JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2003, p. 4004–4005 Vol. 41, No. 8
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.8.4004–4005.2003

Distribution of *fsr* among *Enterococcus faecalis* Isolates from the SENTRY Antimicrobial Surveillance Program

Pillai and colleagues (3) in 2002 reported a striking correlation (100.0% positive; $P = 0.005$) of the *fsr* virulence gene with *Enterococcus faecalis* isolated from a collection of endocarditis cases. The comparison group of stool culture isolates had a significantly lower rate of positive *fsr* tests (53%) by methods described earlier by Qin et al. (4, 5). The *fsr* locus has been noted to be widely distributed in *E. faecalis* (70% of isolates) and regulates virulence-associated gelatinases and serine proteases (4, 5).

To expand the understanding of *fsr* related to contemporary prevalence, we screened a collection of *E. faecalis* isolates from the SENTRY Antimicrobial Surveillance Program selected to achieve a broad range of infection types, geographic samplings, years of isolation, and antibiogram features (vancomycin only). A total of 109 strains were chosen from the 1999 to 2002 SENTRY Program organism bank for the United States, Canada, Latin America, and Europe. Strains were single, unique infection episodes without duplication of strains (pulsed-field gel electrophoresis screened) indexed by patient or medical center. A total of 49 medical centers contributed samples of *E. faecalis* distributed geographically as follows: United States (59 strains; 24 centers), Canada (9 strains; 7 centers), Latin America (19 strains; 7 centers) and Europe (22 strains; 13 sites). These strains occurred among documented infections within the monitored years at the following body sites in patients residing in intensive care units (11 strains) or in general hospital wards (9 strains): bloodstream (51 strains sampled in all regions), lower respiratory tract (7 strains; United States only), skin and soft tissue (27 strains; all regions), and urinary tract (11 sites in all regions).

The *fsr* locus was amplified by the methods described earlier (3, 5) using the following primer sequences: 5′-AACCAGA ATCGACCAATGAAT-3′ (upstream primer) and 5′-GCCCC TCATAACTCAATACC-3′ (downstream primer). The PCR testing conditions utilized were those published by Pillai et al. (3), and the *fsr*-positive *E. faecalis* ATCC 51299 was used as a control.

Table 1 shows the results of the PCR *fsr* screen for all 109 *E. faecalis* strains. The gene was quite ubiquitous across all infection types, geographic areas, times, and susceptibility types. The *fsr*-positive *E. faecalis* isolates were detected in 15 of 24 (62.5%) medical centers in the United States, all Canadian hospitals (100.0%), 4 of 7 (57.1%) Latin American medical centers, and 5 of 13 (38.5%) European participant hospitals (data not shown). Rates of *E. faecalis* isolates with *fsr* were highest (63.6 to 88.9%) among urinary tract infection isolates (Table 1) and lowest for the bloodstream infection strains (23.5%). These findings were consistent across all regions where samples were available. Less variation in the prevalence of the *fsr* was noted between geographic samples of all specimen types combined. Highest *fsr*-positive *E. faecalis* rates were encountered in North America (42.4 to 44.4%). All four vancomycin-resistant *E. faecalis* strains were *fsr* positive (three isolates from the United States [New York and Massachusetts] and one isolate from Brazil).

These results broaden the understanding of the *fsr* range among contemporary isolates of *E. faecalis* in the Americas and Europe. The prevalence of *fsr* can differ significantly among isolates when comparing types (sites) of infection and among geographic areas. The high prevalence in urinary tract infections described here was similar to the finding of other *E. faecalis* surface proteins (*esp*) associated with ascending urinary tract infections (6) and among hospitalized patients with antimicrobial-resistant clones (1). In contrast, the *fsr*-positive rate was low (23.5%) compared to that of the bacteremic endocarditis isolates reported by Pillai et al. (3), indicating a distinct difference between these two types of blood culture isolates. Some investigators have also reported that putative virulence factors among *E. faecalis* did not contribute to increased mortality rates (7). Other enterococcal virulence factors may be greater contributors to invasive disease and have measurable effects on patient outcomes (7).

