

## Community-associated meticillin-resistant *Staphylococcus aureus* pneumonia in China

We read with interest the Article by Stephano Aliberti and colleagues,<sup>1</sup> in which the investigators reported a low global prevalence of meticillin-resistant *Staphylococcus aureus* (MRSA) pneumonia and specific MRSA risk factors in community-dwelling patients admitted to the hospital with pneumonia.

Their Article fails to include data from China. To address this, we retrospectively retrieved clinical information of patients with community-acquired pneumonia from our previous published national survey of community-acquired infections in 31 county hospitals in China.<sup>2</sup> 529 patients (microbiological culture positive) were admitted to hospital because of community-acquired pneumonia. 263 were adults and 266 were children. Among adult patients, 23 patients were identified as *S aureus* positive, including nine (3%) testing positive for MRSA and 14 (5%) testing positive for meticillin-sensitive *S aureus*. By contrast, in 266 children patients, 30 were *S aureus* positive, including two (1%) positive for MRSA and 28 (11%) positive for meticillin-susceptible *S aureus*.

We then assessed the epidemiology and molecular features of these isolates (appendix). Diverse resistance profiles were observed; however, all isolates were susceptible to seven drugs. Of the typed isolates, six isolates (55%) belonged to ST239-t030, and two isolates (18%) were ST59-437. SCCmec and agr typing showed that the majority of the isolates belonged to SCCmecIII/agr type I, except for isolates 1709 and 2271, both of which were SCCmecIV/agr type I. Nine isolates (82%) were negative for Pantone-Valentine leukocidin virulence gene; however, the leukocidin ED gene was detected in nine (82%) isolates.

$\gamma$ -hemolysin was also identified in all isolates, and nine (82%) isolates harboured enterotoxin K, enterotoxin Q, or exfoliative toxin B.

So far, only limited data are available for community MRSA epidemiology in China. A prospective cohort showed that 3% (5/164) of community-associated MRSA isolates, which included two ST239 isolates, caused skin and soft tissue infection in adults.<sup>3</sup> Moreover, a previous study confirms a high prevalence of ST239 in both community-associated MRSA and health-care-associated MRSA isolates in south China, indicating possible transmission from health-care-associated MRSA to the community.<sup>4</sup> Of note, ST239-SCCmecIII has recently been reported as the prevalent community-associated MRSA clone in Korea.<sup>5</sup> Our findings further suggest that China is facing a similar situation. Although this study is limited by small case numbers, these findings emphasise the importance of monitoring community-associated MRSA pneumonia in China.

This work was supported by the National Basic Research Program of China (973 program, number 2015CB554201), the National Key Research and Development Program of China (number 2016YFD0501105), and the National Natural Science Foundation of China (numbers 81361138021, 81301461, and 41406140). We thank Andrew Hastings at Yale University for his linguistic assistance during the preparation of this manuscript. We thank Chaoqun Ying, Xin Wang, and Lihua Guo for their experimental assistance. All authors declare no competing interests.

Beiwen Zheng, Hao Xu, Ang Li, Jinru Ji, Yu Wang, \*Yonghong Xiao, Lanjuan Li  
xiao-yonghong@163.com

Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, State Key Laboratory for Diagnosis and Treatment of Infectious Disease, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, China

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## Plasmid-mediated or chromosomally mediated colistin resistance in *Klebsiella* *pneumoniae*?

Stefan Nicolet and colleagues<sup>1</sup> described a pair of sequential KPC-producing *Klebsiella pneumoniae* isolates from the same patient, including a colistin-susceptible isolate and a colistin-resistant isolate selected after 18 days of colistin treatment. Comparative genome analysis revealed that the two isolates differed by two missense mutations in chromosomal genes, plus some rearrangements and duplications, none of which could explain the acquisition of the colistin-resistant phenotype by the second isolate. Since the main difference between the two isolates was the presence of a 205 kb plasmid (accession CP015823.1, named plasmid 1) in the colistin-resistant isolate (accession CP015822.1, named blood sample 2), the authors warned about the possible presence of a new plasmid-mediated, mcr-1-independent mechanism of resistance to colistin, even if a plasmid-mediated transfer of resistance was not experimentally shown, and the plasmid was similar to other plasmids not associated with colistin resistance.

In 2014, we published the genome of a colistin-susceptible

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KPC-producing *K pneumoniae* strain, named KPB-1 (accession AYOV0000000.1),<sup>2</sup> which belongs to the same sequence type (ST512) as the strains analysed by Nicolet and colleagues, and carries a plasmid, named pKPB-1, that is very similar to plasmid 1 (99% of identity over 93% of the plasmid sequence). The differences between the two plasmids included some single nucleotide polymorphisms, single nucleotide deletions or insertions in intergenic regions or in few coding sequences, and two large substitutions (appendix). Since none of these differences had an obvious link with the acquisition of a colistin-resistant phenotype, we also compared the genomes of KPB-1 with the blood sample 2 isolate. Comparative analysis done with CSIPhylogeny 1.4 revealed a high similarity between the two strains (39 single nucleotide polymorphisms), with no differences in the *mgrB*, *pmrAB*, *phoPQ*, and *crrAB* genes.<sup>3</sup> However, in the blood sample 2 isolate, there was an insertion sequence, *IS1R*, between nucleotides 61 and 62 of the putative promoter of the *mgrB* gene—ie, a genetic alteration that has previously been linked to colistin resistance in

an OXA-48-producing *K pneumoniae* strain.<sup>4</sup> Notably, an identical copy of *IS1R* was also present in plasmid 1, but not in other parts of the chromosome or in the other plasmids carried by blood sample 2 isolate.

In conclusion, we think that the colistin-resistant phenotype expressed by this isolate could be chromosomally mediated, whereas acquisition of the resistance mechanism could have been facilitated by the acquisition of plasmid 1, by providing *IS1R*, which probably was later mobilised into the *mgrB* promoter region. Indeed, it has previously been reported that KPC-encoding plasmids might contain *IS5*-like elements that could facilitate the emergence of colistin resistance by disrupting the *mgrB* coding sequence.<sup>5</sup> Transferable plasmids carrying insertion sequences could therefore reshape the bacterial chromosome facilitating the emergence of colistin resistance.

We declare no competing interests. AA and MMD contributed equally.

Alberto Antonelli,  
Marco Maria D'Andrea,  
Tommaso Giani, \*Gian Maria Rossolini  
gianmaria.rossolini@unifi.it

Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy (AA, MMD, GMR); Department of Medical Biotechnologies, University of Siena, Siena, Italy (MMD, TG, GMR); Clinical Microbiology and Virology Unit, Careggi University Hospital, Florence, Italy (GMR); and IRCCS Don Carlo Gnocchi Foundation, Florence, Italy (GMR)

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