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Type 1 Fimbrial Shafts of *Escherichia coli* and *Klebsiella pneumoniae* Influence Sugar-Binding Specificities of Their FimH Adhesins

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The type 1 fimbriae of enterobacteria comprise FimA, which constitutes most of the fimbrial shaft, and a cassette of three minor ancillary subunits including FimH, the mannose-binding moiety. The sugar-binding specificities of *Escherichia coli* and *Klebsiella pneumoniae* type 1 fimbriae were examined by determining the relative activities of two aromatic mannosides in inhibiting the yeast aggregation caused by the fimbriated bacteria. 4-Methylumbelliferyl α-mannoside (MeUmbαMan) was approximately 10-fold more effective than *p*-nitrophenyl α-mannoside (*p*-NPαMan) in inhibiting the yeast aggregation caused by the recombinant expressing native *E. coli* type 1 fimbriae. In contrast, MeUmbαMan was only fourfold more effective than *p*-NPαMan in assays employing the recombinant expressing native *K. pneumoniae* type 1 fimbriae. In order to elucidate the molecular mechanisms underlying the sugar-binding specificities of type 1 fimbriae in the two species, transcomplementation studies were performed and resulted in the creation of recombinants expressing two types of hybrid fimbriae: one consisting of a cassette of minor subunits of *E. coli* fimbriae borne on a filamentous shaft of *K. pneumoniae* FimA subunits and the other consisting of a cassette of *K. pneumoniae* minor fimbrial subunits borne on a shaft of *E. coli* FimA subunits. Although the heterologous FimH was incorporated into the fimbrial filaments in amounts comparable to those observed in native fimbriae, the hemagglutination activities of recombinants expressing hybrid fimbriae were significantly lower than those of their counterparts bearing native fimbriae. The sugar-binding specificity of the recombinant expressing hybrid fimbriae consisting of an *E. coli* shaft bearing *K. pneumoniae* FimH was different from those of recombinants expressing native *K. pneumoniae* fimbriae in its affinity for the two aromatic sugars but was remarkably similar to the specificities exhibited by recombinants expressing native *E. coli* fimbriae. Conversely, the sugar-binding specificity of the recombinant expressing hybrid fimbriae consisting of a *K. pneumoniae* shaft bearing *E. coli* FimH was different from that of the recombinant expressing native *E. coli* fimbriae but was very similar to those of recombinants expressing native *K. pneumoniae* fimbriae. We conclude that the differences in the sugar-binding specificity between *E. coli* and *K. pneumoniae* FimH fimbrial subunits is influenced by the fimbrial shafts which carry the adhesin molecules in a functionally competent form at the distal tips.

The specific coupling of adhesion-mediating molecules, also termed adhesins, to their complementary receptors on various host tissues is crucial to the initiation and establishment of many bacterial infections (5, 6). It now appears that in a number of enterobacterial species, the adhesins are part of complex heteropolymeric structures protruding from the bacterial surface which are referred to as fimbriae or pili (7, 11, 20). One of the fimbriae most commonly expressed by *Escherichia coli* is mannose-specific type 1 fimbria (4, 8, 12), which consists of a major subunit (FimA) and a cassette of at least three ancillary subunits (FimF, FimG, and FimH) (2, 20, 25, 27, 31). There is compelling evidence to suggest that FimH contains the mannose-binding site responsible for mediating the adhesion of fimbriated bacteria to mannoligosaccharide-containing receptors, summarized as follows. (i) Deletion or inactivation of the *fimH* gene results in the loss of the binding activity of the fimbriae (19, 24, 27, 28); (ii) antibodies directed at FimH but not at other subunits of *E. coli* type 1 fimbriae block fimbrial binding activity (1, 3); and (iii) isolated FimH binds mannosylated glycoproteins (1, 25) and, perhaps more importantly, exhibits biological activities such as binding to and activation of human neutrophils in a manner that mimics the activity of type 1-fimbriated *E. coli* (33).

