Genetic Similarity of *Candida albicans* Strains from Vaginitis Patients and Their Partners

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The moderately repetitive sequence Ca3 was used to fingerprint strains of *Candida albicans* isolated from vulvovaginal infections of 10 women and strains isolated from their male partners. The Dendron software package was then used to compare the DNA fingerprints of these strains with those of vaginal commensals from women from the same geographical locale, vaginal commensals from women from a different geographical locale, and commensals from male partners of asymptomatic women from the same geographical locale. The results demonstrate that, in the majority of cases (8 of 10), strains from symptomatic patients and their partners are either identical or more similar to each other than to other strains, infecting strains do not represent a group genetically distinguishable from vaginal commensal isolates from women from the same geographical locale, and both infecting strains and commensals from individuals in the test locale can be distinguished from commensals obtained in another geographical locale. The results also suggest that women with vaginal infections are responsible for strain replacement in their male partners.

The reasons for single and recurrent episodes of yeast vaginitis remain elusive (21, 22). It has been generally assumed that healthy women carry commensal strains of *Candida albicans* and that these strains are the etiological agents in subsequent episodes of vulvovaginal infection as a result of a physiological change in the host (9, 14, 30). In patients with recurrent infections, it has been suggested that the anorectal region of the patient or a commensal strain carried by the infected patient's partner is the source of reinfection following drug therapy (6, 10). However, there have been a number of observations which complicate these simple scenarios. First, the vulvovaginal region of a healthy woman does not always carry a commensal strain of *C. albicans*. In a recent analysis of 52 healthy young women, samples were taken from 17 body locations. While 73% of the women carried *C. albicans* in one or more body locations, only 40% carried *C. albicans* in the vulvovaginal region (26). Therefore, if a commensal strain is the source of infection in a woman not carrying a commensal strain in the vulvovaginal region, it would have to be derived from a commensal strain in another body location. In addition, one-fourth of all women tested were yeast-free in the 17 body locations within the stringency of the conditions in that study (26). In those cases, the source of subsequent infection would have to be exogenous. Second, it was demonstrated by DNA fingerprinting that, in the majority of cases in which healthy women carried *C. albicans* in both the oral and vulvovaginal regions, the strains in the different body locations were genetically distinct (26). Therefore, if a commensal strain were to be the source of subsequent infection in these individuals, one would have to ask which strain and, then, from which body location the infecting strain was derived. In recurrent vaginal infections, the limited results suggest that the same strain is usually responsible for successive episodes, but again it is not clear what the source of

reinfection is after drug therapy (25). Several studies in which male partners were treated with antifungal drugs suggested that male partners were not the source of reinfection (1a–3). Furthermore, a genetic analysis of the anatomical distribution of *C. albicans* during sequential episodes in a single patient with recurrent episodes demonstrated that the infecting strain could be cloned from the groin region even when the vulvovaginal region was yeast-free immediately after drug treatment, suggesting that reinfecting yeast strains may survive therapy in other body locations (25).

Recently, DNA fingerprinting methods employing moderately repetitive DNA probes were developed to assess the genetic similarity of strains of *C. albicans* (12, 17, 19, 27), and a computer program was developed to assist in quantitating differences and to handle comparisons of large numbers of strains (18, 19, 23). Here, we have used these computer-assisted fingerprinting methods to assess genetic similarity between isolates from vulvovaginal infections in 10 women and (i) isolates from their male partners, (ii) vaginal commensals from the same geographical locale, (iii) vaginal commensals from a different geographical locale, and (iv) isolates from male partners of asymptomatic women of the same geographical locale. The results of this study represent a first step in a detailed etiological analysis of yeast vaginitis.

MATERIALS AND METHODS

Sampling procedures and stock maintenance. Women who exhibited symptoms of vulvovaginitis when examined at one of two family practice offices in the Ann Arbor, Mich., locale were enrolled in this study. Control individuals, in the same age distribution, who had routine pelvic examinations at the same offices were also enrolled. Each woman had a male sexual partner willing to participate.

