Comparison of Genotypic Resistance Pattern Between Enterococcus *Faecium* and Enterococcus *Faecalis* to Better Understand Selection of Antibiotics For Treatment Purposes.

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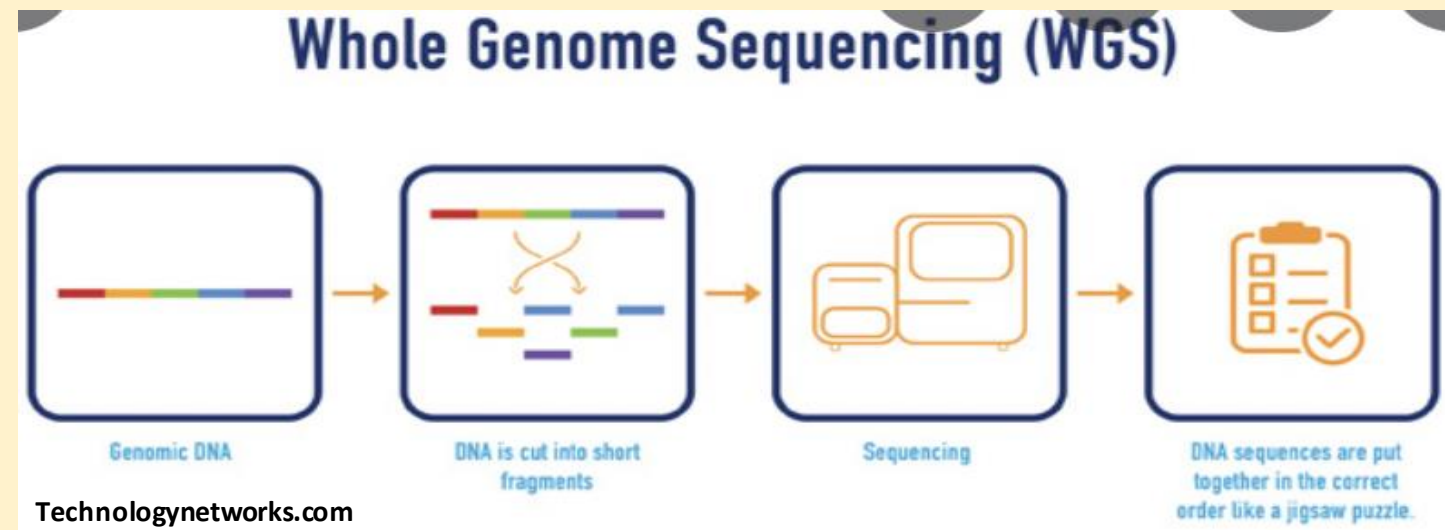
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BACKGROUND

Enterococcus is one of the major causes of nosocomial infections, many with vancomycin resistance. About 50,000 infections are reported per year due to vancomycin-resistant Enterococci (VRE). VRE variants can be challenging to manage and has been shown to increase cost and mortality rates. Understanding the genotypic mutations can help recognize the potential burden for antibiotic resistance that exists in a population and guide in antibiotic selection. In this study, using whole genome sequencing (WGS) we aim to analyze the prevalence of genetic resistance markers for commonly used antibiotics for Enterococcal treatment.

METHODS

Whole genome sequencing was performed using the NextSeq (Illumina Inc., CA) on 60 isolates of *E. faecium* and 29 isolates of *E. faecalis*. The isolates were obtained from two different Detroit area hospitals from 2017-2019. The data from WGS was analyzed using EPISEQ CS™ (BIOMÉRIEUX, Marcy l 'Etoile, France) bioinformatic database to obtain specific resistance genes which would correspond to commonly used antibiotics for treatment of *Enterococcal* infections.

