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## Rare mechanisms of resistance in Belgian enterococci identified by WGS

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**Background:** Enterococci, particularly vancomycin-resistant *Enterococcus faecium* (VRE), are important nosocomial pathogens with limited treatment options. They can acquire high-level resistance to a broad spectrum of antibiotics. Nine types of vancomycin resistance gene clusters have been characterized. *Van*B positive strains are generally resistant to vancomycin and sensitive to teicoplanin. Emergence of linezolid resistance has been limited so far. Non-susceptible organisms usually demonstrate alterations in the 23S rRNA target. A few reports have described the detection of *cfr*-mediated and/or *optrA*-mediated linezolid resistance in *E. faecalis* and *E. faecium*. Here, we report the identification of the first *vanB* positive teicoplanin resistant *E. faecium* strain and the first *optrA* positive *E. faecalis* strain in Belgium.

**Material/methods:** Species identification was performed using Malditof (Bruker). MICs for ampicillin, linezolid, teicoplanin and vancomycin were determined by e-test and interpreted according to EUCAST. Additionally, susceptibility to chloramphenicol was tested. DNA was extracted using the NucliSens EasyMAG (BioMérieux). The presence of *van-genes* was examined by PCR. WGS was performed using Nextera XT (2 x250bp), MiSeq (Illumina Inc.). The sequences were preprocessed by de-novo assembled (Spades v3.9.1) and annotated using RAST online server.
**Results:** An *E. faecium* was isolated from a screening stool of a 62-year-old man with B-cell chronic lymphocytic leukemia (B-CLL) who received chemotherapy prior to allogeneic stem cell transplantation. During chemotherapy, he received multiple doses of meropenem and vancomycin due to neutropenic fever. PCR analyses of the *van* genes, revealed a *vanB* subtype, although the strain was phenotypically teicoplanin resistant (MIC > 256 µg/ml). The strain belonged to CC17, ST17. In a

follow-up sample, an *E. gallinarum* was cultured also carrying the *vanB* gene next to *vanC*. However, in this strain, the *vanC* phenotype was noticed (MIC vancomycin 8.0µg/ml, MIC teicoplanin 0.50µg/ml). WGS analysis of both strains revealed a *vanB* gene with a non synonymous mutation (Q124R). The *E. gallinarum* strain has a deletion in $vanS_B$.

In another patient, an *E. faecalis* strain was isolated from a 85-year-old woman with a urinary tract infection. MIC values were 1.0, 1.0, 0.064, 16, 0.064 µg/ml, for ampicillin, vancomycin, teicoplanin, linezolid and tigecyclin respectively; the strain was resistant to chloramphenicol (MIC value 64µg/ml, CLSI). By using WGS, it was shown that the strain belonged to ST480. The suspected presence of *optrA* was confirmed. *cfr* was not present.

**Conclusions:** WGS was used to investigate the teicoplanin resistance in a *vanB* positive *E. faecium* strain. Here, the long-term treatment with vancomycin might have triggered the teicoplanin resistance. In addition, application of WGS revealed the presence of *optrA* as a cause of linezolid resistance in an *E. faecalis* strain.