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Characterization of tigecycline (tet(X)) and multidrug-resistant *Acinetobacter lwoffii/pseudolwoffii* from French animals

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Leila Hamze, Antoine Drapeau, Pierre Châtre, Estelle Saras, Jean-Yves Madec, et al.. Characterization of tigecycline (tet(X)) and multidrug-resistant *Acinetobacter lwoffii/pseudolwoffii* from French animals. 13th International Symposium on the Biology of *Acinetobacter*, Jun 2023, Coimbra, Portugal. anses-04276211

HAL Id: anses-04276211

<https://anses.hal.science/anses-04276211v1>

Submitted on 8 Nov 2023

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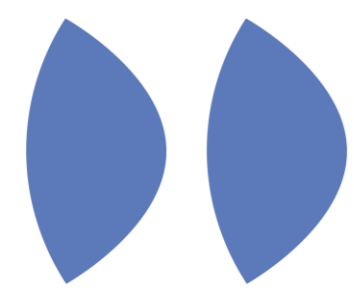


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Background

Tigecycline is a last-resort antibiotic restricted to humans for treating severe infections caused by multidrug-resistant bacteria.

Plasmid-located tigecycline-resistance genes *tet(X)* have been characterized since 2019 in Enterobacterales and *Acinetobacter* species.

In the current study, the genetic content of animal *Acinetobacter lwoffii/pseudolwoffii* exhibiting tigecycline non-susceptibility was characterized.

Results

rMLST confirmed *A. lwoffii* identification for two isolates, whereas two were assigned to *A. pseudolwoffii*. All of them belonged to novel sequence types and carried numerous antibiotic resistance genes (Table 1).

The four tigecycline-non susceptible strains carried gene *tet(X3)*. Full assembly in strains 43620 and 49430 revealed that *tet(X3)* was located on a IS91 mediated transposon (Figure 1).

In turn, these elements were located on plasmids with predicted structures for self-transfer (Figure 2).

