Colistin resistance gene mcr-1 harboured on a multidrug resistant plasmid

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Colistin resistance conferring *mcr-1* isolated from Belgian bovine and pig farms is harbored on a novel multi-drug resistant plasmid

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In the November 18, 2015 issue, Liu *et al* reported, for the first time, plasmid-mediated colistin resistance in *Escherichia coli* isolated from animals, food and patients in China.[1] These data bring to the fore an as yet unknown facet of colistin resistance and yet again highlight the impact of antibiotic use in animal farming on human health.[2, 3] Here, we screened a selection of 105 colistin-resistant *E. coli* strains (sensititre MICs of colistin ≥ 4 mg/L) isolated during 2011-12 from a passive surveillance of *E. coli* diarrhea in calves (n=52) and piglets (n=53) from the Walloon and Flanders regions of Belgium, respectively. All strains were screened for the presence of *mcr-1* using PCR and Sanger sequencing. The gene was detected in 13/105 (12.4%) *E. coli* (macrobroth dilution MICs of colistin 4 and 8 mg/L), of which 6 (11.5%) and 7 (13.2%) were isolated from calves and piglets, respectively. The *mcr-1* allele showed 100% sequence similarity to the Chinese allele.[1] Plasmid sequencing (MiSeq, Illumina) from one bovine strain isolated pKH-457-3-BE that showed an IncP backbone and a size of 79,798 bp (Figure). Blast comparison with pHNSHP45 showed 100% similarity only in a short, 2604 bp region that included *mcr-1* (1626 bp) and a truncated IS*ApII* mobile element that did not include the transposase-encoding *tnpA* gene. pKH-457-3-BE showed 99% similarity (73% query coverage) to plasmid pHXY0908 (acc. no. KM877269) found in *Salmonella enterica subsp. enterica serovar typhimurium* isolated from

chicken stool in China. In contrast to pHNSHP45, pKH-457-3-BE harbored multiple resistance-encoding genes to trimethoprim (*dfrA1*), tetracycline (*tetA*), aminoglycoside (*aadA1, aph(6)-Id or strA,* and *aph(3'')-Ib/strB*) and sulphonamide (*sul1*) antibiotics. Phenotypic testing showed absence of extended-spectrum beta-lactamase and carbapenemase production in all *mcr-1* positive strains.

We demonstrate here a marked presence of *mcr-1* in animal pathogenic bacteria in Europe, an indication that this is already a truly global phenomenon. That *mcr-1* was present in *E. coli* circulating in Belgian farm animals during 2011-2012 and was harbored on a different plasmid backbone than the one isolated from pigs in China (IncI2) or from imported chicken meat in Denmark (IncX4),[1, 4] indicates a high promiscuity of this gene guided by the adjoining mobile element. Of note, majority of the *mcr-1* positive *E. coli* isolated here were enterotoxigenic (ETEC) and verocytotoxic (VTEC) strains that affect animals but do not cause pathology in humans. It will be of utmost importance to assess transfer frequencies and sustainability of the *mcr-1* harboring genetic elements in human-associated *E. coli* and other Gram-negative pathogens to fully delineate the impact of these findings. Finally, also noteworthy are the 92 colistin-resistant *E. coli* wherein *mcr-1* was not detected and might potentially harbor other (transferable) colistin-resistant mechanism(s) or even novel *mcr-1* alleles. These findings highlight the importance of a more proactive ‘one health’ screening approach to identify novel mechanisms and vectors of antibiotic resistance.

References

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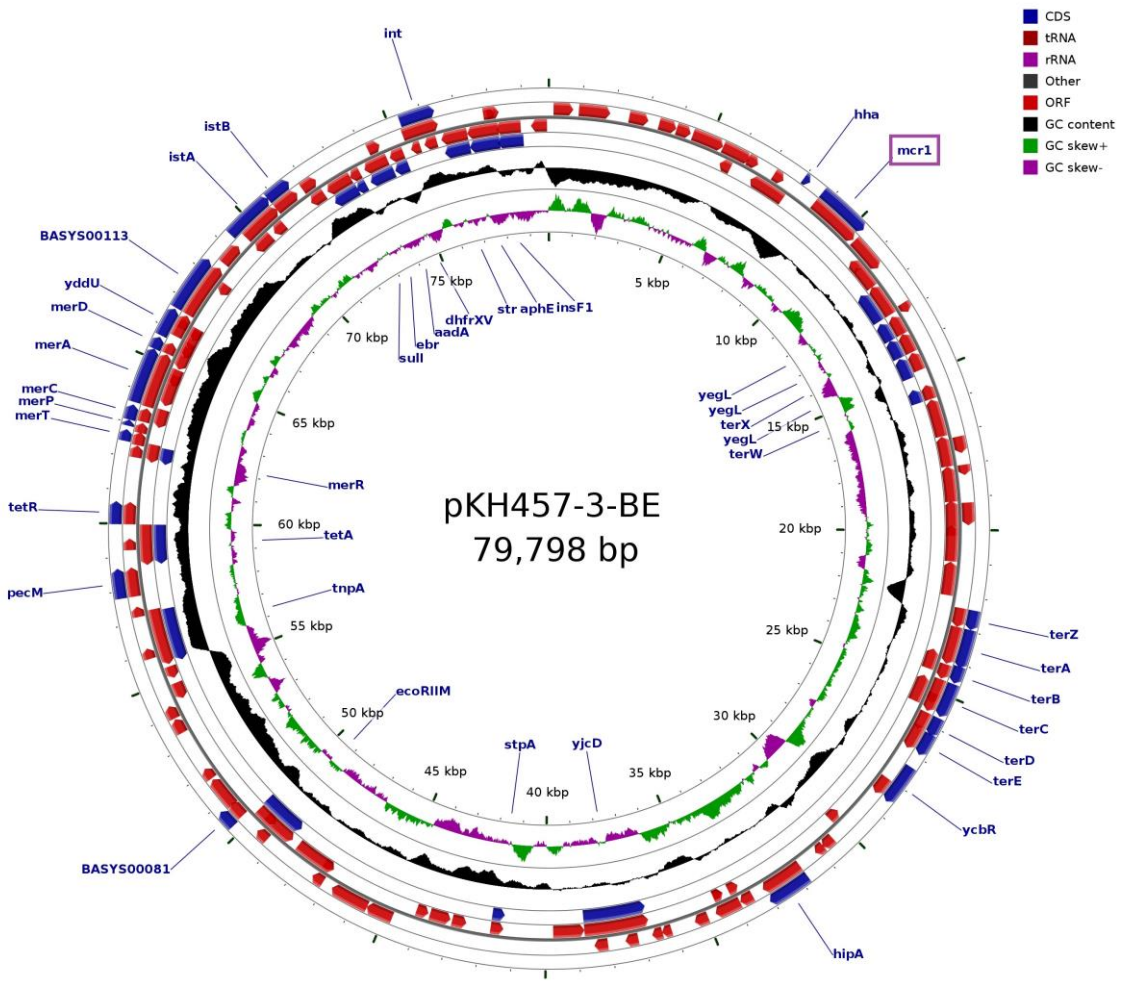

Figure: Genetic organization and structure of *mcr-1* harboring plasmid pKH-457-3-BE. Figure was generated using http://stothard.afns.ualberta.ca/cgview_server/