Proteins corresponding in size, antigenicity, and function to *E. coli* FimH have been detected in type 1 fimbriae expressed by other member species of the family *Enterobacteriaceae*, indicating that the compositions and mechanisms of binding amongst the type 1 fimbriae are similar (3, 9, 18, 19). In spite of the apparent conservation in their adhesin moieties, there appears to be remarkable heterogeneity in their fine sugar specificities (14–16). For example, aromatic α-mannosides and the trisaccharide Manα3Manβ4GlcNAc were weak inhibitors of yeast aggregation (YA) caused by type 1-fimbriated strains of *Salmonella typhimurium*, whereas these mannosides were strong inhibitors of the YA activities caused by fimbriated strains of *E. coli* and *Klebsiella pneumoniae* (14–16). These findings were interpreted to suggest that the mannose-combining site of FimH on type 1 fimbriae of *E. coli* and *K. pneumoniae* is in the form of a pocket that corresponds to the size of a trisaccharide and is situated adjacent to a hydrophobic region (15, 16). Furthermore, the putative binding pocket of *S. typhimurium* is probably smaller and is devoid of an adjacent hydrophobic region. Different specificities and hence different sugar-combining sites appear to be exhibited by FimH adhesins of several other type 1-fimbriated members of the *Enterobac-*

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teriaceae (15). These differences in sugar specificity may be responsible for the strictly different interspecies hemagglutination patterns of type 1-fimbriated bacteria seen when tested with a panel of animal erythrocytes (12). Because short oligomannose chains or hybrid units in glycoproteins on animal cells are preferentially recognized by type 1 fimbriae (13, 29), it is likely that the interspecies differences in the sugar specificities of the fimbrial adhesins influence the tissue tropism of various fimbriated enterobacteria.

In order to better understand the structure-function relationship of fimbrial adhesins, we initiated studies of mannose-specific type 1 fimbriae. We focused our studies on *E. coli* and *K. pneumoniae* type 1 fimbriae because the composition of the fimbrial structure and the genetic organization of their respective gene clusters are known and, more importantly, because recombinant clones expressing *E. coli* and *K. pneumoniae* type 1 fimbriae and their genetic variants are available (9, 23, 28, 30). In the present study, with the help of *p*-nitrophenyl α-mannoside (*p*-NPαMan) and 4-methylumbelliferyl α-mannoside (MeUmbαMan), which has not previously been tested, we were able to discriminate between the sugar-binding specificities of *E. coli* and *K. pneumoniae* fimbriae. Furthermore, transcomplementation experiments with plasmids coding for the minor fimbrial subunits FimH, FimG, and FimF or for FimH-deficient fimbriae revealed that the fimbrial shafts of both bacterial species influence the sugar-binding specificity of the FimH adhesin.

MATERIALS AND METHODS

Bacterial strains and culture conditions. *E. coli* ORN103 [*thr-1 leu-6 thi-1* Δ(*argF-lac*)*U169 xyl-7 ara-13 mtl-2 gal-6 rpsL tonA2 fhuA2 minA minB recA13* Δ(*fimABCDEFGH*)] (27, 30, 31) is a nonfimbriated K-12 strain which was used as the host strain for the introduction of various plasmids. *E. coli* 346 and *K. pneumoniae* Kb1 are strains isolated from clinical specimens (26). For the best expression of type 1 fimbriae for YA assays, the bacterial strains were grown in Luria broth under static conditions for 18 h (26). To maintain the appropriate plasmids in the host, 40 μg of chloramphenicol per ml and/or 50 μg of ampicillin per ml was incorporated into the medium.

Recombinant DNA techniques. Isolation of plasmid DNA was carried out by the minilysate method (24). Restriction endonuclease mapping, ligation, and transformation of plasmid DNA were performed as described before (28). Analyses of DNA fragments were performed on 1% agarose gels.

