

TITLE: HEAVY METAL AND BIOCIDES RESISTANCE GENES AND THEIR CO-OCCURRENCE WITH VIRULENCE FACTORS IN ENTEROCOCCI

AUTHORS: GUERRA, C.F.^{1,2}; FARIA, A.R.^{1,2}; SANTOS, M. R. S.¹; LEITE, V.L.M.¹; FREITAS, A.A.R.¹; SOUZA, S.S.R.⁴; MORAIS, J.M.^{1,3}; MERQUIOR, V.L.C.³; TEIXEIRA, L.M.¹.

INSTITUTION: INSTITUTO DE MICROBIOLOGIA PAULO DE GÓES, CCS-UFRJ, RIO DE JANEIRO, RJ (AV. CARLOS CHAGAS FILHO, 373, BLOCO I, 2º ANDAR, CEP 21941-590, RIO DE JANEIRO - RJ, BRAZIL);

²FACULDADE DE MEDICINA, UFRJ, RIO DE JANEIRO, RJ (RUA BRUNO LOBO, 50, 5º ANDAR, CEP 21044-020, RIO DE JANEIRO- RJ, BRAZIL);

³FACULDADE DE CIÊNCIAS MÉDICAS, UERJ, RIO DE JANEIRO, RJ (AV. PROFESSOR MANOEL DE ABREU, 444, 2º ANDAR, CEP 20550-170, RIO DE JANEIRO - RJ, BRASIL);

⁴DEPARTMENT OF BIOLOGICAL SCIENCES, UNIVERSITY AT ALBANY, STATE UNIVERSITY OF NEW YORK (1400 WASHINGTON AVE, ALBANY, NY 12222).

ABSTRACT:

Enterococci have become important nosocomial pathogens worldwide, primarily due to their remarkable ability to acquire and transmit resistance and virulence genes. The relationship between biocides and heavy metals and antimicrobial resistance has been examined previously, but reports linking resistance to nonantibiotic compounds and the maintenance of virulence factors are still scarce. Therefore, we investigated the co-occurrence of heavy metal resistance genes (HMRG) and/or biocide resistance genes (BRG) with virulence factors (VFG) and population diversity in 174 enterococcal isolates (63 *E. faecalis* and 111 *E. faecium*) recovered from hospitalized patients in the state of Rio de Janeiro. The isolates were characterized by MALDI-TOF MS, and the presence of HMRG [copper (*tcrB* and *cueO*), mercury (*merA*), and cadmium (*cadA*)] and nine VFG were determined by PCR. The population diversity was analyzed by MLST. Whole genome sequencing was performed, and thirteen BRG and eleven VFG were detected by using the BLAST tool. Among the *E. faecalis* isolates, *cadA* was the predominant (94%). However, in *E. faecium*, *tcrB* was more frequent (30%), followed by *cueO* (26%), *merA* (23%), and *cadA* (4%). At least one BRG was found in 81% (n=141/174) of the isolates. Regarding BRGs, *efrA/B* were prevalent in both species, 97% in *E. faecalis* and 77% in *E. faecium*; *emeA* was only detected in *E. faecalis* (33%). Each isolate had at least one gene associated with VFG. The *pilB* (96%), *ecbA* (85%), *fsr1/3* (80%), *acm* (67%), and *fms8* (61%) genes were the most abundant VFG in both species. In addition, VFG were frequently detected along with HMRG and BRG. VFG *efaA*, *eeP*, *cpd*, *cad*, *ccf*, *asa1*, *agg*, *sprE*, *gelE*, and *cylA* were only found in *E. faecalis* and were mostly associated with *emeA* and *cadA*. Also, *srgA*, *fsm*, and *esp*, which were most frequently found in *E. faecium*, were often correlated with the presence of copper and mercury resistance genes. Three of the major sequence types showed BRG with HMRG and VFG. *E. faecalis* belonging to ST525 (n=26) and ST6 (n=19) carried VFG in addition to *cadA* and *emeA*. *E. faecium* ST78 isolates (n=21) carried VFG along with *tcrB*, *cueO*, and *merA*. These results, indicating the coexistence of HMRG, BRG, and VFG in multidrug-resistant enterococci, suggest that an even larger arsenal of genes is involved in selection events that contribute to the maintenance and transmission of isolates with features of outstanding clinical relevance.

Keywords: *Enterococcus*, heavy metals, biocides, virulence factors, population diversity.

Development Agency: CNPq, INPRA, CAPES and FAPERJ.