Specimens were collected in the Michigan locale with sterile Dacron swabs which were passed several times across the surface of the vulva, vaginal canal, rectum, and back of the tongue. Their male partners collected urine, semen, feces, and tongue swabs at home and delivered

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samples to the participating clinics. All specimens were plated on Sabouraud agar and typed for species by sugar assimilation patterns, using the commercial kit API20C (Analytab Products, Plainview, N.Y.). Slants of isolates identified as *C. albicans* in the Michigan locale were then mailed to Iowa City, Iowa, for fingerprinting. Commensal, infecting, and partner strains from the Michigan locale were obtained during the same 11-month period. Strains isolated from vulvovaginal infections were coded V, patient numbers 1.1 to 1.11, and body location "vag" (for vaginal canal) or "vul" (for vulva). Therefore, a strain from the vaginal canal of patient 1.3 would be coded V1.3vag. Strains isolated from the partners of vaginitis patients were coded VP, corresponding patient numbers 1.1 to 1.11, and body location "ton" (for tongue) or "fec" (for feces). Strains isolated from healthy women in the Ann Arbor, Mich., locale were coded C, individual numbers 2.1 to 2.10, and body location as above. Strains isolated from healthy women in the Iowa City, Iowa, locale were coded CI, individual numbers 11 to 49, and body location "vw" (for vaginal wall) or "vp" (for vaginal pool). Strains isolated from healthy males with partners not infected by *C. albicans* were coded CP, individual numbers 2.1 to 2.6, and body location as above.

DNA fingerprinting. Southern blot hybridization was performed by methods previously described (19). Cells from stored slants were grown in YPD medium (2% dextrose, 2% Bacto Peptone, 1% yeast extract) to late log phase or early stationary phase, and DNA was prepared by the method of Scherer and Stevens (16). DNA concentration was estimated by the dot blotting technique. DNA was digested with *EcoRI*, separated on a 0.8% (wt/vol) agarose gel, transferred to a nitrocellulose membrane, and hybridized with labeled Ca3 probe (19). Washed membranes were then pressed against XAR-S film (Eastman Kodak Co., Rochester, N.Y.) with a Cronex Lightning-Plus intensifying screen (Du Pont Co., Wilmington, Del.) in a lightproof box.

Probe Ca3 contains approximately 11 kb containing moderately repetitive sequences and was obtained by partial *EcoRI* digestion of whole-cell DNA (15). The Ca3 fragment hybridizes to all but two chromosomes separable by transverse alternating field electrophoresis (1) and is species specific (15, 27, 28). When used to probe a Southern blot of *EcoRI*-digested, whole-cell DNA of the reference strain 3153A, it hybridizes to 12 bands in the size range of 2.25 to 19.00 kb at varying intensities (Fig. 1).

Analysis of fingerprints. The Southern blot hybridization pattern of each strain was analyzed for band positions and intensities (0 to 3) in the size range 2.25 to 19.00 kb by methods previously described (19). The similarity coefficient (S_{AB}) for each pair of strains, A and B, was calculated by the formula

$$S_{AB} = \frac{\sum_{i=1}^k (a_i + b_i - |a_i - b_i|)}{\sum_{i=1}^k (a_i + b_i)}$$

where a_i and b_i are the intensities of band i in patterns A and B, and k is the number of bands. It was demonstrated in a previous study that the average S_{AB} for 46 independently isolated test strains was 0.69 ± 0.11 , providing an average measure of dissimilarity, and that the average S_{AB} for the same strain compared on different gels was 0.96 ± 0.02 , providing an average measure of identicalness (19). An S_{AB} value of 0.85 was arbitrarily used as the threshold for clustering of similar strains since it is roughly halfway between the average values for dissimilarity and identical-

TABLE 1. Characteristics of test populations from the Michigan locale^a

Test population	Age (yr)	No. of partners in lifetime	No. of mo with current partner ^b
Symptomatic			
Females			
Mean	37	3.5	142
Range	20-47	1-8	8-324
Male partners			
Mean	40	16.1	163
Range	28-53	1-60	24-324
Asymptomatic			
Females			
Mean	31	7	118
Range	23-46	1-18	10-360
Males			
Mean	38	17	85
Range	30-45	6-40	26-240

^a The median income for all test groups was in the range of \$35,000 to \$49,000.

^b The discrepancy in the number of months with current partner for symptomatic females and partners is due to separate estimates provided by individual partners.

ness (18, 26). Dendrograms based on S_{AB} s were created with the Dendron software program (19, 23) by the unweighted pair group method (20). In the Dendron program, the two strains with the highest S_{AB} s are grouped, with a branch point corresponding to that S_{AB} . The program then searches for the strain-strain or strain-unit pair with the next highest S_{AB} and groups them, with a branch point corresponding to that S_{AB} . The process continues to include all strains. A unit can be two or more strains, and a branch point for a unit-strain or unit-unit is determined by the average S_{AB} between each member of the unit and another strain or unit. Therefore, branch points involving a unit are not as accurate as S_{AB} s calculated for two strains.