These reported findings must be further documented by resistance surveillance networks using a larger selection of enterococcal virulence genes, especially with our discovery of all of the vancomycin-resistant *E. faecalis* isolates (four strains) being *fsr* positive. Finally, these enterococcal virulence factors appear to be more prevalent among human isolates of enterococci (34.5 to 41.7%) compared to those of strains of swine or poultry origin (6 of 276 samples; 2.2%), thus minimizing food animals as a significant reservoir and source of these genetic elements (A. M. Hammerum and L. B. Jensen, Letter, J. Clin.

TABLE 1. Occurrences of *fsr*-positive strains of *E. faecalis* in various SENTRY Antimicrobial Surveillance Program objectives (body sites of infection) and geographic areas and nations and among vancomycin-resistant strains (109 isolates)[a]

Parameter	No. of isolates tested	No. (%) of positive isolates
Body site of infection or patient or medical facility category		
Bloodstream	51	12 (23.5)
Hospitalized patients with pneumonia	11	4 (36.4)
Skin and soft tissues	27	10 (37.0)
Urinary tract infections		
ICU[c]	9	8 (88.9)
Non-ICU medical facility	11	7 (63.6)
Geographic location		
North America		
United States	59	25 (42.4)
Canada	9	4 (44.4)
Latin America	19	5 (26.3)
Europe	22	7 (31.8)
Resistance phenotype		
Vancomycin resistant (*vanA*)[b]	4	4 (100.0)
Total	109	41 (37.6)

[a] Strains selected randomly to represent participating medical centers by geographic area or nation and site of infection (24 hospitals in the United States, 4 centers in Canada, 7 hospitals in Latin America and 13 centers in Europe).
[b] Result from reference MIC testing (3).
[c] ICU, intensive care units.

Microbiol. **40:**4396, 2002). We encourage expanded studies of these genes among human and environmental enterococcal strains to determine their epidemiologic significance.

REFERENCES

1. **Coque, T. M., R. Willems, R. Canton, R. Del Campo, and F. Baquero.** 2002. High occurrence of *esp* among ampicillin-resistant and vancomycin-susceptible *Enterococcus faecium* clones from hospitalized patients. J. Antimicrob. Chemother. **50**:1035–1038.
2. **National Committee for Clinical Laboratory Standards.** 2003. Methods for dilution antimicrobial tests for bacteria that grow aerobically. Approved standard M7-A6. National Committee for Clinical Laboratory Standards, Wayne, Pa.
3. **Pillai, S. K., G. Sakoulas, H. S. Gold, C. Wennersten, G. M. Eliopoulos, R. C. Moellering, Jr., and R. T. Inouye.** 2002. Prevalence of the *fsr* locus in *Enterococcus faecalis* infections. J. Clin. Microbiol. **40**:2651–2652.
4. **Qin, X., K. V. Singh, G. M. Weinstock, and B. E. Murray.** 2000. Effects of *Enterococcus faecalis fsr* genes on production of gelatinase and a serine protease and virulence. Infect. Immun. **68:**2579–2586.
5. **Qin, X., K. V. Singh, G. M. Weinstock, and B. E. Murray.** 2001. Characterization of *fsr*, a regulator controlling expression of gelatinase and serine protease in *Enterococcus faecalis* OG1RF. J. Bacteriol. **183:**3372–3382.
6. **Shankar, N., C. V. Lockatell, A. S. Baghdayan, C. Drachenberg, M. S. Gilmore, and D. E. Johnson.** 2001. Role of *Enterococcus faecalis* surface protein *esp* in the pathogenesis of ascending urinary tract infection. Infect. Immun. **69:**4366–4372.
7. **Vergis, E. N., N. Shankar, J. W. Chow, M. K. Hayden, D. R. Snydman, M. J. Zervos, P. K. Linden, M. M. Wagener, and R. R. Muder.** 2002. Association between the presence of enterococcal virulence factors gelatinase, hemolysin, and enterococcal surface protein and mortality among patients with bacteremia due to *Enterococcus faecalis.* Clin. Infect. Dis. **35:**570–575.

Ronald N. Jones*
Tufts University School of Medicine
Boston, Massachusetts

Lalitagauri M. Deshpande
The JONES Group/JMI Laboratories, Inc.
North Liberty, Iowa

*Phone: (319) 665-3370
Fax: (319) 665-3371
E-mail: ronald-jones@jmilabs.com