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Onward clonal transmission of blaKPC-2 and mcr-1 harbouring Klebsiella pneumoniae in a hospital environment: analysis of whole-genome sequences and shoe-leather epidemiology

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Background: Optimal infection prevention strategy for control of *mcr-1* harbouring Enterobacteriaceae is still unknown, contributed in part by the lack of understanding of the transmission patterns of these organisms in the healthcare environment. In this study, we investigate the horizontal transmission of

Enterobacteriaceae harbouring *mcr-1* in Singapore acute care hospitals, using whole genome sequencing (WGS) and shoe-leather epidemiology.

Material/methods: *mcr-1* harbouring Enterobacteriaceae isolates were identified via two approaches: 1) prospective PCR screening for *mcr-1* from January – May 2016 (*n*=350); 2) retrospective analysis of WGS data of carbapenemase-producing Enterobacteriaceae (CPE) which included, New Delhi Metallo-β-lactamase (NDM) isolates (*n*=91) and, Klebsiella pneumoniae carbapenemase (KPC)–producers (*n*=210) from seven healthcare facilities in Singapore from October 2010 – April 2014. We investigated the patient-to-patient transmission of *mcr-1* by analysing overlaps in ward stays, admitting disciplines, endoscopic procedures, and place of residence in the community; by WGS using plasmid identity (*mcr-1*, bla_{NDM}, bla_{KPC}), bacterial chromosomal core genome cluster assignment, and single nucleotide polymorphism (SNP).

Results: We identified six patients carrying *mcr-1* Enterobacteriaceae (5 *E. coli* and 1 *K. pneumoniae*). Considerable plasmid diversity was noted, with 4 of the six isolates bearing different *mcr-1* plasmids. Three out of the five *E. coli* isolates co-carried plasmid-borne bla_{KPC-2}. Two *E. coli* isolates (ENT 563 and ENT 564) harbouring both *mcr-1* and bla_{KPC-2} fulfilled clinical and genomics criteria for horizontal transmission. The host patients had temporal overlap in the same ward under the same clinical discipline. They stayed at different residential areas in Singapore suggesting nosocomial transmission. Based on core chromosomal analysis, the two *E. coli* isolates, met the criteria for phylogenetic transmission clustering, with identical core chromosome (pairwise SNP = 10) and plasmids carrying *mcr-1* (FAP1 plasmid) and bla_{KPC-2} (pHS102707 plasmid).

Conclusions: Our results show that it is possible for *mcr-1* and KPC-plasmids to be co-transferred among hospitalised patients. Hence, screening of CPE carriers for co-carriage of *mcr-1* should be considered. Transmission-based precaution for CPE carriers as recommended by the current guidelines remain relevant.

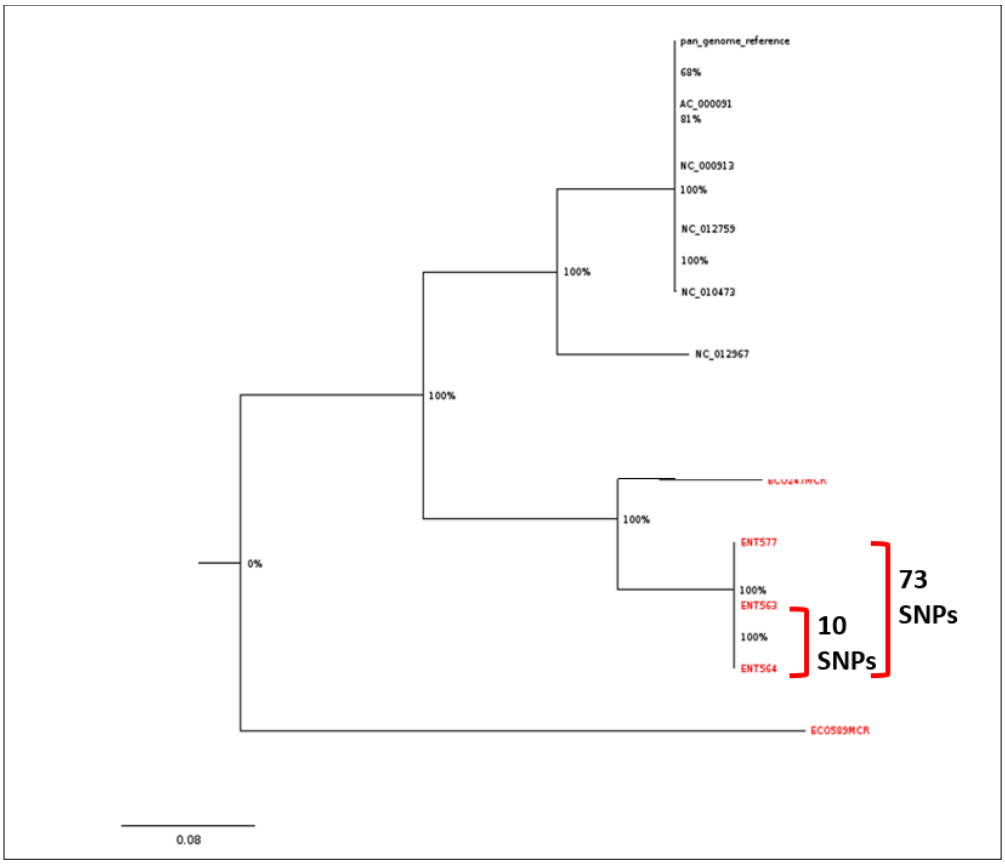

FIG. 1. Maximum likelihood phylogenetic tree based on the core genome of *E. coli* isolates. Brackets denote a transmission cluster as was defined as isolates which (i) shared the same *mcr-1* positive plasmid, (ii) had the same ST and (iii) had ≥99% bootstrap support at all nodes in the chromosomal core genome phylogeny tree.