

27th **ECCMID**

Vienna, Austria
22 – 25 April 2017

The congress of  ESCMID

Session: OS175 Origin, dissemination and impact of *mcr* genes

Category: 3b. Resistance surveillance & epidemiology: Gram-negatives

25 April 2017, 09:48 - 09:58
OS0870

Heterogeneous location of the *mcr-1* gene in colistin-resistant *Escherichia coli* strains from humans and chicken meat

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Background: The recent discovery of transferable *mcr-1*-mediated colistin resistance has raised considerable public health concern. To date, the *mcr-1* has been found in many different genetic backgrounds and in strains isolated from several reservoirs. The aim of our study was to characterize the genetic environment of *mcr-1* in colistin-resistant *Escherichia coli* strains isolated from human and chicken meat at retail.

Material/methods: Nine *mcr-1*-carrying *E. coli* strains from humans (n=3) and poultry meat (n=6) isolated in Switzerland between 2014 and 2016 were included in our study. Total DNA (genomic and plasmidic) was extracted, and whole genome and plasmid sequencing were performed with the fourth-generation sequencer MinION (Oxford Nanopore). 2D passed reads were converted to fastq format with poretools and assembled with the Canu pipeline. Plasmid-, resistance-, and virulence gene-typing were performed implementing PlasmidFinder, ResFinder, and VirulenceFinder, respectively.

Results: The *mcr-1* was found both integrated into plasmids (n=7), as well as on the bacterial chromosome (n=2). The *mcr-1*-harboring plasmids identified in the human isolates consisted of a 33 kb IncX4, a 230 kb IncHI2, and a 250 kb IncHI2 plasmid. The IncX4 plasmid was identified in a strain exhibiting no additional resistance genes, but virulence genes indicative for an enteropathogenic *E. coli*, whereas the other two IncHI2 plasmids harbored additional antimicrobial resistance determinants

for macrolide, aminoglycoside, beta-lactam and quinolone resistance. An identical IncX4 plasmid was also found in one of the poultry meat isolates. Plasmids carrying *mcr-1* from the remaining four *E. coli* from poultry meat consisted of two 100 kb IncK2 (n=2) and of one 64 kb IncI2 plasmid. In two strains, the IS*ApI1-mcr-1* element was found integrated into the chromosome in different genomic loci in single or duplicate copies, highlighting once more the ability of such element to mobilize across diverse plasmidic and chromosomal locations.

Conclusions: The genetic location of *mcr-1* in 9 colistin-resistant *E. coli* strains isolated from different sources was highly heterogeneous. The identified IncHI2, IncX4 and IncI2 plasmids found in human and poultry meat isolates were highly similar to the ones previously described in several ecological niches worldwide, indicating a possible clonal spread and transfer among different reservoirs. The presence of the same IncX4 plasmid in *E. coli* from chicken meat and from human strongly suggests that contaminated food may be a primary source of transmission to humans.