Recombinant plasmids. The construction and characterization of plasmids encoding the expression of native *E. coli* (pSH2) and *K. pneumoniae* (pBP7) type 1 fimbriae and their respective adhesin-deficient fimbrial shafts (pUT2002 and pBP799) have been described elsewhere (17, 18, 28, 32). Plasmid pBM10 was created by inserting a 5.5-kb *Bam*HI-*Sal*I fragment of pBP7 into a similarly cut site on pUC18. Plasmid pBM20 was made by inserting a 5.0-kb *Bam*HI fragment from pSH2 into pUC18. For transcomplementation analyses, the plasmids used contained compatible replicons. Double transformants were screened for the presence of two distinct plasmid molecules as previously described (19). Transformant designations, such as A_E-H_E, A_E/H_K, etc., show the presence of shaft and FimH subunits (A and H, respectively), the *E. coli* and *K. pneumoniae* sources (E and K, respectively), and transformation by one or two plasmids (hyphen and slash, respectively).

Isolation and purification of type 1 fimbriae. Type 1 fimbriae were isolated and purified from *E. coli* strains by the method of Dodd and Eisenstein (10).

SDS-PAGE and immunoelectroblotting. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed in a 1.5-mm-thick 15% slab gel (3). Samples of fimbriae were dissociated before electrophoresis by heating in acid (10). After SDS-PAGE, the bands of fimbrial protein were electrophoretically transferred onto nitrocellulose as described previously (2). After transfer, the nitrocellulose paper strips were incubated first with *E. coli* FimH antisera raised in rabbits, then with enzyme-linked goat anti-rabbit immunoglobulin G antibody, and finally with the substrate (2). The FimH-specific antibodies react with homologous and heterologous FimH because of conserved regions in the FimH of various enterobacterial species (3).

Electron microscopy. Samples of type 1-fimbriated bacteria or isolated type 1 fimbriae were applied to Formvar-coated copper grids and then stained with 2% phosphotungstic acid (1). Negatively stained preparations were examined on a Philips transmission microscope.

Determination of relative inhibitory activity of mannoglycosides. The YA activity of the bacterial suspension was determined with a Payton aggregometer as previously described (15). Each value was expressed as the rate of aggregation deduced from the steepest slope of the curve recorded after adding the bacterial suspension (10 μl of a solution with an optical density of 1.00 in phosphate-buffered saline [PBS]) to a yeast suspension (0.25 mg [dry weight]/0.5 ml of PBS). The inhibitory activity of each sugar was determined by adding 10 to 50 μl of a solution containing various concentrations of the test sugar to the yeast suspension and then adding the bacterial suspension. For each inhibitory sugar, the concentrations causing 50% inhibition of the YA activities of the test bacteria were determined, and the inhibitory activities relative to that of methyl α-mannoside (MeαMan), which was arbitrarily set at 1.00, were calculated as described previously (15, 16).

RESULTS

Characterization of binding specificity of *E. coli* and *K. pneumoniae* type 1 fimbriae. The YA and hemagglutinating (HA) activities of *E. coli* ORN103 transformants expressing *E. coli* type 1 fimbriae encoded by pSH2 were significantly higher than those of transformants expressing native *K. pneumoniae* fimbriae encoded by pBP7 (Tables 1 and 2). Both activities were sensitive to MeαMan, and the concentrations of MeαMan causing 50% inhibition of YA activities were 1.6 mM for *E. coli* fimbriae and 1.0 mM for *K. pneumoniae* fimbriae. The relative inhibitory activities of *p*-NPαMan with bacteria expressing *E. coli* (A_E-H_E) and *K. pneumoniae* (A_K-H_K) fimbriae were determined to be 70 and 14, respectively, indicating a fivefold difference in affinity between the two fimbriae for the inhibitor (Table 1). An even greater difference in affinity (11-fold) for MeUmbαMan between *E. coli* (relative inhibitory activity, 733) and *K. pneumoniae* (relative inhibitory activity, 66) fimbriae was observed (Table 1). For comparative purposes, we also examined the relative inhibitory activities of *p*-NPαMan and MeUmbαMan on the YA activities of an *E. coli* isolate (strain 346) and a *K. pneumoniae* isolate (strain Kb1) randomly selected from our collection of clinical strains. The binding specificities of the type 1-fimbriated clinical isolate of *E. coli* for the two aromatic mannosides were remarkably similar to those exhibited by the recombinant clone ORN103 (pSH2), expressing *E. coli* type 1 fimbrial genes. Similarly, the binding specificities of the clinical *K. pneumoniae* strain were identical to those exhibited by the recombinant clone ORN103(pBP7), expressing type 1 fimbrial genes of *K. pneumoniae*. Taken together, these findings suggest that *E. coli* and

