr-1*-*orf*, which was also detected in pECHN-15-61(IncI2), pECFJ-B42-63(IncI2), and pECS-B60-267(IncHI2) plasmids,²⁴ while the *fosA3* gene had the common genetic background of ΔISE*cp1*-*bla*_{CTX-M-14}-IS903*B*-*fosA3*-*orf* located in pYZU1189. IncHI2 plasmids harboring antimicrobial resistance genes found in this study were also reported in *Enterobacteriaceae*, such as *E. coli* and *Salmonella* spp.^{6,7,24} The sequence alignment showed that an IncHI2-type plasmid pHNSHP45-2 harboring a similar genetic background with *mcr-1*, *bla*_{CTX-M-14} and

fosA3 in *E. coli* (Figure 1). Five *Salmonella* Typhimurium isolates carrying co-transferred *fosA3*, *bla*_{CTX-M-14}, *mcr-1*, *oqxAB* and *floR* genes from food animals between 2016 and 2017 in China have been previously reported.⁶ More importantly, *mcr*-positive *Salmonella* 4,[5],12:i:- isolates with multiple antimicrobial resistance genes have been frequently reported from different sources in multiple countries worldwide,^{25–32} indicating the increasing risk potential of this pathogen transmitting worldwide. Also, *mcr*-positive *Salmonella* 4,[5],12:i:- isolates from different sources showed a potential dissemination between food animals and humans, which remains a significant threat to human health.

Conclusion

In conclusion, this study reported an ESBL-producing *Salmonella* 4,[5],12:i:- isolate of human origin carrying a colistin resistance gene *mcr-1*, a fosfomycin resistance

Figure 1 Sequence alignment of pYZU1189 and pHNSHP45-2 (GenBank no. KU341381). The pHNSHP45-2 was used as a reference to compare with *mcr-1*-bearing plasmid which possess the IncHI2 replicon in this study. Red arrows represent the plasmid pHNSHP45-2.

gene *fosA3* and a rare sulfonamide resistance gene *sul3*. The occurrence of *mcr-1* and *fosA3* genes in a transferable IncHI2 plasmid pYZU1189 from a ESBL-producing *Salmonella* 4, [5],12:i:- isolate brings great considerable public health threat. Great concern should be taken for the spread of multi-drug-resistant ESBL-producing *Salmonella* isolates from food catering workers to consumers. In the “One Health” aspect, quick and thorough action should be taken to reduce the use of colistin in food-producing animals in the farming industry. Interventions of restricting antibiotic use in food-producing animals should also be applied to reduce the prevalence of MDR bacteria.

Funding

This research was funded by National Natural Science Foundation of China, grant number 3192010301, and 31730094; The Priority Academic Program Development of Jiangsu Higher Education Institution (PAPD) and Jiangsu Key Laboratory of Zoonosis (R1703).

Disclosure

The authors report no conflicts of interest in this work.

