Clonal Spread of Acinetobacter baumannii Sequence Type 25 Carrying bla OXA-23 in Companion Animals in France

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Acinetobacter baumannii causes life-threatening infections in critically ill patients, with subsequent treatments mostly based on carbapenems. Unfortunately, oxacillinases (OXAs) that hydrolyze carbapenems, especially OXA-23, have dramatically spread in humans and even started to be reported in animals (1–4). As OXA-producing isolates are still rare in nonhuman sources, a comprehensive picture of their occurrence in animals is lacking.

We analyzed 41 *A. baumannii* isolates from nonduplicate diseased animals from 2011 to 2015 in the framework of the French Surveillance Network for Antimicrobial Resistance in Animal Pathogens (RESAPATH; https://www.resapath.anses.fr/) for susceptibility to carbapenems, the presence of bla_{OXA} genes, and clonal relatedness.

Identification was based on *rpoB* gene sequencing (5). According to the CA-SFM/EUCAST breakpoints (http://www.sfm-microbiologie.org/UserFiles/files/casfm/CASFM2016_V1_0_FEVRIER.pdf), seven isolates demonstrated high-level resistance to meropenem and imipenem (MICs of >32 μg/ml) and were also multidrug resistant (Table 1).

PCR screening, performed as previously described (6), demonstrated the presence of bla_{OXA-23} in the seven isolates. IS*Aba1* was inserted 34 bases upstream from the starting codon of bla_{OXA-23}. This organization, resembling that of transposons Tn*2008B*, Tn*2006*, and Tn*2009*, provided a −35 (TCGTTA) and −10 (TGACATTAT) extended promoter region for the overexpression of bla_{OXA-23} (7). Similarly to Tn*2008B*, no copy of IS*Aba1* was present downstream of bla_{OXA-23} in our isolates. According to DNA-DNA hybridization, bla_{OXA-23} was located on the bacterial chromosome and attempts of conjugation with *Escherichia coli* K-12 strain J53 (8) did not produce transconjugants on selective medium containing rifampin (250 μg/ml) and imipenem (2 μg/ml) or ticarcillin (8 μg/ml).

The seven isolates were clonally related (similarity, ≥98.8%) according to repetitive-sequence-based PCR performed with DiversiLab (bioMérieux, Marcy l'Etoile, France) (9). Multilocus sequence typing based on the Pasteur scheme (10) assigned the isolates to sequence type 25 (ST25). Remarkably, the isolates were found to be associated with urinary tract infections in pets originating in five departments in two regions (Ile de France and Rhône-Alpes) from 2013 to 2015, for the first time demonstrating the clonal dissemination of OXA-23-producing *A. baumannii* among companion animals. Three isolates (40293, 41133, and 41134) were recovered from pets attending the same clinic, outlining the occurrence of a small outbreak. The remaining isolates (38208, 40104, 34972, and 41833) originated from unrelated and distant animals, suggesting a nationwide spread of OXA-23-

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TABLE 1 Origins and antimicrobial resistance profiles of ST25 OXA-23-producing *A. baumannii* isolates from companion animals in France

					Inhibition zone diam, mm (category)[b]											
Isolate	Host	Disease[a]	Yr	Municipality	CTX	CTX + CLO[c]	CAZ	CAZ + CLO	FEP	FEP + CLO	TOB	GN	AK	NET	CIP	SXT
34972	Cat	UTI	2013	94110	14 (R)	16	21 (S)	24	8 (R)	11	19 (S)	6 (R)	27 (S)	14 (R)	6 (R)	6 (R)
38208	Cat	UTI	2014	94000	15 (I)	16	21 (S)	24	10 (R)	11	18 (S)	6 (R)	26 (S)	11 (R)	6 (R)	6 (R)
40104	Cat	UTI	2015	94140	11 (R)	15	19 (S)	23	12 (R)	14	21 (S)	6 (R)	29 (S)	13 (R)	6 (R)	6 (R)
40293	Dog	UTI	2015	95600	12 (R)	18	22 (S)	24	9 (R)	11	25 (S)	23 (S)	26 (S)	21 (S)	6 (R)	6 (R)
41133	Cat	UTI	2015	75020	14 (R)	18	23 (S)	25	9 (R)	12	19 (S)	6 (R)	26 (S)	9 (R)	6 (R)	6 (R)
41134	Dog	UTI	2015	77230	15 (I)	17	22 (S)	23	8 (R)	11	17 (S)	6 (R)	26 (S)	10 (R)	6 (R)	6 (R)
41833	Cat	UTI	2015	69240	16 (I)	19	22 (S)	28	11 (R)	16	21 (S)	9 (R)	28 (S)	14 (R)	6 (R)	6 (R)

[a]UTI, urinary tract infection.

[b]Isolates were highly resistant to imipenem and meropenem (MICs of >32 μg/ml). Categorization was based on the breakpoints provided by CA-SFM/EUCAST for *Acinetobacter* spp. (www.sfm-microbiologie.org/UserFiles/files/casfm/CASFM2016_V1_0_FEVRIER.pdf). Abbreviations (breakpoints): CTX, cefotaxime (S, ≥23; R, <15); CAZ, ceftazidime (S, ≥18; R, <15); FEP, cefepime (S, ≥18; R, <15); TOB, tobramycin (S, ≥17; R, <17); GN, gentamicin (S, ≥17; R, <17); AK, amikacin (S, ≥18; R, <15); NET, netilmicin (S, ≥16; R, <16); CIP, ciprofloxacin (S, ≥21; R, <21); SXT, trimethoprim-sulfamethoxazole (S, ≥16; R, <13).

[c]Cloxacillin (CLO) was added to the medium at a concentration of 250 μg/ml to unveil the hydrolytic mechanism responsible for β-lactam resistance.

producing ST25 *A. baumannii* in pets. Our findings expand recent data on two isolates recovered from healthy dogs in the region of Nantes (11) and highlight an emerging and worrying epidemiological picture, with a possible endemicity of OXA-23-producing ST25 *A. baumannii* in pets in France.

So far, OXA-23-producing *A. baumannii* isolates from animals have belonged to ST2 (3, 4, 12), suggesting cross-transmission of such isolates from humans to animals (4). Looking at human clinics in France, OXA-23-producing ST2 *A. baumannii* is the predominant clone (2, 13). However, Jeannot et al. have also reported the occurrence of ST25 *A. baumannii* among human isolates, albeit mostly harboring OXA-58 (2). Our results suggest that the epidemiology of carbapenem-resistant *A. baumannii* in companion animals might be independent of that in humans. Nonetheless, incidental transmission of OXA-23-producing ST25 *A. baumannii* from humans to pets cannot be excluded, even though the process that might favor the persistence and circulation of this clone among different individuals remains to be elucidated. On the other hand, carbapenems do not belong to the therapeutic arsenal used in veterinary medicine but penicillins or penicillin–β-lactamase inhibitor combinations might select for OXA-23-producing *A. baumannii*. Moreover, many other veterinary antibiotics can coselect intrinsic resistances of *A. baumannii* and contribute to a further clonal spread. In light of the remarkable prevalence of ST25 *A. baumannii* associated with urinary tract infections in our study, a possible special tropism of such a clone as a uropathogen needs further evaluation. These findings make it urgent to investigate the processes favoring the emergence and spread of OXA-producing *A. baumannii* in veterinary settings.

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