TABLE 1. Relative inhibition by aromatic mannosides of yeast aggregation caused by various *E. coli* and *K. pneumoniae* strains

Transformant or strain (plasmid[s])[a]	Type of fimbriae	Relative inhibition by[b]:	
		p-NPαMan	MeUmbαMan
Recombinant strains of *E. coli* ORN103			
A_E-H_E (pSH2)	Native	70 ± 10	733 ± 16
A_E/H_E (pUT2002/pBM20)	Native complemented	65 ± 9	905 ± 20
A_E/H_K (pUT2002/pBM10)	Hybrid complemented	55 ± 12	570 ± 17
A_K-H_K (pBP7)	Native	14 ± 5	66 ± 8
A_K/H_K (pBP799/pBM10)	Native complemented	20 ± 6	73 ± 10
A_K/H_E (pB799/pBM20)	Hybrid complemented	8 ± 3	45 ± 11
Clinical isolates			
E. coli 346	Native	50 ± 8	560 ± 18
K. pneumoniae Kb1	Native	17 ± 3	49 ± 12

[a] For transformant designations, see Materials and Methods.
[b] Inhibition by MeαMan was set at 1, and all values are relative to it.

K. pneumoniae fimbriae exhibit distinctly different binding specificities, presumably reflecting differences in the configurations of their respective mannose-combining sites on the fimbriae. These findings also confirm that the binding specificities of recombinant clones expressing either *E. coli* or *K. pneumoniae* type 1 fimbriae are identical to those exhibited by wild-type strains of *E. coli* and *K. pneumoniae*.

Transposition of FimH subunits between *E. coli* and *K. pneumoniae* type 1 fimbriae. Because the mannose-binding site resides in FimH, we attempted to transpose the binding specificities of *E. coli* and *K. pneumoniae* fimbriae by transposing their respective FimH subunits. Our strategy was to delete the *fimH* gene from the *E. coli* and *K. pneumoniae* gene cluster and then complement the deletion by introducing heterologous *fimH* in *trans*. Because recent studies have suggested that FimH forms a distinct fibrillar structure along with FimF and FimG (23a), we optimized the functional activity of FimH on heterologous fimbrial filaments by maintaining as much of the structural organization of the native fibrillar structure as possible. Thus, each *fimH* gene was transposed along with homologous *fimF* and *fimG* genes into the heterologous gene cluster. The plasmids employed in this study are depicted in Fig. 1. Because the hybrid fimbriae are derived from genes encoded on two separate replicons, the stoichiometry of the different fimbrial proteins produced may not be the same as that of proteins encoded by fimbrial genes clustered on a single replicon (e.g., pSH2 or pBP7). Therefore, for comparative purposes, we created "native fimbriae" with the plasmids employed to create hybrid fimbriae by complementing *fimH*-deficient fimbrial gene clusters with homologous *fimH*. A list of strains expressing native or hybrid fimbriae resulting from these transcomplementation experiments and a description of their fimbrial phenotypes are presented in Table 1.

