The structure of the N-terminal truncated Type IVb pilin (t-PilS) from *Salmonella typhi* was determined by NMR. Although topologically similar to the recently determined x-ray structure of pilin from *Vibrio cholerae* toxin-coregulated pilus, the only Type IVb pilin with known structure, t-PilS contains many distinct structural features. The protein contains an extra pair of β-strands in the N-terminal αβ loop that align with the major β-strands to form a continuous 7-stranded antiparallel β-sheet. The C-terminal disulfide-bonded region of t-PilS is only half the length of that of toxin-coregulated pilus pilin. A model of *S. typhi* pilus has been proposed and mutagenesis studies suggested that residues on both the αβ loop and the C-terminal disulfide-bonded region of PilS might be involved in binding specificity of the pilus. This model structure reveals an exposed surface between adjacent subunits of PilS that could be a potential binding site for the cystic fibrosis transmembrane conductance regulator.

Type IV pili have long been recognized as major bacterial virulence-associated adhesins that promote bacterial attachment to host cells (1). The genome of the typhoid fever bacterium, *Salmonella typhi*, contains a large insertion or “pathogenicity island” that is not found in the chromosome of the non-invasive *Salmonella typhimurium* (2). DNA sequencing within the novel pathogenicity island (*Salmonella* pathogenicity island 7) identified a pil operon (11 genes, from PilL to PilV) that the novel pathogenicity island (pathogenicity island/*Salmonella* pathogenicity island 7) contains a pil operon (11 genes, from PilL to PilV) that was identified by NMR. Although topologically similar to the recently determined x-ray structure of pilin from *Vibrio cholerae* toxin-coregulated pilus, the only Type IVb pilin with known structure, t-PilS contains many distinct structural features. The protein contains an extra pair of β-strands in the N-terminal αβ loop that align with the major β-strands to form a continuous 7-stranded antiparallel β-sheet. The C-terminal disulfide-bonded region of t-PilS is only half the length of that of toxin-coregulated pilus pilin. A model of *S. typhi* pilus has been proposed and mutagenesis studies suggested that residues on both the αβ loop and the C-terminal disulfide-bonded region of PilS might be involved in binding specificity of the pilus. This model structure reveals an exposed surface between adjacent subunits of PilS that could be a potential binding site for the cystic fibrosis transmembrane conductance regulator (CFTR).

The structural differences between these two Type IVb pilins allow a very different surface to be exposed on *S. typhi* pilus, which may represent a potential binding site for CFTR.
BL21(DE3) E. coli cells as inclusion bodies (induction with 0.3 mM final concentration of isopropyl-1-thio-β-D-galactopyranoside; cells were grown at 37 °C). Nine extra residues from the vector (GSAMADIGS) remain N-terminal to residue Met-26 of PilS after thrombin cleavage. The pellet of the expressed inclusion bodies was purified with nickel-nitrilotriacetic acid resin (Qiagen) using buffers containing 6 M GdnCl. The purified protein was refolded by rapid dilution (30 °C) into ice-cold buffer (50 mM Tris, pH 7.9) for NMR studies.

The DNA fragments for PilS (residues 1–181) and its mutants were subcloned between BamHI and EcoRI site of the same vector. All subcloned mutants were confirmed by DNA sequencing. The proteins were expressed as inclusion bodies in BL21(DE3) by inducing at a cell density of 0.6 and at 30 °C. The inclusion body pellets were resuspended in binding buffer (20 mM Tris, pH 7.9, 0.5 M NaCl, 5 mM Imidazole) with 2% v/v Triton-X100 and 0.1 mM phenylmethylsulfonyl fluoride. The inclusion body pellets were resuspended with nickel-nitrilotriacetic acid resin (Qiagen) before being used for binding assays.

**NMR Spectroscopy and Structure Calculation**—Purified t-PilS protein was concentrated to ~1 mM and buffer-exchanged to 50 mM phosphate, pH 6.0, with 0.5 mM sodium sulfate for NMR studies. NMR experiments were performed on a 500-MHz Bruker DRX spectrometer equipped with cryoprobe or a 750-MHz Varian Inova spectrometer at 30 °C. NMR spectra were acquired using a 1H-13C uniformly labeled sample. The stereo-specific assignment of methyl groups was obtained by analyzing the 1H-13CHSQC spectrum of a 10% 13C-labeled sample (24).