References

- Zhang J, Jin H, Hu J, et al. Serovars and antimicrobial resistance of non-typhoidal *Salmonella* from human patients in Shanghai, China, 2006–2010. *Epidemiol Infect.* 2014;142:826–832.
- European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA and ECDC). The European union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. *EFSA J.* 2018;16(12):e5500.
- CDC (Centers for Disease Control and Prevention). National *Salmonella* surveillance annual report, 2016; 2018. Available from: <https://www.cdc.gov/national-surveillance/salmonella-surveillance.html>. Accessed September 2, 2020.
- Biswas S, Li Y, Elbediwi M, Yue M. Emergence and dissemination of *mcr*-carrying clinically relevant *Salmonella* Typhimurium monophasic clone ST34. *Microorganisms.* 2019;7.
- Yi LX, Wang J, Gao YL, et al. *Mcr-1*-harboring *Salmonella enterica* serovar Typhimurium sequence type 34 in pigs, China. *Emerg Infect Dis.* 2017;23:291–295.
- Mulvey MR, Bharat A, Boyd DA, Irwin RJ, Wylie J. Characterization of a colistin-resistant *Salmonella enterica* 4,[5],12:i:- harbouring *mcr-3.2* on a variant IncHI-2 plasmid identified in Canada. *J Med Microbiol.* 2018;67:1673–1675.
- Monte DF, Nelson V, Cerdeira L, et al. Multidrug- and colistin-resistant *Salmonella enterica* 4,[5],12:i:- sequence type 34 carrying the *mcr-3.1* gene on the IncHI2 plasmid recovered from a human. *J Med Microbiol.* 2019;68:986–990.
- Yang X, Wu Q, Zhang J, et al. Prevalence and characterization of monophasic *Salmonella* serovar 1,4,[5],12:i:- of food origin in China. *PLoS One.* 2015;10:e0137967.
- Medalla F, Gu W, Mahon BE, et al. Estimated incidence of antimicrobial drug-resistant nontyphoidal *salmonella* infections, United States, 2004–2012. *Emerg Infect Dis.* 2017;23:29–37.
- Food and Drug Administration (FDA). National antimicrobial resistance monitoring system-enteric bacteria (narms): 2015 integrated report. Rockville,MD, USA: US Department of Health and Human Services, FDA; 2017. Available from: <https://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM581468.pdf>. Accessed September 2, 2020.
- Wu H, Xia X, Cui Y, et al. Prevalence of extended-spectrum β -lactamase producing *Salmonella* on retail chicken in six provinces and two national cities in the People's Republic of China. *J Food Prot.* 2013;76:2040–2044.
- Xu H, Zhang W, Guo C, et al. Prevalence, serotypes, and antimicrobial resistance profiles among *Salmonella* isolated from food catering workers in Nantong, China. *Foodborne Pathog Dis.* 2019;16(5):346–351.
- Tennant SM, Diallo S, Levy H, et al. Identification by PCR of non-typhoidal *Salmonella enterica* serovars associated with invasive infections among febrile patients in Mali. *PLoS Negl Trop Dis.* 2010;4.
- Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. M07 Standard.* 11th ed. Wayne, PA: CLSI; 2018.
- Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing. M100 Standard.* 28th ed. Wayne, PA: CLSI; 2018.
- Liu YY, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis.* 2016;16:161–168.
- Amavisit P, Boonyawiwat W, Bangtrakulnont A. Characterization of *Salmonella enterica* serovar Typhimurium and monophasic *Salmonella* serovar 1,4,[5],12:i:- isolates in Thailand. *J Clin Microbiol.* 2005;43:2736–2740.
- Bankevich A, Nurk S, Antipov D, et al. SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. *J Comput Biol.* 2012;19:455–477.
- Seemann T. Prokka: rapid prokaryotic genome annotation. *Bioinformatics.* 2014;30:2068–2069.
- Zankari E, Hasman H, Cosentino S, et al. Identification of acquired antimicrobial resistance genes. *J Antimicrob Chemother.* 2012;67:2640–2644.
- Larsen MV, Cosentino S, Rasmussen S, et al. Multilocus sequence typing of total-genome-sequenced bacteria. *J Clin Microbiol.* 2012;50:1355–1361.
- Capuano F, Mancusi A, Capparelli R, Esposito S, Proroga YTR. Characterization of drug resistance and virulotypes of *Salmonella* strains isolated from food and humans. *Foodborne Pathog Dis.* 2013;10:963–968.
- Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect.* 2012;18(3):268–281.
- Li RC, Xie MM, Zhang JF, et al. Genetic characterization of *mcr-1*-bearing plasmids to depict molecular mechanisms underlying dissemination of the colistin resistance determinant. *J Antimicrob Chemother.* 2017;72:393–401.
- Fang LX, Jiang Q, Deng GH, et al. Diverse and flexible transmission of *fosA3* associated with heterogeneous multidrug resistance regions in *Salmonella enterica* serovar Typhimurium and indiana isolates. *Antimicrob Agents Chemother.* 2020;64.
- Li XP, Fang LX, Song JQ, et al. Clonal spread of *mcr-1* in PMQR-carrying ST34 *Salmonella* isolates from animals in China. *Sci Rep.* 2016;6:38511.
- Doumith M, Godbole G, Ashton P, et al. Detection of the plasmid-mediated *mcr-1* gene conferring colistin resistance in human and food isolates of *Salmonella enterica* and *Escherichia coli* in England and Wales. *J Antimicrob Chemother.* 2016;71:2300–2305.

28. Campos J, Cristino L, Peixe L, Antunes P. MCR-1 in multidrug-resistant and copper-tolerant clinically relevant *Salmonella* 1,4,[5],12:i:- and *S. Rissen* clones in Portugal, 2011 to 2015. *Euro Surveill.* **2016**;21.
29. Litrup E, Kiil K, Hammerum AM, et al. Plasmid-borne colistin resistance gene *mcr-3* in *Salmonella* isolates from human infections, Denmark, 2009–17. *Euro Surveill.* **2017**;22.
30. Saavedra SY, Diaz L, Wiesner M, et al. Genomic and molecular characterization of clinical isolates of *Enterobacteriaceae* harboring *mcr-1* in Colombia, 2002 to 2016. *Antimicrob Agents Chemother.* **2017**;61.
31. Arnott A, Wang Q, Bachmann N, et al. Multidrug-resistant *Salmonella enterica* 4,[5],12:i:- sequence type 34, New South Wales, Australia, 2016–2017. *Emerg Infect Dis.* **2018**;24:751–753.
32. Borowiak M, Hammerl JA, Deneke C, et al. Characterization of *mcr-5*-harboring *Salmonella enterica* subsp. *enterica* serovar Typhimurium isolates from animal and food origin in Germany. *Antimicrob Agents Chemother.* **2019**;63.

Infection and Drug Resistance

Dovepress

Publish your work in this journal

Infection and Drug Resistance is an international, peer-reviewed open-access journal that focuses on the optimal treatment of infection (bacterial, fungal and viral) and the development and institution of preventive strategies to minimize the development and spread of resistance. The journal is specifically concerned with the epidemiology of

antibiotic resistance and the mechanisms of resistance development and diffusion in both hospitals and the community. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/infection-and-drug-resistance-journal>