TABLE 2. HA and YA activities of various *E. coli* and *K. pneumoniae* strains

Plasmid content or strain no.	Fimbrial phenotype[a]	HA titer[b]	Rate of YA (T/min)[b,c]
ORN103 transformants			
pSH2	A_E-H_E	128	17.0 ± 3.0
pBP7	A_K-H_K	32	19.0 ± 1.6
pUT2002/pBM20	A_E/H_E	128	6.0 ± 1.0
pBP799/pBM10	A_K/H_K	32	5.6 ± 1.4
pUT2002/pBM10	A_E/H_K	4	2.1 ± 0.8
pBP799/pBM20	A_K/H_E	8	3.2 ± 0.9
pUT2002	A_E	0	0
pBP799	A_K	0	0
pBM20	H_E	0	ND[d]
pBM10	H_K	0	ND
Clinical isolates			
E. coli 346	A_E-H_E	ND	16 ± 2.0
K. pneumoniae Kb1	A_K-H_K	ND	25 ± 4.0

[a] For transformant designations, see Materials and Methods.
[b] Each value is the average of three tests.
[c] T, relative transmission.
[d] ND, not done.

Characterization of *E. coli* and *K. pneumoniae* fimbriae bearing heterologous ancillary subunits. No significant difference in the average number of fimbriae (approximately 98 per cell) between transformants bearing native (A_E/H_E and A_K/H_K) and hybrid (A_E/H_K and A_K/H_E) fimbriae was observed (Fig. 2). Similarly, no obvious difference between the thickness of either hybrid fimbria and those of the native fimbriae was observed. Interestingly, the hybrid fimbriae were significantly shorter than native fimbriae. This was especially noticeable when isolated fimbriae of both types were examined. The average length of isolated native fimbriae was 0.46 ± 0.06 μm; in contrast, the average length of hybrid fimbriae was 0.23 ± 0.07 μm.

Purified fimbriae from each transformant were obtained and

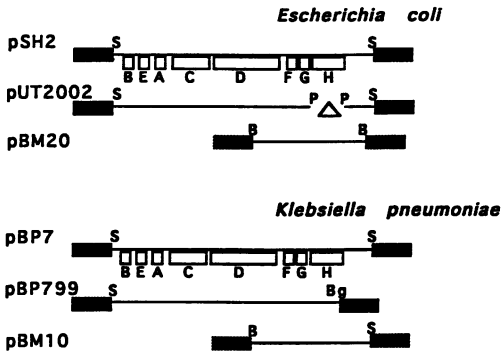

FIG. 1. Organization of genes in plasmids employed in this study. Abbreviations for restriction endonuclease sites: P, *Pvu*II; S, *Sal*I; B, *Bam*HI; Bg, *Bgl*III; H, *Hin*dIII. Solid bars indicate pACYC184 DNA, and hatched bars indicate pUC18 DNA. The products encoded by the type 1 fimbrial genes in each gene cluster are indicated by open rectangles.