Hydrogen bond restraints from amide hydrogen exchange were derived from Thr-15N-HSQC spectrum of a sample left in 99% D2O buffer for 6 h. Proton distance constraints were derived from three-dimensional 15N-edited NOESY (mixing time 150 ms) and three-dimensional 13C-edited NOESY. NMR data were processed using the MMRPipe/NMRDraw (25) suite and analyzed by NMRView (26).

The initial structures of t-PilS were generated by DYANA (27) using manually assigned unambiguous NOE restraints from 15N-NOESY and 13C-NOESY and dihedral angle restraints predicted by TALOS (28). Many other NOE cross-peaks in the two NOESY spectra were further assigned by CYANA (29) automatically. The unambiguous NOE restraints, automatically assigned NOE restraints, dihedral angle restraints, and hydrogen bond restraints were used for structure calculation.

One hundred structures were calculated by DYANA using standard TAD protocol, and 20 conformers with the lowest target function values were selected for further energy refinement in AMBER 7.0 (30). The final ensemble of 10 structures with the lowest amber energies was checked by Procheck-NMR (31) and deposited at the Protein Data Bank.

**Model of PilS Pili**—The two subunits of PilS were first docked manually using the program “O” in such a manner that α2 is in close vicinity to α4. The interface was then refined using the program MULTIDOCK with the following parameters. To define the interface, a distance cut-off of 15 Å was used. The criterion for convergence in terms of change in energy was set at 0.4 kcal/mol (emax). For rigid body energy minimization, a distance cut-off of 15 Å was used. The model was further energy minimized and docked into the receptor structure. The maximum rotation step size was 1° and max-
mum translation step size 0.3 Å. Minimization continued until the energy of the system decreased by less than 1 × 10⁻³ kcal/mol (ftol) for any given step. The energy cap for the number of atom-atom van der Waals clashes was set at 2.5 kcal/mol (eatmax).

Inhibition of Bacterial Entry Experiment—The procedures for inhibition of bacterial entry into human intestinal cells by recombinant PilS proteins were described elsewhere (3). Human embryonic intestinal cells INT407 were grown in tissue culture flasks and seeded in 24-well plates to obtain a monolayer in basal medium Eagle's with 15% calf serum (BME) by cultivating overnight at 37 °C in a CO₂ incubator. The medium was removed, and the cells were washed with 1× PBS. 0.35 ml of fresh BME was added, followed by 100 µl of solutions of PilS or mutant PilS to a final protein concentration of 2 × 10⁻² M (1× PBS was used as a control for 100% invasion) and then 50 µl of S. typhi bacterial cells in saline (−3.6 × 10⁶ cells). The mixture was centrifuged for 10 min at 2,164 × g and incubated for 2 h to allow bacterial invasion. The culture medium was removed, and the cells were washed once with 1× PBS. 0.35 ml of fresh BME with 100 µg/ml gentamycin was added, and the cells were incubated for 1 h to kill S. typhi that remained outside the intestinal cells. The medium was removed, and the cells were washed twice with 1× PBS to remove any trace of gentamycin. 1 ml of 0.02% Triton X-100 was added, and the cells were pipetted up and down to ensure that the intestinal cells were detached and lysed to release the S. typhi cells. The mixture was incubated at 37 °C for 1 h before spreading onto agar plates (with kanamycin) for cell counts.

RESULTS

Structure of S. typhi PilS—The construct used for the PilS structural determination is N-terminal-truncated (Met-26-Gly-181, referred as t-PilS), and the truncation of the N-terminal 25 residues is necessary to prevent the pilin from oligomerization. The three-dimensional structure of t-PilS was solved by NMR spectroscopy (Table I). Fig. 2A shows a stereoview of the best fit superposition of the family of 15 final structures of t-PilS. The N-terminal five residues of t-PilS (residues 26–30) are not well

TABLE I

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<th>Structural statistics for the S. typhi t-PilS protein</th>
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Fig. 2. NMR structure and topology of t-PilS. A, stereoview showing the best fit superposition of the backbone atoms of the final 15 structures of the S. typhi t-PilS protein. B, ribbon diagrams of the three-dimensional structure of t-PilS. Panels A and B were prepared with the program MOLMOL (37). C, secondary structure topologies of t-PilS and Tcp pilin. The αβ loop and D region are shown with shaded background. Locations of the disulfide bonds are indicated with open circles.
defined because of the lack of structural restraints. The other less defined regions in the protein include the loop between helices α1 and -2 (residues 49–60), the loop between strands β1 and -2 (residues 84–86), the loop between strands β3 and -4 (residues 105–112), and the loop between helix α4 and strand β7 (residues 164–171). Residues in these regions have relatively fewer NOE restraints compared with the well-defined regions and are likely to be intrinsically more flexible.

