Letters to the Editor

Disruption of vanS by IS1216V in a Clinical Isolate of Enterococcus faecium with VanA Glycopeptide Resistance

The elements that mediate VanA glycopeptide resistance in enterococci are heterogeneous. Twenty-four distinct VanA elements were identified among a collection of enterococci isolated from hospital patients and nonhuman sources in the United Kingdom (9). Despite their diversity, all these elements showed extensive homology with the prototype VanA transposon, Tn1546, from Enterococcus faecium BM4147 (2); specifically, the vanRHSAX genes, which are critical for the expression of glycopeptide resistance, were conserved in all 24 elements (8).

We recently identified a blood culture isolate of E. faecium (designated ARMRL 26) in which the vanRHSAX gene cluster was distinct from that observed in all the other United Kingdom strains examined. The strain yielded a long PCR (L-PCR) amplicon larger than the expected size of 4.4 kb (8), and digestion of this amplicon with DdeI indicated loss of the 418-bp fragment present in Tn1546 digests and the appearance of a new fragment of ca. 1 kb (Fig. 1). As the 418-bp fragment results from digestion of Tn1546 at nucleotide positions 5382 and 5800, the loss of this fragment suggested an intragenic insertion located towards the 3' end of vanS. Sequencing detected a copy of the insertion sequence IS1216V (1) flanked by 8-bp direct repeats of GCTTCCAG (corresponding to Tn1546) and 57861 to 57868) and consistent with target site duplication following a transposition event. Insertion at this position would be predicted to cause the loss of 11 amino acids (AMPDLVDKRRS) from the C terminus of the VanA peptide and their possible replacement by 10 amino acids (GFCCKVL BKE) resulting from read-through of the inserted IS1216V sequence. It is unlikely that this change would affect the function of the VanS sensor peptide, because the critical residues remain intact (7). Even if the insertion did cause a functional change, VanS is not essential for expression of glycopeptide resistance (3). Strain ARMRL 26 had a normal VanA phenotype (vancomycin and teicoplanin MICs of >32 μg/ml).

To our knowledge, E. faecium ARMRL 26 is only the second glycopeptide-resistant enterococcus in which an insertion has been identified within a van gene; disruption of vanY by IS1476 has been reported previously (6). L-PCR has been stated previously to be a useful method for fingerprinting and comparing glycopeptide resistance elements for epidemiological and evolutionary purposes (4, 8). This report further emphasizes the ability of L-PCR to identify rapidly enterococci that have insertions within the vanRHSAX gene cluster. It would therefore detect readily strains that carry copies of IS1251 in the vanS-vanH intergenic region which have been documented in the United States (5). Furthermore, restriction fragment length polymorphism analysis of the resulting amplicons can be used to pinpoint the likely position of the insertion and so permit relevant sequencing, allowing cost-effective analysis of VanA elements to be undertaken.

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REFERENCES


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