For neighboring lanes from different gels or different regions of the same gel, the gel images were digitized into the Dendron data base in a Macintosh II computer with a Sharp scanner, normalized according to invariable band positions, and relocated with Dendron software. Neighbored lanes were then photographed from the computer monitor.

RESULTS

Test populations from the Michigan locale. Of 47 male partners of women with symptomatic vulvovaginal candidiasis, 11 (23.4%) had positive cultures in the feces ($n = 7$) or on the tongue ($n = 6$). None had positive cultures in the urine or semen. Isolates from 10 of these couples were available for further analysis. Of 15 asymptomatic couples, none had positive cultures in both partners. Six (40%) of the male partners of asymptomatic women had positive cultures for *C. albicans* (three fecal and four tongue cultures). Samples from the six partners of the asymptomatic women from whom *C. albicans* was isolated were not available.

The average age, number of lifetime sexual partners, number of months with current partner, and household income levels of the study participants with positive cultures are presented in Table 1. The characteristics of the symptomatic and asymptomatic female populations were similar, as were those of the two male populations (Table 1). The patient data also indicate that the individuals in the test

FIG. 1. Ca3-probed Southern blots of *EcoRI*-digested, whole-cell DNA of *C. albicans* isolates from the vaginal canals of vaginitis patients from the Ann Arbor, Mich., locale (A), vulvovaginal regions of asymptomatic women from the same geographical locale (B), and feces and tongues of the male partners of the symptomatic women (C). Each blot contains one or more lanes of the standard laboratory strain 3153A for normalization by the Dendron program. The sizes (in kilobases) of select bands in the 3153A pattern are presented to the left of panels A and C for reference.

groups were not from high-risk groups for secondary yeast infections.

Infecting strains do not represent a distinct genetic group. To determine whether the 10 infecting strains of *C. albicans* isolated from symptomatic women represent a distinct genetic group, they were compared with a set of commensal isolates obtained from the vulvovaginal regions of asymptomatic women during the same time period in the same clinics in Ann Arbor, Mich. Examples of the patterns of six infecting strains and six commensal strains are shown in Fig. 1A and B, respectively. By examining the patterns, one can determine, without the aid of the computer-assisted Dendron program, that the patterns of infecting and commensal strains differed within each group and between the two groups by the position of one or more bands. However, some patterns were similar. For instance, the patterns of

FIG. 2. Dendrograms based on S_{AB} s for the group of isolates from symptomatic women (V) from the Ann Arbor locale (A) and asymptomatic women (C) from the same locale (B) and for the combination of isolates from the two groups (C). A dashed line is drawn at $S_{AB} = 0.85$ to denote the threshold for clustering. vag, vagina; vul, vulva.

V1.6vag and V1.9vag (Fig. 1A) differed by the position of only one intense band, and the pattern of V1.4vag (Fig. 1A) differed from that of C2.1vul (Fig. 1B) by the presence of one intense band in the former pattern. The relationships between strains and patterns are best visualized in dendrograms based on computed similarity coefficients (S_{AB}) (Fig. 2). In the dendrogram for the 10 infecting strains (Fig. 2A), there were various relationships ranging from 0.93 between V1.4vag and V1.6vag to 0.61 between V1.11vag and the group containing all other strains. Half of the strains, including V1.6vag, V1.4vag, V1.9vag, V1.8vag, and V1.10vag,

formed a cluster of genetically similar strains with S_{ABs} equal to or greater than 0.85. Three of the 10 strains, including V1.6vag, V1.4vag, and V1.9vag, formed a cluster of highly similar strains with S_{ABs} above 0.90. In a similar fashion, three of the seven control strains, including C2.9vag, C2.1vul, and C2.10vag, formed a cluster of highly related strains with S_{ABs} above 0.90 (Fig. 2B).

When S_{ABs} were computed among all pairs of strains from symptomatic and asymptomatic women (Fig. 2C), apparently random mixing occurred, demonstrating that infectious strains in this Michigan locale did not represent a group which was genetically distinct from commensal strains, within the resolution of the Ca3 probe. Interestingly, the cluster of infectious strains (Fig. 2A) and the cluster of commensal strains (Fig. 2B) with S_{ABs} of 0.90 or greater formed a single mixed cluster of highly similar strains (Fig. 2C).