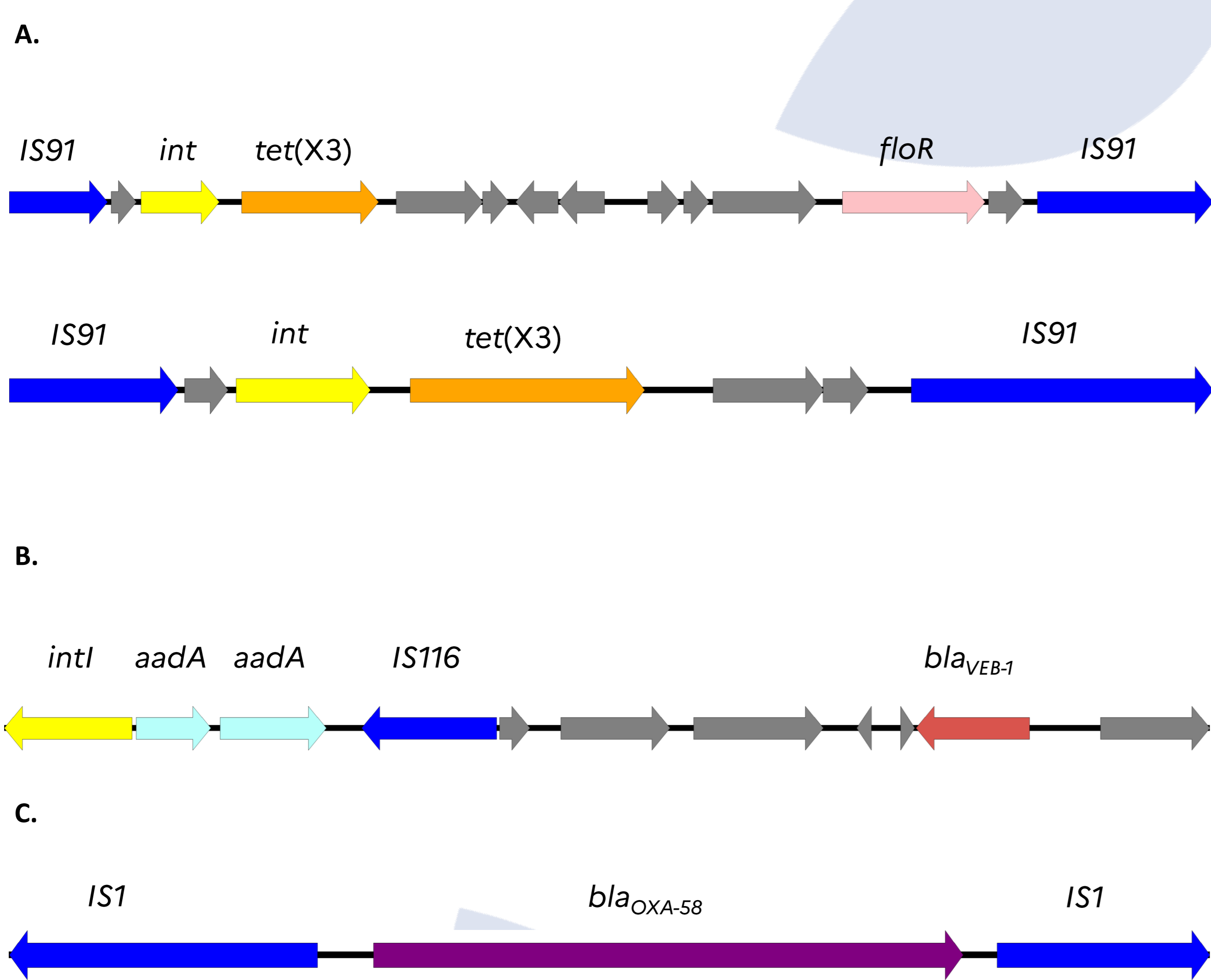


Figure 1. A. Graphical representation of the genetic environment surrounding *tet(X)* gene in 43620 and 49430 (A), *bla_{VEB-1}* gene in 43620 (B), and *bla_{OXA-58}* in 49430 (C) (Easyfig v.2.5.).

Conclusion

Genes *tet(X)* and tigecycline resistance in *Acinetobacter* spp. were so far unreported among French animals. In general, *tet(X)* occurrence in Europe is rare, with two reports in tissues of dead animals from Italy and one from environmental source from Norway.

However, their localization on predicted mobile elements could rapidly change the epidemiological picture.

Surveillance of this major resistance mechanism is important for animal and human health.

Furthermore, these results underline the necessity of rationale usage of “old” antibiotics such as tetracycline, which regained interest to avoid the use of last-generations antibiotics but could co-select multiple and major resistance mechanisms in animals.

Material and methods

During 2016-2022, four tigecycline non-susceptible *A. lwoffii* isolates (E-test 2 mg/L) were collected through the diagnostic laboratories of the Resapath (<https://resapath.anses.fr>).

Genomes were sequenced by short (Illumina) and, for two isolates, by long reads (Oxford Nanopore) approaches. Assembly was performed using Shovill v.1.0.4 and Unicycler v.0.4.8. Antibiotic resistance genes and sequence type were analyzed on the BV-BRC platform based on the CARD database and the Institut Pasteur scheme, respectively.

Isolate	Identification	Year of isolation	Host	Source	ST*	Antibiotic resistance genes
43620	<i>A. pseudolwoffii</i>	2016	Horse	Endometre	1792	<i>bla_{VEB-1}</i> , <i>bla_{TEM-2}</i> , <i>aadA1</i> , <i>strA</i> , <i>strB</i> , <i>sul1</i> , <i>sul2</i> , <i>tet(A)</i> , <i>tet(X3)</i> , <i>mph(E)</i> , <i>msr(E)</i> , <i>floR</i> , <i>arr-3</i>
48934	<i>A. lwoffii</i>	2017	Cat	Nose	1960	<i>bla_{CARB-5}</i> , <i>bla_{TEM-2}</i> , <i>strA</i> , <i>strB</i> , <i>aph(3')-Ia</i> , <i>aac(3)-IIa</i> , <i>sul2</i> , <i>tet(X3)</i> , <i>floR</i> , <i>InuG</i>
49430	<i>A. pseudolwoffii</i>	2018	Horse	Peritoneum	1968	<i>bla_{CARB-5}</i> , <i>bla_{OXA-58}</i> , <i>strA</i> , <i>strB</i> , <i>aph(3')-Ia</i> , <i>aac(3)-IIa</i> , <i>sul2</i> , <i>dfrA36</i> , <i>tet(X3)</i> , <i>cat(A1)</i> , <i>mph(E)</i> , <i>msr(E)</i>
61450	<i>A. lwoffii</i>	2022	Horse	Endometre	2258	<i>bla_{VEB-1}</i> , <i>strA</i> , <i>strB</i> , <i>aac(3)-IIa</i> , <i>aac(6)-Ib-cr</i> , <i>sul1</i> , <i>sul2</i> , <i>tet(A)</i> , <i>tet(X3)</i> , <i>mph(E)</i> , <i>msr(E)</i> , <i>floR</i> , <i>arr-3</i>

