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## Hospital wastewater as a reservoir for the tigecycline resistance gene cluster *tmexCD-toprj*

We read with great interest the recent Article by Ning Dong and colleagues<sup>1</sup> in *The Lancet Microbe* on the transmissible, tigecycline-resistant RND efflux pump *tmexCD-toprj* that was widely distributed in clinically important pathogens. As a last-resort antibiotic used to treat severe infections caused by antimicrobial-resistant organisms, the efficacy of tigecycline could be compromised by the presence of *tmexCD-toprj*. It has been reported that *tmexCD1-toprj1* could be detected in food market sewage, and several variants of *tmexCD4-toprj* have been reported so far.<sup>2,3</sup> To supplement the epidemiological findings in this study, we conducted surveillance of *tmexCD-toprj* and other important antimicrobial resistance (AMR) genes in bacteria in hospital wastewater, which is considered to be an important source of AMR genes and a reflection of the AMR genes and pathogens that are prevalent in the hospital.

We surveyed the hospital wastewater in ten hospitals located in different regions of Zhejiang province in China in September to December, 2021, for the presence of bacterial pathogens that were resistant to last-resort antibiotics including carbapenems, colistin, and tigecycline. Among 417 strains of *Aeromonas* spp, 174 *Klebsiella* spp, seven *Citrobacter* spp, and 98 *Raoultella* spp that exhibited resistance to carbapenems, we detected 37 *tmexCD-toprj*-positive bacterial strains including 27 *Aeromonas* spp, four *Klebsiella michiganensis*, one *Klebsiella oxytoca*,

one *Citrobacter youngae*, and four *Raoultella ornithinolytica* strains. All of these strains carried *tmexCD-toprj2* except for two *Klebsiella michiganensis* strains carrying *tmexCD-toprj1* and two *Aeromonas* spp strains carrying *tmexCD-toprj3*. All except for three *Aeromonas* spp strains carried different carbapenemase genes including *bla<sub>NDM-1</sub>*, *bla<sub>KPC-2</sub>* and its variants, and *bla<sub>IMP-1</sub>* with some of them carrying more than one carbapenemase gene—in particular *Raoultella ornithinolytica*. In addition, a high proportion of the coexistence of *mcr-3*, *tmexCD2-toprj2*, and *bla<sub>KPC-2</sub>* genes were observed in *Aeromonas* spp strains (21 [77.8%] of 27). The coexistence of *tmexCD-toprj*, *mcr-3*, and carbapenemase genes in bacterial strains might pose potential risks of AMR development and spread. The results of antimicrobial susceptibility testing showed that all the *tmexCD-toprj*-positive Enterobacteriaceae strains were resistant to tigecycline (minimum inhibitory concentration range: 1–4 mg/L), although most of the *tmexCD-toprj*-positive *Aeromonas* spp strains (25 [92.6%] of 27) were susceptible to tigecycline (minimum inhibitory concentration range: <0.5–1 mg/L) according to the European Committee on Antimicrobial Susceptibility Testing guidelines (appendix). This study implied that *Aeromonas* spp in water systems might be an important reservoir for important AMR genes and play an important role in the transmission of AMR genes, which warrants further monitoring.

Currently *tmexCD-toprj* has been reported mainly in China, from different geographical locations and origins including humans, chicken, pork, slaughterhouses, and food market sewage.<sup>4</sup> However, as mentioned by Dong and colleagues, those *tmexCD-toprj*-positive strains have been recorded in the National Center for Biotechnology Information

database from countries across three continents since 1997, although few epidemiological studies have revealed the prevalence of *tmexCD-toprj* in other countries or worldwide. Strengthening global monitoring of *tmexCD-toprj* under the One Health framework, in particular its simultaneous presence with other important AMR genes, is necessary.

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