A statistical analysis of the similarity matrix, which was performed by the method of Schmid et al. (18), confirmed that infectious strains were as likely to have another infectious strain as their most similar counterpart as they were to have a commensal strain. In addition, the group of infectious strains (Fig. 2A), the group of commensal strains (Fig. 2B), and the combined groups (Fig. 2C) had similar average S_{AB} values and standard deviations of 0.73 ± 0.10 , 0.78 ± 0.08 , and 0.75 ± 0.10 , respectively.

Strains do exhibit geographical distinctions. Although no genetic distinctions were observed between infectious and commensal strains isolated from the vulvovaginal regions of women in the Ann Arbor, Mich., locale, differences were evident between these Ann Arbor strains and a set of commensal strains isolated from the vulvovaginal regions of healthy women in Iowa City, Iowa (26). The set from Iowa City contained a cluster of highly similar strains (CI33vw, CI22vw, CI49vp, and CI39vw) with S_{ABs} of 0.96 or greater and a cluster (CI11vu, CI29vu, CI27vw, and CI37vp) with S_{ABs} of 0.85 or greater (Fig. 3A). When a combined dendrogram was generated for Iowa City and Ann Arbor strains from asymptomatic women, there was very little mixing in clusters (Fig. 3B). The cluster of four Ann Arbor strains with S_{ABs} of 0.85 and above (Fig. 2B) remained intact, with no penetrating Iowa City strains, and the two clusters of Iowa strains (Fig. 3A) remained intact, with no penetrating Michigan strains (Fig. 3B). If one scans the order of strains at the end of the dendrogram in Fig. 3B, one distinguishes runs of either Iowa City or Ann Arbor strains, with little mixing. A statistical analysis of the similarity matrix of the 7 commensal strains from Michigan and the 12 commensal strains from Iowa, performed by the method of Schmid et al. (18), determined that in 15 of 19 cases strains were most similar to other strains from the same geographical locale. If associations were random, this should have happened in only 10 cases. In a z test, the difference between the observation and prediction for random association was statistically significant, with $P < 0.05$, using one-sided percentage points of the normal distribution. This geographical distinction was retained in a combined dendrogram of Iowa City commensal strains, Ann Arbor commensal strains, and Ann Arbor infectious strains (Fig. 3C). In this case, the mixed cluster of three infectious and three commensal strains from Ann Arbor with S_{ABs} of 0.90 and above remained intact, and the cluster of four highly similar strains from Iowa City with S_{ABs} above 0.95 remained intact. The cluster of four moderately similar Iowa City strains was penetrated by a single infectious strain from Ann Arbor, V1.8vag (Fig. 3C).

Strains from women with vulvovaginal infections are highly

FIG. 3. Dendrograms based on S_{ABs} for the group of commensal strains from asymptomatic women (CI) from the Iowa City locale (A), the combination of Iowa City commensals (CI) and commensal strains (C) from the Ann Arbor locale (B), and the combination of Iowa City commensals (CI), infecting strains (V) from the Ann Arbor locale, and commensal strains (C) from the Ann Arbor locale (C). A dashed line is drawn at $S_{AB} = 0.85$ to denote the threshold for clustering. vw, vaginal wall; vp, vaginal pool; vu, vulva; vag, vaginal canal.

similar to strains carried by their partners. In Fig. 1C, Southern blot hybridization patterns are presented for strains carried by the partners of the 10 symptomatic women. If one compares the patterns of the male partner

FIG. 4. Dendrograms based on S_{AB} s for the isolates from the male partners of symptomatic women (VP) from the Ann Arbor locale (A) and the combination of counterpart isolates from male partners (VP) and symptomatic women (V) of the Ann Arbor locale (B). A dashed line is drawn at $S_{AB} = 0.85$ to denote the threshold for clustering. ton, tongue; fec, feces; vag, vagina; vul, vulva.