*: most similar sequence type from the Institut Pasteur scheme

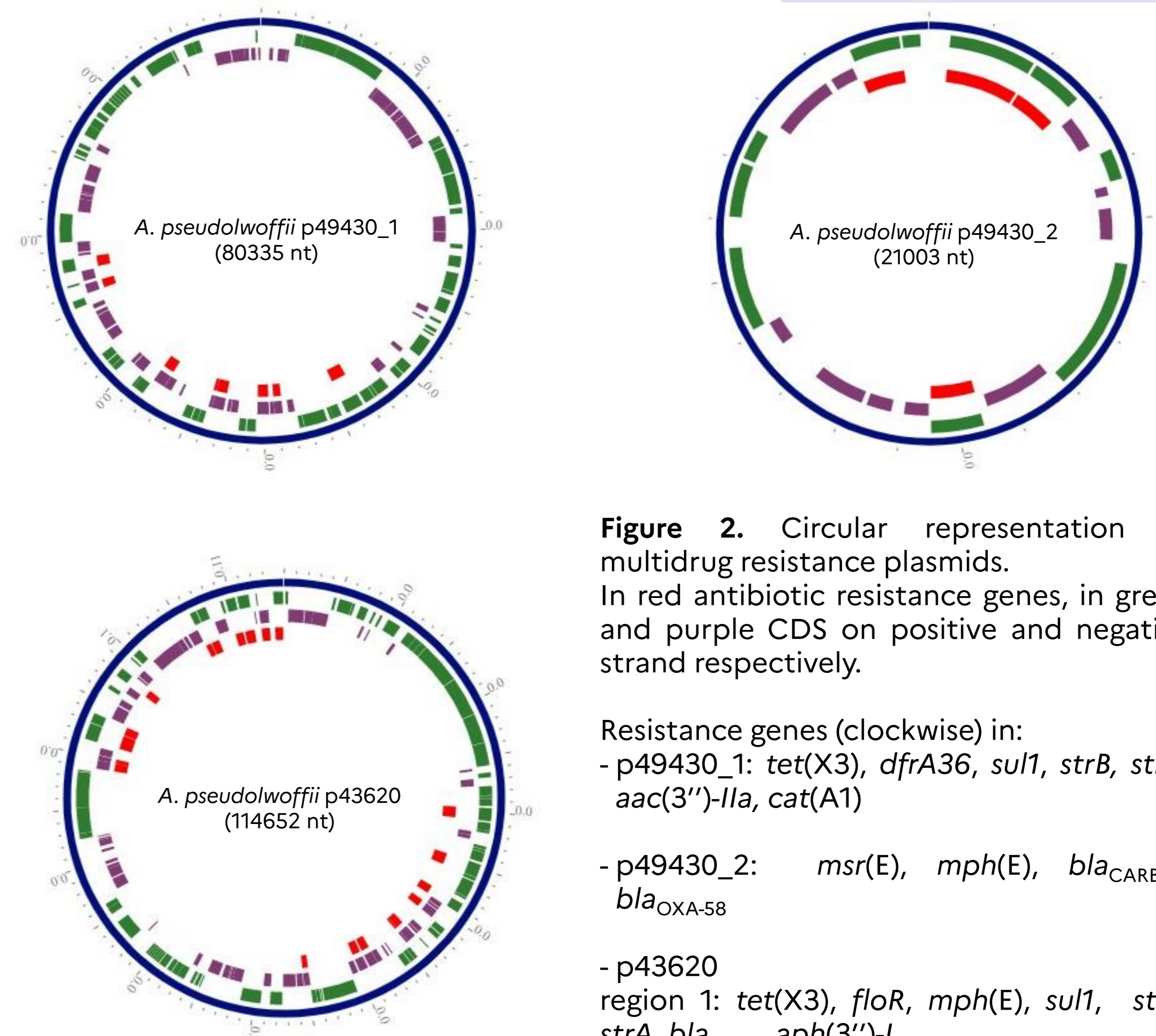


Figure 2. Circular representation of multidrug resistance plasmids.

In red antibiotic resistance genes, in green and purple CDS on positive and negative strand respectively.

- Resistance genes (clockwise) in:
- p49430_1: *tet(X3)*, *dfrA36*, *sul1*, *strB*, *strA*, *aac(3')-IIa*, *cat(A1)*
 - p49430_2: *msr(E)*, *mph(E)*, *bla_{CARB-16}*, *bla_{OXA-58}*
 - p43620
region 1: *tet(X3)*, *floR*, *mph(E)*, *sul1*, *strB*, *strA*, *bla_{TEM-1}*, *aph(3')-I*
region 2: *strB*, *strA*, *msr(E)*, *mph(E)*, *aph(3')-I*, *ant(3')-Ia*, *sul1*, *tetA*, *bla_{VEB-1}*, *sul1*