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126 Emergence of plasmid-mediated high-level tigecyclineresistance genes in animals and humans

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Background: Tigecycline is the last-resort antibiotic that is used to treat severe infections caused by extensively drug-resistant bacteria. The tigecycline-resistance gene *tet*(X) has been shown to encode a flavin-dependent monooxygenase that modifies tigecycline, while few *tet*(X) or its variant genes were reported in animal or clinical isolates.

Materials/methods: Tigecycline-resistant *Acinetobacter baumannii* 34AB and *Escherichia coli* 47EC were firstly isolated from pigs during our annual surveillance. Screening for *tet*(X) was conducted in various samples of animal origin collected during 2017–2018. All samples were incubated and then detected *tet*(X) by PCR. The minimal inhibitory concentration values of all *tet*(X)-positive isolates were recommended by the EUCAST. Genomic DNA of all *tet*(X)-positive isolates was subjected to analysed using whole-genome sequencing. Inverse PCR assays were conducted for circular intermediate IS*Vsa3*-*tet*(X3) and *tet*(X4). Transposition experiments were performed to determine whether IS*Vsa3* could mediate the transposition of *tet*(X)-carrying cassettes.

Results: Two unique mobile tigecycline-resistance genes, *tet*(X3) and *tet*(X4), were identified in 34AB and 47EC, respectively. Retrospective screening revealed that these two genes were also detected in numerous Enterobacteriaceae and *Acinetobacter* that were isolated from animals, meat for consumption and humans. Both *tet*(X3) and *tet*(X4) increase (by 64–128-fold) the tigecycline minimal inhibitory concentration values for *E. coli*, *Klebsiella pneumoniae* and *A. baumannii*. A total of 77 tigecycline-resistant isolates were positive for *tet*(X3) (n = 48) or *tet*(X4) (n = 29) by retrospective screening analyses, and most *tet*(X3) and *tet*(X4) in these isolates are adjacent to insertion sequence IS*Vsa3*, which could form a circular IS*Vsa3*-*tet*(X) variant intermediate for transposition. Moreover, data mining from NCBI Genbank confirm that *tet*(X3) and *tet*(X4) are globally present in clinical bacteria.

Conclusions: Our findings suggest that both the surveillance of *tet*(X) variants in clinical and animal sectors and the use of tetracyclines in food production requires urgent global attention.