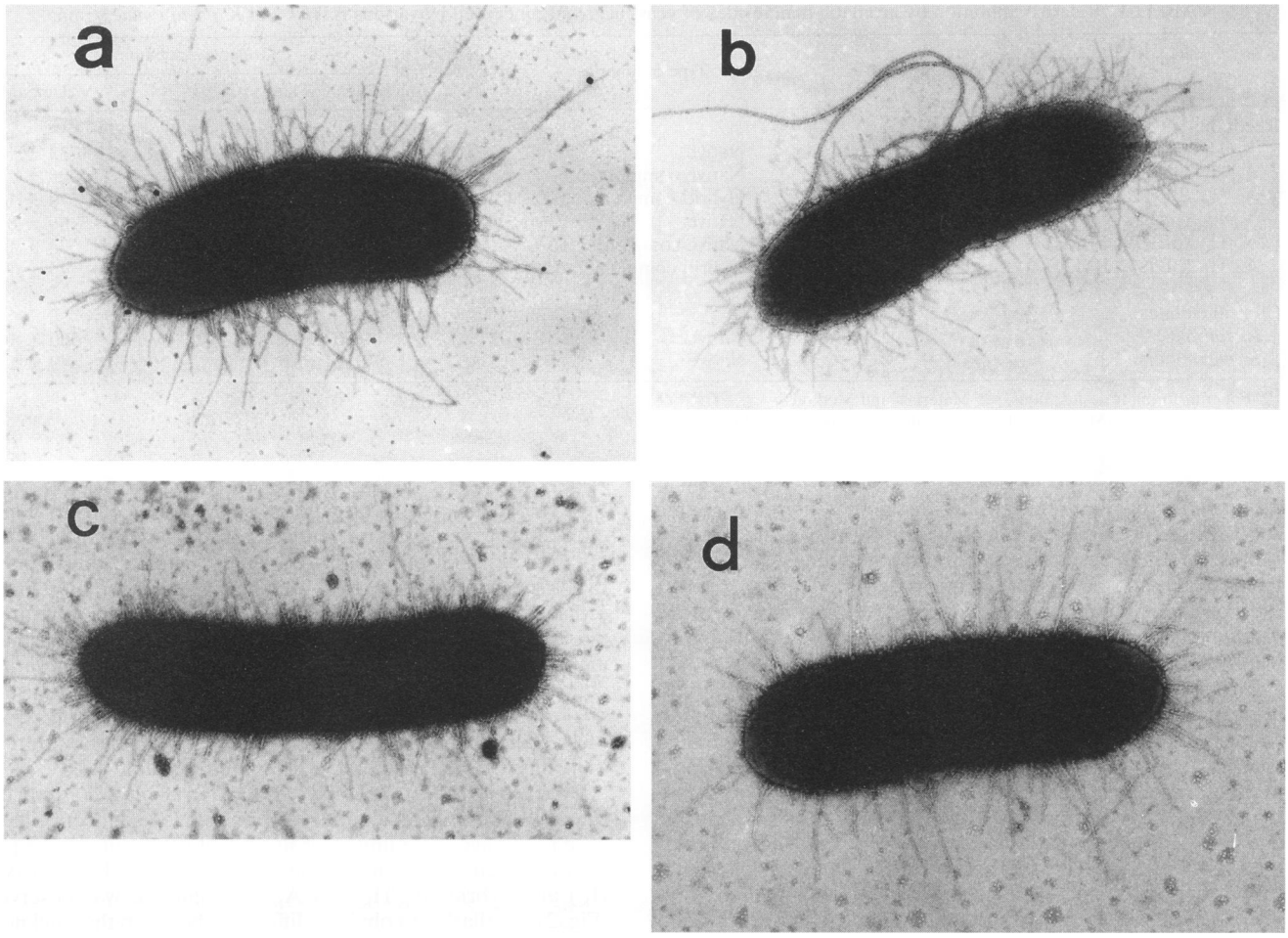

FIG. 2. Electron micrographs of negatively stained recombinant *E. coli* ORN103 expressing native *E. coli* A_E/H_E fimbriae (a), native *K. pneumoniae* A_K/H_K fimbriae (b), hybrid A_E/H_K fimbriae (c), and hybrid A_K/H_E fimbriae (d).

subjected to SDS-PAGE and immunoblot analysis employing antibodies to FimH as a probe. Figure 3a shows a Coomassie blue-stained gel preparation of fimbriae obtained from each of the transformants (A_K/H_K, A_K/H_E, A_E/H_E, and A_E/H_K), revealing prominent bands corresponding to the major subunit, FimA. Since the adhesin moiety FimH and the ancillary subunits FimF and FimG are only minor components of the fimbriae, these proteins were not visible with the relatively insensitive Coomassie blue stain. It is noteworthy that the size of *E. coli* FimA is 17 kDa, whereas that of *K. pneumoniae* FimA is 18 kDa. An immunoblot of the same group of fimbriae (Fig. 3b) reacted with polyclonal antibodies to *E. coli* FimH shows the presence of FimH in native and hybrid fimbriae of both bacterial species. *K. pneumoniae* FimH has a size of 30 kDa, whereas that of *E. coli* is 29 kDa. Notice that both hybrid fimbriae (A_E/H_K and A_K/H_E) appear to contain heterologous FimH in amounts comparable to those seen with native fimbriae (A_E/H_E and A_K/H_K).

