Multilevel population genetic analysis of vanA and vanB Enterococcus faecium causing nosocomial outbreaks in 27 countries (1986-2012) - DTU Orbit (18/12/2018)

Vancomycin-resistant Enterococcus faecium (VREfm) have been increasingly reported since the 1980s. Despite the high number of published studies about VRE epidemiology, the dynamics and evolvability of these microorganisms are still not fully understood. A multilevel population genetic analysis of VREfm outbreak strains since 1986, representing the first comprehensive characterization of plasmid content in E. faecium, was performed to provide a detailed view of potential transmissible units. From a comprehensive MeSH search, we identified VREfm strains causing hospital outbreaks (1986-2012). In total, 53 VanA and 18 VanB isolates (27 countries, 5 continents) were analysed and 82 vancomycin-susceptible E. faecium (VSEfm) were included for comparison. Clonal relatedness was established by PFGE and MLST (goeBURST/Bayesian Analysis of Population Structure, BAPS). Characterization of van transposons (PCR mapping, RFLP, sequencing), plasmids (transfer, ClaI-RFLP, PCR typing of relaxases, replication-initiation proteins and toxin-antitoxin systems, hybridization, sequencing), bacteriocins and virulence determinants (PCR, hybridization, sequencing) was performed. VREfm were mainly associated with major human lineages ST17, ST18 and ST78. VREfm and VSEfm harboured plasmids of different families [RCR, small theta plasmids, RepA_N (pRUM/pLG1) and Inc18] able to yield mosaic elements. Tn1546-vanA was mainly located on pRUM/Axe-Txe (USA) and Inc18-pIP186 (Europe) plasmids. The VanB2 type (Tn5382/Tn1549) was predominant among VanB strains (chromosome and plasmids). Both strains and plasmids contributed to the spread and persistence of vancomycin resistance among E. faecium. Horizontal gene transfer events among genetic elements from different clonal lineages (same or different species) result in chimeras with different stability and host range, complicating the surveillance of epidemic plasmids.

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