The structure of t-PilS reinforces that Type IVb pilins adopt very different folding topologies compared with the structures of Type IVa pilin. The extended N-terminal α-helix (helix α1) is packed against three antiparallel β-strands (strands β3, -4, and -7) to form the hydrophobic core of the protein. The N-terminal αβ loop on one edge of the β-sheet contains a short α-helix (helix α2) and a pair of well-defined antiparallel β-strands (strands β1 and -2). This is in contrast to the sugar loop and minor β-strands found in the αβ loop of MS11 and PAK pilins, respectively. The C-terminal disulfide-bonded region on the other edge of the β-sheet contains a pair of α-helices (helices α3 and -4) lying on top of two shorter antiparallel β-strands (strands β5 and -6). The seven β-strands align in an antiparallel manner to form a continuous but twisted β-sheet with all helices on one side of the β-sheet (Fig. 2, A and B). In Type IVa pilins, the hypervariable disulfide loop contains either a β-hairpin connected to a loop (12) or β-turns connected to each other (14, 32). These differences may relate to the fact that Types IVa and IVb pili have completely different receptor substrate specificities.

Although topologically similar, t-PilS contains distinct structural features in both the αβ loop and D region when compared with Tcp (Fig. 2C). The αβ loop of t-PilS contains an extra pair of antiparallel β-strands (strands β1 and -2) between helix α2 and strand β3. The corresponding region in the Tcp pilin, between helix α2 and strand β1, is replaced with an extended loop of 18 residues (Fig. 1). The extra pair of β-strands in t-PilS aligns continuously at the edge of the major β-sheet (strands β3, -4, and -7) and allows helix α2 to pack on top at an angle of ~124° to helix α1. In the Tcp pilin, helix α2 lies perpendicular to helix α1 (~90°) and across on the outside of the major β-sheet. Consequently, helix α2, strand β1, and the α1-α2 loop of t-PilS are exposed at the edge of the molecule, whereas only helix α2 is exposed at the same edge in the Tcp pilin (Fig. 3, A and B).

Even larger differences between the structures of t-PilS and Tcp pilin are found in the disulfide-bonded D region (19). The D region of Tcp pilin -- the hypervariable region of the pilin from enteropathogenic E. coli is somewhat shorter, being composed of 49 residues. PilS and pilin of R64 thin pilus have the shortest D regions among Type IVb pilins, consisting of only 36 residues, similar in length to that of the Type IVa pilin of N. gonorrhoeae pilus (29 residues) (Fig. 1). The extra length in the D region of the Tcp pilin is contributed by two extended loops between strands β3 and -4 (24 residues) and between strand β4 and helix α4 (12 residues). These loops contain overlapping epitopes for protective Tcp antibodies and encompass most of the functional domain residues (19). The corresponding regions in t-PilS, between strands β3 and -6 and between strand β6 and helix α4, are only 2 and 6 residues in length, respectively. The β3-β4 loop in Tcp pilin is highly exposed on the surface of the pilus and covers most of the β-sheet on the opposite side of the N-terminal α-helix (Fig. 3A). In contrast to Tcp pilin, the β5-β6 loop is relatively short in t-PilS; most of the residues on the β-sheet opposite to the N-terminal helix are thus predicted to be exposed on the surface of the pilus. In addition to covering the β-sheet, the β3-β4 loop in Tcp pilin is also extended over the edge of the β-sheet at the D region. To expose functional residues found mainly in the β4-α4 loop and helix α4, the β4-α4 loop is extended and helix α4 packs loosely away from helix α3 and makes an angle of around 50° with the helical axis of the pilus (Fig. 3B). On the contrary, helices α3 and -4 of t-PilS align tightly with each other, and both are almost parallel along the helical axis of the pilus.