	E. Faecium	E. Faecalis
# of Unique Resistance genes	12	7
Unique drug classes	efmA, pbp5, tet(L), liar, liaS	emeA

Table 2: Comparison of mutations unique to Enterococcus *faecium* and E. *faecalis*

www.idimages.org/enterococcus
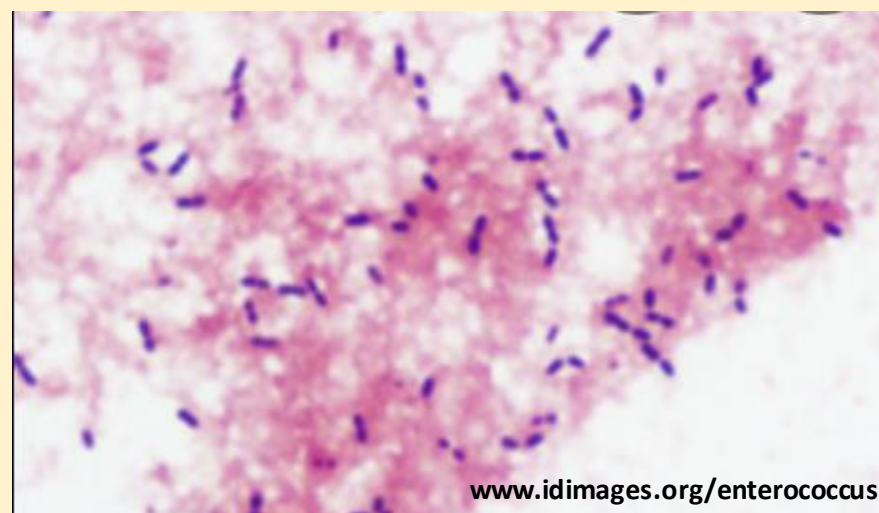
Gram-positive facultative anaerobic cocci in short and medium chains

Enterococcus faecium and **E. faecalis**

Whole Genome Sequencing (WGS)

Technologynetworks.com

RESULTS

Among the 89 *Enterococcus faecium* and *E. faecalis* investigated, we identified a total of 33 unique resistance genes across 16 classes of antibiotics (Table 1). The most common antibiotic classes include aminoglycosides, tetracyclines, quinolones, beta-lactams, glycopeptides, macrolides, and pyrimidine analogs. *E. faecium* and *E. faecalis* share 14 similar resistance genes from 10 classes of antibiotics. *E. faecium* has more number of unique resistance genes when compared to *E. Faecalis* (Table 2). *E. faecium* has resistance genes covering all drug classes except for Acridine, where as *E. faecalis* has resistance genes excluding Beta-lactams and Nitromidazole drug class (Table 1).

CONCLUSION

Enterococcus faecium had a greater number of resistance genes with glycopeptide, aminoglycoside, and beta lactam drugs when compared to *Enterococcus faecalis*. Whereas *Enterococcus faecalis* had more resistance genes associated with macrolides, tetracyclines, pyrimidine analogs, and Bactrim. In general, both appear to have many genes that encode for resistance to major classes of antibiotics which are used for treatment of Enterococcal infections. Further comparison with phenotypic susceptibility testing data would help better understand the practical implications of our resistance gene testing.

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ANTIBIOTIC RESISTANCE

Drug class resistance	E. faecium (n=60) Genes	E. faecalis (n=29) Genes
Aminoglycosides	aac(6')-l, aac(6')-li, ant(9)-la, aad(6), aacA/aphD, aph(3')-llla, sat4	aadD1, aad(6), aacA/aphD, aph(3')-llla, sat4
Nucleoside	sat4, efmA	sat4
Pyrimidine analogs	dfrG	dfrC, dfrG
Trimethoprim/sulfonamides	dfrG	dfrC, dfrG
Pleuromutilins	eat(A)	lsa(A)
Acridine		emeA
Quinolones	efmA, tet(L)	emeA
Tetracyclines	efmA, msrC, tet(M), tet(S), tet(L)	emeA, tet(M), lsa(A)
Beta-lactams	efmA, pbp5, tet(L)	
Macrolides	efmA, msrC, erm(A), erm(B), tet(L)	erm(B), erm(C), lsa(A)
lincosamides	efmA, msrC, erm(A), erm(B), tet(L)	erm(B), erm(C), lsa(A)
streptogramins	efmA, msrC, erm(A), erm(B), tet(L)	erm(B), erm(C), lsa(A)
Nitroimidazole	efmA, tet(L)	
Peptides	efmA, liaS, erm(A), erm(B)	erm(B), erm(C)
Glycopeptides	vanA, vanR, vanS, vanX-A, vanY-A, vanZ-A, vanH-A	vanA, vanR, vanS, vanX-A, vanY-A, vanZ-A, vanH-A

Green = both
Yellow = E. faecium
Red = E. faecalis

Table 1. Enterococcus *faecium* and E. *faecalis* genetic mutations and drug class resistance

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