Transformants bearing single plasmids encoding either the fimbrial shaft or its ancillary minor subunits lacked HA activity, whereas transformants expressing both the fimbrial shaft and the minor subunits including the adhesin exhibited HA and YA activities (Table 2). These findings confirm earlier studies of the adhesive role of FimH but also emphasize the importance of the fimbrial shaft in presenting FimH in a functionally competent manner. It is noteworthy that transformants A_E/H_K and A_K/H_K expressing hybrid fimbriae exhibit significantly ($P < 0.05$) reduced HA and YA activities compared with those of the corresponding A_E/H_E and A_E/H_K transformants expressing native fimbriae (Table 2).

The relative inhibitory activities of *p*-NPαMan on the YA of the transformant A_E/H_K which expresses hybrid fimbriae were in the same range (ca. 55) as those of the corresponding transformants A_E/H_E (ca. 65) and A_E-H_E (ca. 70), which express native fimbriae (Table 1). Similarly, the relative inhibitory activity of the aromatic MeUmbαMan on the YA of the transformant A_K/H_E, which expresses hybrid fimbriae, was in the same range (ca. 8) as those of the corresponding transformants A_K/H_K (ca. 20) and A_K-H_K (ca. 14) which express native fimbriae (Table 1).

DISCUSSION

In the present study, we have utilized the relative inhibitory activities of two aromatic mannosides to differentiate between the binding specificities of *E. coli* and *K. pneumoniae* type 1 fimbriae. *E. coli* type 1 fimbriae exhibited 5-fold more sensitivity to *p*-NPαMan and 11-fold more sensitivity to MeUmbαMan than *K. pneumoniae* fimbriae. Having demonstrated quantifiable differences in sugar-binding specificities

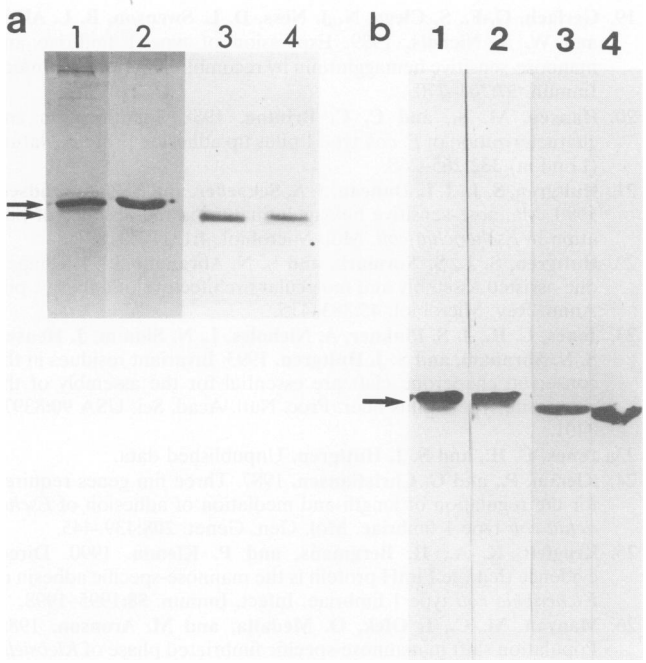

FIG. 3. SDS-PAGE (a) and immunoblot (b) analysis of isolated fimbriae obtained from various double transformants after Coomassie blue staining. (a) Lane 1, A_K/H_K; lane 2, A_K/H_E; lane 3, A_E/H_E; lane 4, A_E/H_K. Only the major subunit FimA is detectable in each preparation. The upper arrow marks 18 kDa, and the lower arrow marks 17 kDa. (b) Lane 1, A_K/H_K; lane 2, A_E/H_K; lane 3, A_E/H_E; lane 4, A_K/H_E. Each of the lanes was reacted with polyclonal antibodies to *E. coli* FimH. Notice that the amounts of FimH in both native and hybrid *E. coli* and *K. pneumoniae* fimbriae are comparable. The arrow marks 29 kDa.