FIG. 3. Comparison of the structures of t-PilS and Tcp pilin in two different views. In both panels, the central hydrophobic core, the αβ loop, and the D region are red, green, and blue, respectively. The extended β3-β4 and β4-α4 loops in Tcp pilin and their corresponding counterparts in t-PilS are yellow. A, the extended loops in Tcp pilin are highly exposed and cover most of the β-sheet. The much shortened β5-β6 and β6-α4 loops in t-PilS allow different parts of the protein to be exposed. B, during pilus assembly, helix α4 of PilS is aligned almost parallel to the helical axis of the pilus; helix α4 of Tcp pilin makes an angle of around 50° with the helical axis. The figure was prepared with the program MOLMOL (37).
A model of PilS pilus assembly—A model of S. typhi pilus was built based on our t-PilS structure and the model of Tcp (19). The postulated association interface (a2 against a4) between two adjacent t-PilS subunits was energy-refined (total energy = −34.6 kcal/mol) using the program MULTIDOCK (33). The refined dimeric subunit was used to build a single helical strand that was subsequently intertwined with another two identical helical strands to form the pilus model. The model shows that t-PilS can also be arranged into a left-handed three-start helix. Each turn of the helical strand contains six subunits of t-PilS with their a2 helices interacting with the a4 helices of an adjacent subunit. α-helices and loops are red; β-sheets are cyan. B, the PilS pilus can form a three-start helix with a pitch of 30 Å between each helical strand and an outer diameter of ~100 Å. The N-terminal hydrophobic helices of each subunit are packed at the central core of the pilus. The 3 helical strands of the PilS pilus are red, yellow, and blue. The figure was prepared with the program MOLMOL (37).

FIG. 4. A model of PilS pilus assembly. A, each left-handed helical strand of the pilus contains six subunits of PilS with their a2 helices interacting with a4 helices of an adjacent subunit. α-helices and loops are red; β-sheets are cyan. B, the PilS pilus can form a three-start helix with a pitch of 30 Å between each helical strand and an outer diameter of ~100 Å. The N-terminal hydrophobic helices of each subunit are packed at the central core of the pilus. The 3 helical strands of the PilS pilus are red, yellow, and blue. The figure was prepared with the program MOLMOL (37).

Model of S. typhi Pilus Assembly—A model of S. typhi pilus was built based on our t-PilS structure and the model of Tcp (19). The postulated association interface (a2 against a4) between two adjacent t-PilS subunits was energy-refined (total energy = −34.6 kcal/mol) using the program MULTIDOCK (33). The refined dimeric subunit was used to build a single helical strand that was subsequently intertwined with another two identical helical strands to form the pilus model. The model shows that t-PilS can also be arranged into a left-handed three-start helix. Each turn of the helical strand contains six subunits of t-PilS with their a2 helices interacting with the a4 helices of an adjacent subunit in a perpendicular fashion (Fig. 4A). The helix a4 of t-PilS, unlike that of Tcp, is almost parallel to the helical axis of the pilus. Three such helical strands intertwine to form a cylindrical pilus with a helical pitch of around 30 Å and an outer diameter of around 100 Å (Fig. 4B). This arrangement of the pilus places the hydrophobic N-terminal helix (helix a1) of every subunit at the innermost core of the PilS pilus, where it can pack to form a coiled coil providing mechanical strength and stability.

In addition to the N-terminal hydrophobic helix, there are polar interfaces buried between stacked subunits of t-PilS from different helical strands. These potential “structural” charged residues at the “tip” side of the molecule are located on the α1–α2 loop (Lys-51), helix α3 (Arg-135), and helix α4 (Glu-157). Those at the “base” side of the molecule are located on the α2–β1 loop (Lys-75), the β4–α3 loop (Lys-120), and the α4–β7 loop (Asp-166 and Arg-169). These charged residues found in both the αβ loop and D region are not exposed but could form salt bridges or side chains to main chain hydrogen bonds to secure the position of neighboring helical strands. In Tcp, these structural charged residues are found within the D region spanning helix α3 to strand β4. In contrast to the above-mentioned residues, charged residues found among the interface formed between a2 and -4 of two adjacent subunits or on the β-sheet of each subunit are exposed on the surface of the pilus. These exposed charged residues in the aβ loop are found mainly on the a1–a2 loop (Asp-54), helix α2 (Lys-63 and Asp-66), and the β1–β2 loop (Asp-82). Those found in the D region are mainly located on or around helix α4 (Asp-151, Lys-153, and Glu-162). Asp-103 and Lys-143 are the two exposed charged residues that are found on β3 and -5 of each PilS subunit, respectively (Fig. 5A). All these charged residues are exposed (Fig. 5B) and could be involved in a functional role of the PilS pilus by interacting directly with the first extracellular domain of CFTR.

