

Letters to the Editor

Identification of the Aminoglycoside Resistance Determinants *armA* and *rmtC* among Non-Typhi *Salmonella* Isolates from Humans in the United States^V

Aminoglycosides are an important class of antimicrobial agents for the treatment of life-threatening bacterial infections. Several mechanisms for aminoglycoside resistance have been described previously (5). Among these mechanisms, 16S rRNA methyltransferases are especially troublesome due to their wide target range and their ability to confer high levels of resistance.

In the United States, antimicrobial resistance among enteric pathogens in humans is monitored by the National Antimicrobial Resistance Monitoring System (NARMS) at the CDC. From 1996 to 2006, 18,281 non-Typhi *Salmonella* isolates were submitted to the CDC. MICs of 14 to 17 antimicrobial agents were determined by broth microdilution using the Sensititre system (Trek Diagnostics, Westlake, OH). Two isolates displayed resistance to three aminoglycosides, with resistance defined by a MIC of ≥ 64 $\mu\text{g/ml}$ for amikacin, ≥ 16 $\mu\text{g/ml}$ for gentamicin, and ≥ 64 $\mu\text{g/ml}$ for kanamycin (Table 1). Isolate AM04864 was *Salmonella enterica* serotype Stanley, submitted in 1999. Additional information from the patient was not available. AM23818 was *S. enterica* serotype Virchow, submitted in 2005. The patient was an 11-month-old Asian male from Hartford, CT. Prior to the onset of illness, he visited a farm in India and had exposure to farm animals. The patient became ill with nonbloody diarrhea in India. Upon returning to the United States, he was taken for medical care. Oral antibiotics were prescribed following specimen collection; the antibiotic name could not be recalled. The patient was ill with diarrhea for 6 weeks, during which he was presented for medical care two additional times.

Screening for methyltransferase genes was performed by PCR using previously described primers for six genes: *armA*, *rmtA*, *rmtB*, *rmtC*, *rmtD*, and *npmA* (2). AM04864 was positive for *armA*, while AM23818 was positive for *rmtC*. Sequence analysis confirmed that the *armA* gene was identical to that observed in *Acinetobacter baumannii* (GenBank accession number EU014811) and *S. enterica* serotype Oranienburg (GenBank accession number DQ177329). Sequence analysis also confirmed that *armA* was located between *mpU* and *mpD*, genes associated with the Tn1548 transposon (3, 4). Tn1548 typically carries additional genes which confer resistance to azithromycin, streptomycin-spectinomycin, sulfonamides, and trimethoprim. This may explain the additional resistance phenotype of AM04864 (Table 1). Sequence analysis of the *rmtC* gene confirmed that the gene was identical to that observed in

Proteus mirabilis (GenBank accession number EU144360) (7). To our knowledge, *rmtC* has not been identified outside of *P. mirabilis*. Upstream of the *rmtC* sequence, we identified the 3' end of the *ISEcp1* element, along with one of the inverted repeat regions. *ISEcp1* has been shown previously to promote the expression and transposition of *rmtC* (6).

Although *ArmA* is one of the most widespread methyltransferases in the world, it has been identified only in *A. baumannii* in the United States (1). *RmtC* has not previously been observed in the United States. All of the *rmtC*-positive isolates reported up to now have been *P. mirabilis* isolates from patients in Japan, with the exception of a single isolate from Australia (8). The patient infected with the *Salmonella* strain carrying the *rmtC* gene had recently traveled to India, suggesting that the infection originated in India. Identification of methyltransferase genes among non-Typhi *Salmonella* isolates from humans in the United States suggests the existence of a potential reservoir for these resistance mechanisms.

Nucleotide sequence accession numbers. The nucleotide sequences of *armA* and *rmtC* have been deposited in GenBank under accession numbers FJ788923 and FJ807682.

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TABLE 1. Antimicrobial susceptibilities and characteristics of NARMS non-Typhi *Salmonella* isolates resistant to amikacin, gentamicin, and kanamycin^a

Isolate	Year	Serotype	MIC ($\mu\text{g/ml}$) of:			rRNA methyltransferase gene	Additional resistance profile
			AMI	GEN	KAN		
AM04864	1999	Stanley	>64	>16	>64	<i>armA</i>	AMP, AZM, CHL, FIS, STR, TET, SXT
AM23818	2005	Virchow	>64	>16	>64	<i>rmtC</i>	NAL, FIS, SXT

^a AMI, amikacin; AMP, ampicillin; AZM, azithromycin; CHL, chloramphenicol; FIS, sulfisoxazole (sulfafurazole); GEN, gentamicin; KAN, kanamycin; NAL, nalidixic acid; STR, streptomycin; SXT, trimethoprim-sulfamethoxazole; TET, tetracycline. Additional drugs tested: amoxicillin-clavulanic acid, ceftriaxone, ciprofloxacin, ceftiofur.

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Jason P. Folster*

*National Antimicrobial Resistance Monitoring System
Centers for Disease Control and Prevention
CCID/NCZVED/DFBMD/EDLB
1600 Clifton Road
Atlanta, Georgia 30333*

Regan Rickert

Ezra J. Barzilay

Jean M. Whichard

*Division of Foodborne, Bacterial and Mycotic Diseases
Centers for Disease Control and Prevention
Atlanta, Georgia*

*Phone: (404) 639-4948

Fax: (404) 639-4290

E-mail: gux8@cdc.gov

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