between the two fimbriae, we investigated if we could achieve transposition of binding specificities between *E. coli* and *K. pneumoniae* fimbriae by exchanging FimH proteins. Hybrid type 1 fimbriae were genetically created by coexpressing genes encoding the fimbrial shaft from one species and genes encoding minor subunits, including FimH, of the second species through transcomplementation experiments. By comparing the relative inhibition by the two aromatic mannosides, we determined that the sugar-binding activity of the transformant expressing hybrid A_E/H_K fimbriae was virtually identical to that of recombinants expressing native A_E-H_E or A_E/H_E *E. coli* fimbriae. The sugar-binding activity of the transformant expressing hybrid A_K/H_E fimbriae was comparable to the binding specificity of recombinants expressing native A_K-H_K or A_K/H_K *K. pneumoniae* fimbriae. Apparently, *E. coli* FimH exhibits a lower affinity for the aromatic mannosides when it is presented on a *K. pneumoniae* shaft than when it is presented on its homologous shaft. Conversely, *K. pneumoniae* FimH exhibits a stronger affinity for the mannoglycosides when it is presented on an *E. coli* shaft than when it is presented on the *K. pneumoniae* shaft. Taken together, these findings suggest that the binding specificities of *K. pneumoniae* and *E. coli* type 1 fimbriae were not transposed with the exchange of their respective mannose-specific FimH moieties. Furthermore, the fimbrial shaft on which the cassette of minor subunits is presented may play a hitherto unrecognized role in modulating the sugar-binding specificity of the fimbrial adhesin.

It is not known how the fimbrial shaft modulates the sugar-binding activity of the fimbrial adhesin. Unlike the high level of homology (88%) in the primary structure between FimH proteins of *E. coli* and *K. pneumoniae* examined so far (18), there are remarkable differences in the sizes and antigenic properties of FimA proteins among different species of enterobacteria (4, 17). It is conceivable that the heterogeneity among the major components of the fimbrial shaft of each species results in the imposition of particular conformational constrains on its FimH proteins. These quaternary structural constraints imposed by the fimbrial shaft of each species could alter the shape of the mannose-combining site within the FimH proteins, resulting in a distinctive sugar-binding activity. The conformational pressures imposed by each fimbrial shaft may affect not only the sugar-binding specificity of the adhesins but also the potency of their binding activity, as evidenced by our finding that the HA and YA titers of hybrid fimbriae were significantly lower than those of native fimbriae even though similar amounts of FimH were incorporated into each type of fimbria. At this time, it is not possible to make any predictions about the shape of the mannose-combining sites of the FimH molecule on either *E. coli* or *K. pneumoniae* fimbrial shafts, primarily because of the limited number of structurally defined mannoglycosides used in this study. Furthermore there is a possibility that the relatively large hydrophobic groups on *p*-NPαMan and MeUmbαMan may be indirectly influencing the binding specificities of FimH by mediating nonspecific interactions with molecules adjacent to the adhesin.

Transformants containing a single plasmid coding for FimH and its ancillary subunits FimG and FimF were not fimbriated and did not exhibit any YA or HA activity. This is not surprising because the plasmids lack *fimA*, the structural gene of the fimbriae. Furthermore, the genes coding for the chaperone and anchor proteins which are required to stabilize and anchor the minor fimbrial subunits in the periplasmic space and outer membrane, respectively, are also lacking (22, 23). In another study, the deletion of the *fimA* gene from the gene cluster of *E. coli* type 1 fimbriae caused the loss of the fimbrial shaft, and the resulting mutant exhibited HA activity but unlike native fimbriae failed to bind tissue culture cells (21). This finding lends support to the notion that the fimbrial shaft influences the fimbrial binding specificity.

In conclusion, because the fimbrial shaft exhibits considerable antigenic and structural interspecies variation (4, 17), it is possible that some of this heterogeneity is reflected in the variations of the fine sugar specificity of the carbohydrate-binding sites of the minor fimbrial subunits in enterobacteria. It remains to be seen whether variation in fimbrial sugar-binding activity influences the tissue tropism of type 1-fimbriated enterobacteria.

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