strains in Fig. 1C with those of the six counterpart infectious strains in Fig. 1A, one finds that in most cases the paired strains are similar. The dendrogram for partner strains (Fig. 4A) has several of the features observed for the dendrogram for infectious strains (Fig. 2A). Male partner strains VP1.6, VP1.10, VP1.8, VP1.3, VP1.4, and VP1.9 (Fig. 2A) cluster with S_{AB} s of 0.85 or greater (Fig. 4A). This group is similar to the cluster of infectious strains from counterpart female partners V1.6, V1.10, V1.8, V1.4, and V1.9. The only difference is the inclusion of VP1.3 in the partner cluster. In addition, strains VP1.7ton, VP1.5fec, and VP1.11fec separate in the partner strain dendrogram (Fig. 4A) in the same manner as counterpart strains V1.7vul, V1.5vag, and V1.11vag in the dendrogram of strains from symptomatic women (Fig. 2A). The similarity between most counterpart strains is demonstrated in the combined dendrogram in Fig. 4B. Nine of the ten pairs (V1.11vag-VP1.11fec, V1.1vag-VP1.1fec, V1.9vag-VP1.9fec, V1.8vag-VP1.8fec, V1.6vag-VP1.6ton, V1.4vag-VP1.4fec, V1.10vag-VP1.10ton, V1.7vul-VP1.7ton, and V1.5vag-VP1.5fec) exhibited S_{AB} s of 0.85 or greater (Table 2). An analysis of the similarity matrix of all strains from the 10 couples revealed that, in 8 of the 10 cases, the strains of the two partners were more similar to each other than to any other strain. Upon random associa-

TABLE 2. S_{AB} values computed for strains from symptomatic women and their male partners

Counterpart pair	S_{AB}^a
V1.1vag-VP1.1fec.....	0.91
V1.3vag-VP1.3fec.....	0.81
V1.4vag-VP1.4fec.....	0.89
V1.5vag-VP1.5fec.....	0.95
V1.6vag-VP1.6ton.....	0.94
V1.7vul-VP1.7ton.....	1.00
V1.8vag-VP1.8fec.....	0.93
V1.9vag-VP1.9fec.....	0.96
V1.10vag-VP1.10ton.....	0.85
V1.11vag-VP1.11fec.....	1.00

^a S_{AB} s were computed for each pair and represent a far more accurate calculation than those obtained from a dendrogram in which S_{AB} s are averaged between groups at branch points. V1.1 to V1.11, strains from symptomatic women; VP1.1 to VP1.11, strains from counterpart male partners.

tion between strains from different couples, this could only be expected to occur by chance in one case (10×0.1).

Although the majority of partner strains were similar, they were not always identical. In Fig. 5, we have used an image-processing feature of the Dendron software program to "neighbor" Southern blot hybridization patterns of partner strain pairs analyzed on different gels. Since no two gels are identical and since they can be geometrically distorted, the digitized images of the gels were straightened, or unwarped, and then lanes were "neighbored" and normalized so that invariant bands matched. Counterpart pairs V1.1vag-VP1.1fec, V1.3vag-VP1.3fec, and V1.4vag-VP1.4fec varied by the position of one to two bands (Fig. 5), and counterpart pair V1.10vag-VP1.10ton varied by several band positions. These pairs had S_{AB} s varying between 0.81 and 0.91 (Table 1). Counterpart pairs V1.5vag-VP1.5fec, V1.6vag-VP1.6ton, V1.8vag-VP1.8fec, and V1.9vag-VP1.9fec had similar, if not identical, patterns (Fig. 5) and S_{AB} s varying between 0.93 and 0.96 (Table 2).

In two cases (VP1.3 and VP1.9), strains were obtained from both the tongue and feces of the male partner. In the case of V1.3-VP1.3, the fecal and tongue samples of the male partner varied by a single band, and the infectious strain from the vaginitis patient was identical to the tongue isolate of the male partner (Fig. 5). In the case of V1.9-VP1.9, the sample from the symptomatic woman and the oral and fecal samples from the male partner were all identical (Fig. 5).

Strains from partners of uninfected women are genetically more diverse. The isolates of six male partners of asymptomatic, culture-negative women (Fig. 6) were genetically more diverse (i.e., formed clusters to a lesser degree) than strains in the three other test groups. The percentage of comparisons among these isolates with S_{AB} s equal to or greater than 0.8 was 7%, while those of isolates from vaginitis patients, asymptomatic women, and partners of asymptomatic women were 32, 38, and 33%, respectively. A z test demonstrated that the differences between the percentage of S_{AB} s ≥ 0.8 for isolates from partners of asymptomatic women and those from the three other groups were statistically significant ($P < 0.05$). In a combined dendrogram of isolates from partners of symptomatic and asymptomatic women (Fig. 6B), there was no penetration of strains of the latter into clusters of strains of the former with S_{AB} s of 0.85 or greater.

