Emergence of new IncHI2 multidrug-resistance plasmids carrying VIM-1 metallo-β-lactamase in *Escherichia coli* in Norway

Carbapenem-resistant Enterobacteriaceae are one of the most substantial threats to human health.[1] In 2021, IncHI2 plasmids carrying resistance genes against carbapenems and colistin were detected in Enterobacteriaceae.[2] In this Correspondence, we show the emergence of new IncHI2 plasmids ranging from 300–385 kb and carrying multiple antibiotic resistance genes (ARGs) and heavy metal resistance genes (HMRGs), including two copies of carbapenemase VIM-1, in *Escherichia coli* in Norway.

We analysed 569 cefotaxime-resistant *E coli* isolates from raw and treated sewage collected from five sewage treatment plants in Bergen, Norway, over a period of 19 months (August, 2020, to February, 2022) for phenotypic antibiotic resistance. Five multidrug-resistant *E coli* strains (appendix p 2) carrying VIM-1, based on Illumina MiSeq sequencing, were detected only in the influents and effluents of the treatment plant receiving hospital sewage. Four of the five strains (ie, 7–390, 8–386, 8–387, and 8–388) belonged to sequence type 536 and were clonally related based on single nucleotide polymorphism analysis, whereas the fifth strain (ie, 3–349)[3] belonged to sequence type 635.

Complete genome sequencing with a combination of Oxford Nanopore MinION and Illumina MiSeq sequencing of strain 8–386 showed the presence of 300 585 bp (p8–386_1, CP101587), of strain 7–390 showed the presence of 301 413 bp (p7–390_1, CP101582), and of strain 3–349 showed the presence of 385 171 bp (p3–349_1, CP101332) IncHI2 plasmids carrying two copies of VIM-1 in an identical class 1 integron gene cassette (appendix p 3). These plasmids carry multiple toxin-antitoxin systems, suggesting potential for persistence.

Conjugation experiments showed that plasmid p3–349_1 was transferred to a green-fluorescent-protein-tagged *E coli* strain at a transfer frequency of 2×10^{-5} per recipient cell,[4] showing transfer of resistance against seven different antibiotic classes (appendix p 2). Plasmids p8–386_1 and p7–390_1 do not have the conjugal transfer genes *traGHI* that are present in plasmid p3–349_1 (appendix p 3), thus explaining the lack of conjugal transfer during repeated experiments.

Plasmid p3–349_1 carries 20 unique ARGs, including $bla_{CTX\text{-}M\text{-}15}$ and two copies of *catA1* and $bla_{VIM\text{-}1}$, whereas plasmids p8–386_1 and p7–390_1 have 15 unique ARGs each (appendix p 5). Furthermore, p3–349_1 carries several HMRGs conferring resistance against arsenic, mercury, tellurium, and copper (appendix p 3), suggesting potential for co-selection of antibiotic resistance.

Carbapenem resistance in Norway is low in clinics, with no VIM-1-carrying *E coli* detected in 2021.[5] However, the emergence of an IncHI2 plasmid carrying VIM-1 carbapenemase with multiple ARGs and HMRGs, and its recurring detection in the treatment plant receiving hospital sewage, suggests a clinical origin and highlights the risks for future dissemination of this plasmid in clinics.

We declare no competing interests.

NPM conceptualised the study, established the methodology, did the investigation, validated and analysed data, wrote the original draft, reviewed and edited the manuscript, acquired funding, and managed the project. VR and FS-S established the methodology, did the investigation, did the bioinformatic analysis, analysed data, and reviewed and edited the manuscript. ERBM did the investigation, validated data, provided critical inputs, and reviewed and edited the manuscript. DHG established the methodology, did the investigation, analysed data, and reviewed and edited the manuscript.

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See Online for appendix

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