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NGS characterization of expanded-spectrum cephalosporins resistant *Morganellaceae* spp. from animal and human origins

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Antibiotic resistance is a major public health problem notably for Gram-negative bacteria. Mechanisms and epidemiology of resistance to expanded-spectrum cephalosporins (ESC) are well known for common *Enterobacteriaceae*, like *Escherichia coli* or *Klebsiella pneumoniae* but little is known for *Morganellaceae* spp. Present in water, soil or inside the intestinal tract of humans and animals, *Morganellaceae* spp. are opportunistic pathogens mainly responsible for urinary tract infections. Since the last decade, there is an increase of reports describing multidrug-resistant (MDR) *Proteus mirabilis* strains harbouring mobile genetic elements with extended-spectrum- β -lactamase (ESBL) and/or AmpC cephalosporinase resistance genes. Several MDR Integrative Conjugative Elements (ICE) or Integrative Mobilizable Elements (IME) belonging to the SXT or SGI1 families have been described. The objective here was to determine, thanks to NGS, the genetic determinants of resistance and the molecular supports of ESC-resistant *Morganellaceae* isolates from animal and human origins.

Sixty-six ESC-resistant *Morganellaceae* strains (mainly *P. mirabilis* and *Morganella morganii* isolated from humans and animals in France, Bulgaria, Taiwan between 1996 and 2017) were whole-genome sequenced using the IonProton[®] system to investigate the resistome and presence of mobile genetic elements. Conjugation assays were performed to assess the horizontal transfer of ESBL and/or AmpC resistance genes.

All ESC-resistant *Morganellaceae* isolates were MDR with additional resistances to other antibiotic families (>3 antibiotic classes). *bla*_{CTX-M} genes were mainly encountered among human isolates (25/48). The AmpC-encoding gene *bla*_{CMY-2} and the ESBL-encoding gene *bla*_{VEB-6} were found more frequent in animal isolates than in human isolates (14/18 vs 10/48, respectively). Chromosomally-integrated mobile genetic elements SXT and SGI1 carried the *bla*_{CMY-2} and *bla*_{VEB-6} genes, respectively. Both elements co-occurred in a few isolates. Broad host range IncC-related mobile elements (plasmids and SXT) were almost the only self-transferable elements by conjugation.

The mobile genetic supports of ESBL and AmpC resistance genes appeared different between *Morganellaceae* isolates of human and animal origins, as well as different from that of *Enterobacteriaceae* such as *E. coli* in which conjugative plasmids carrying *bla*_{CTX-M} genes are mainly responsible for ESC resistance. These results need to be confirmed on larger collections of *Morganellaceae* isolates of different sources.