FIG. 5. Comparison of Ca3 fingerprinting patterns of isolates from symptomatic women and their male partners. Because compared lanes were not in sequence in the original blots, gel images were digitized into the Dendron data file, and through a unique neighboring program, the lanes were placed alongside each other, unwarped, and normalized. No changes in relative band position or intensity were made. Estimated molecular sizes, in kilobases, are presented to the left of the 3153A blot for comparison. The question mark in V1.1vag-VP1.1fec indicates probable change. Dashes represent changes in molecular size.

DISCUSSION

Until quite recently, little was known about the etiology and epidemiology of yeast vaginitis primarily because of the lack of tools for comparing independent isolates at the genetic level. In the past, strains were distinguished by biotyping (5, 11), but this method compares phenotype and therefore runs the risks of separating strains which are genetically similar but phenotypically dissimilar and group-

ing strains which are genetically dissimilar but phenotypically similar (23). Problems with biotyping were compounded by the discovery of reversible switching systems which can dramatically alter the phenotype of *C. albicans* (24). Recently, several methods were developed to fingerprint *C. albicans* at the genetic level (4, 8, 13, 16, 17, 19, 29), and the use of the Ca3 probe to generate strain-specific Southern blot hybridization patterns has proven to be the most sensitive and accurate method (7, 12), especially with

FIG. 6. Dendrograms based on S_{AB} for a group of commensal isolates from male partners of asymptomatic women (CP) from the Ann Arbor locale (A) and for the combination of this group of isolates and the group of isolates from male partners of symptomatic women (VP) from the Ann Arbor locale (B). A dashed line is drawn at $S_{AB} = 0.85$ to denote an arbitrary threshold for clustering. ton, tongue; fec, feces.

the development of the computer-assisted Dendron system for analysis (18, 19). We have used Dendron to compare the Ca3 fingerprints of strains isolated from vaginitis patients, strains from their male partners, vaginal commensals isolated from women in the same geographical region, vaginal commensals isolated from women from a different geographical region, and commensals from males with asymptomatic, culture-negative female partners. Our results demonstrate that, in the Ann Arbor, Mich., locale, infecting strains do not represent a group that is genetically distinct from commensal strains. When a comparative dendrogram based on the S_{AB} values between infecting and commensal strains from this single geographical locale was generated, both types of strains mixed in clusters with similarity values above 0.85. Therefore, within this geographical locale, infecting strains could not be distinguished from commensal strains by their Ca3 Southern blot hybridization patterns. Moreover, the most frequently encountered type of infecting strains, represented by the cluster including V1.6, V1.4, V1.5, V1.8, and V1.10, and the most frequently encountered type of commensal strains, represented by the cluster including C2.9, C2.1, and C2.10, fall into the same cluster in a combined dendrogram. This suggests that strains that are the most successful in being carried in the vulvovaginal region as a commensal are genetically similar to strains that are the most successful pathogens in the vulvovaginal region and

that vaginal commensals may therefore be the direct source of vaginal pathogens. This, however, does not explain the source of infecting strains in women who do not carry a vaginal commensal. A similar conclusion was reached by Schmid et al. (18) for the relationship between oral commensal isolates and oral infecting isolates in AIDS patients.

Although no distinction was evident between infecting and commensal strains from the Ann Arbor locale, genetic differences were evident between vaginal strains from the Ann Arbor and Iowa City locales. A set of commensal strains from Iowa contained a cluster from different healthy women which was highly dissimilar to several hundred other strains in the Dendron data base which had been collected worldwide (26). This cluster also separated from all Ann Arbor strains. In addition, a second cluster of four Iowa City commensal strains with S_{AB} of greater than 0.85 was penetrated by only a single infecting strain from the Ann Arbor set in a combined dendrogram. These results suggest that strains in a particular geographical locale are genetically more similar, on average, than strains from different geographical locales and that genetic similarity based on geographical localization may be far stronger than genetic similarity based on the particular disease state.

Our results also demonstrate that, in 8 of the 10 cases in which infecting and male partner strains were compared, the paired strains were either identical or far more similar to each other than to other strains and that male partner strains were more similar, on average, to vaginal strains than to strains carried as commensals by males with asymptomatic partners lacking a vaginal commensal. These results suggest that strain replacement occurs in male partners of symptomatic women, but they do not distinguish when replacement occurs.

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