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LETTER TO THE EDITOR

Plasmid-Mediated *mcr-1* Gene in Colistin-Resistant Clinical Isolates of *Klebsiella pneumoniae* in France and Laos

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Recently, Yi-Yun Liu et al. reported the emergence of plasmid-mediated colistin resistance involving the *mcr-1* gene from *Escherichia coli* and *Klebsiella pneumoniae* isolates from animals, food, and humans in China (1). Because of the plasmidic location of this new gene, which encodes a phosphoethanolamine transferase, it is transferable laterally between Gram-negative bacteria (1). We have recently reported the isolation of *mcr-1*-positive *E. coli* isolates from animals and humans from Laos (pigs and asymptomatic humans), Thailand (asymptomatic humans), and Algeria (chicken) (2). Although resistance to colistin in humans was believed to be linked only to colistin ingestion in humans, there is evidence of an independent emergence of colistin-resistant bacteria in humans without colistin usage, likely suggesting that such bacteria may preexist in the human gut and be selected upon colistin therapy (3, 4). We have tested by real-time PCR (5) and confirmed by standard PCR and sequencing the possible presence of the *mcr-1* gene in 32 colistin-resistant *K. pneumoniae* isolates previously isolated in Laos (11 isolates), Thailand (14 isolates), France (6 isolates), and Nigeria (1 isolate) (6). We found that 6 isolates, specifically, 4 isolates from humans in Laos and 2 isolates from France (1 from Marseille and 1 from Angers), harbor the *mcr-1* gene sequence (Table 1). MICs were determined by the Etest and interpreted with EUCAST guidelines. Interestingly, two of the four isolates from Laos also had either a stop codon (at Cys28 in strain KP LH131) or a mutation (A14S in strain KP LH61) in the *mgrB* gene sequence; the MICs for them were higher than those for the four other isolates that had only *mcr-1*, which is consistent with previous findings for colistin MICs for isolates with only *mcr-1* (1, 2). These strains were isolated from human stool samples collected in 2012 and 2013 either from healthy individuals (Laos) or from patients at the University Hospital La Timone (Marseille, 4-year-old girl) and the University Hospital Centre (Angers, 83-year-old male) who had never received colistin therapy. Interestingly, although our isolates are resistant to colistin, they remain susceptible to several classes of antibiotics, including cephalosporins and carbapenems (Table 2), but acquisition of additional antibiotic resistance genes within the human gut is a possible scenario (6). To the best of our knowledge, this is the first report of colistin-resistant *mcr-1*-positive *K. pneumoniae* clinical isolates in Marseille and Angers, France, and in Laos. Our report clearly demonstrates that plasmid-mediated colistin resistance has already spread all over the world, including Europe. This is probably due to the fact that colistin is extensively used in animal production, including in Europe (3, 4, 7).

Since colistin is now widely used in Europe (Greece and Italy, for example) to treat patients infected with *K. pneumoniae* carbapenemase producers and also in agriculture production, there is an urgent need to implement a screening strategy for the carriage of colistin-resistant Gram-negative bacteria in hospitalized humans, as has already been done for carbapenemase producers, and to ban the use of colistin in avian and pig production in order to avoid a frightening scenario of the colistin resistance gene spreading to humans, as NDM-1 did 5 years ago.

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TABLE 1 MICs for and genetic features of *Klebsiella pneumoniae* clinical isolates positive for *mcr-1* by PCR[a]

Country	Isolate	Colistin MIC (mg/liter)[b]	ST	*mgrB* feature
Laos	KP LH131	32	1319	Stop (at Cys28)
	KP LH17	12	37	Intact
	KP LH61	24	491	Sub (A14S)
	KP LH92	12	39	Intact
France	KP FHM128 (Marseille)	4	1310	Intact
	KP FHA60 (Angers)	8	8	Intact

[a] All strains were *mcr-1* positive. ST, sequence type; Intact, intact *mgrB* gene with no mutation; Stop, mutation leading to insertion of a stop codon; Sub, mutation leading to an amino acid substitution.
[b] MICs were determined by the Etest assay.

TABLE 2 Antibiotic susceptibility testing results for the 6 *mcr-1*-positive strains

Strain	Susceptibility profile for following antibiotic of the indicated class[a]:																					
	β-Lactams											Aminoglycosides			Quinolones		Cyclins			Sulfamide	Nitrofuran	
	AMX	AMC	TIM	TZP	CRO	CTX	FEP	ERT	MEM	IMP	ATM	GEN	TOB	AMK	NAL	CIP	DOX	MIN	TGC	SXT	NIT	FOF
KP LH17	**R**	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	**R**
KP LH92	**R**	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
KP LH61	**R**	S	**R**	S	S	S	S	S	S	S	S	S	S	S	S	S	**R**	S	S	**R**	S	S
KP LH131	**R**	**R**	**R**	S	S	S	S	S	S	S	S	S	S	S	S	S	**R**	**R**	S	S	S	S
KP FHA60	**R**	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	**R**	S	S	**R**	S	S
KP FHM128	**R**	S	S	S	S	S	S	S	S	S	S	**R**	**R**	S	S	S	**R**	**R**	S	**R**	S	**R**

[a] AMX, amoxicillin; AMC, amoxicillin-clavulanate; TIM, ticarcillin-clavulanate; TZP, piperacillin-tazobactam; CRO, ceftriaxone; CTX, cefotaxime; FEP, cefepime; ERT, ertapenem; MEM, meropenem; IMP, imipenem; ATM, aztreonam; GEN, gentamicin; TOB, tobramycin; AMK, amikacin; NAL, nalidixic acid; CIP, ciprofloxacin; DOX, doxycycline; MIN, minocycline; TGC, tigecycline; SXT, trimethoprim-sulfamethoxazole; NIT, nitrofurantoin; FOF, fosfomycin; R, resistant; S, susceptible.

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