Peptide Binding Surface of the S. typhi Pilus—The first extracellular domain of CFTR (residues 103–117) was identified as a binding receptor on human intestinal cells for S. typhi pilus (4, 5). A 10-residue peptide composed of residues 108–117 (SYDPDNKEER) of CFTR was enough to inhibit entry of S. typhi into intestinal cells. This inhibitory effect was not found in another 10-residue peptide composed of residues 103–112 (GRIIASYDPD) of CFTR, indicating that residues 113–117 (NKEER) of CFTR are essential for S. typhi pilus binding (5). Interestingly, the same 10-residue peptide was also found to be effective in inhibiting entry of P. aeruginosa into corneal cells (34). Because the peptide 108–117 of CFTR contains four neg-
Fig. 5. Peptide binding surface of PilS pilus. A, ribbon diagram showing exposed and charged residues on t-PilS. The two subunits are gray and light blue, respectively. Exposed and charged residues at the subunit interfaces and on the β-sheet are shown in wire-frame models. Positively charged residues are blue. Negatively charged residues are red. Note that residues are labeled only on one of the subunits. B, molecular surface of four subunits of PilS on the pilus model showing the distribution of charges and locations of exposed charged residues. Positively and negatively charged surfaces are blue and red, respectively. Exposed charged residues found to be essential for bacterial cell entry into human intestinal cells are underlined. An asterisk next to the label represents functional residues from adjacent subunits on the same helical strand. A hash sign next to the label represents functional residues from adjacent subunits on a different helical strand. The border of one of the subunits is highlighted for easier identification. The figure was prepared with the program MOLMOL (37).

Positively charged residues and two positively charged residues, the binding site for this peptide on PilS pilus is expected to contain polar or charged residues.

Exposed and charged residues in t-PilS are mainly found on or around the helices α2 (Asp-54, Lys-63, Asp-66, and Asp-82) and α4 (Asp-151, Lys-153, and Glu-162) at the interface between two adjacent subunits and also on the exposed β-sheet (Asp-103 and Lys-143) (Fig. 5A). Fig. 5B shows the locations of all the exposed and charged residues found on the surface of PilS pilus. In an attempt to determine the exact binding site of CFTR on PilS, we have synthesized a 10-residue peptide with a sequence derived from residues 108–117 (SYDPDNKEER) of CFTR. The peptide was titrated into a 15N-labeled t-PilS NMR sample, but to our surprise no binding could be observed (data not shown). The inability of t-PilS to bind CFTR is further confirmed by the loss of its ability to inhibit entry of S. typhi into intestinal cells (Fig. 6). Only full-length PilS protein that contains the N-terminal hydrophobic oligomerization domain retained the ability to bind CFTR and inhibit entry of S. typhi into intestinal cells. To identify the exposed charged residues that could involve direct interaction with CFTR, we have generated eight mutants of the full-length PilS protein and tested their abilities to inhibit entry of S. typhi into intestinal cells (Fig. 6). Asp-66 was not tested because the protein tends to precipitate out of solution. Results of the inhibition of bacterial entry experiment show that most of the “functional” charged residues involved in CFTR binding are located on or around helix α4 in the D region (residues Asp-151, Lys-153, and Glu-162). This agrees with the findings on Tcp pilin in which all of its functional residues are found exclusively on or around α4 (19). Unlike Tcp pilin, the residue on the α1-α2 loop of PilS (Asp-54), which is in close proximity to Lys-153 on helix α4 of an adjacent subunit, is also essential for CFTR binding. Other charged residues that are exposed on the αβ loop (Lys-63 and Asp-82) and the β-sheet (Asp-103 and Lys-143) of PilS are not essential for CFTR binding.

**DISCUSSION**

Type IV pili play a crucial role in pathogenesis of many bacterial species by providing adherence to host cells. All Type IV pilins identified to date adopt an αβ roll fold with the N-terminal hydrophobic helix packed against three antiparallel β-strands to form a ladle-shaped molecule. Different classes of Type IV pili, however, differ substantially in their N-terminal αβ loops and C-terminal disulfide-bonded D regions. Type IVa pilin has either a sugar loop (MS11) or minor β-strands (PAK) in the αβ loop, whereas Type IVb pilin has a well defined α-helix in the αβ loop that is involved in subunit interaction. The disulfide-bonded receptor binding loop in Type IVa pilin is composed of either two type I β-turns joined together (MS11 and K122–4) (14) or one type I β-turn joined to a type II β-turn (PAK) (35). The corresponding region in Type IVb pilin (Tcp) contains a much more elaborate structure of a pair of α-helices packed on top of a pair of antiparallel β-strands.

Here, we have described the structure of the Type IVb pilin from S. typhi, which has an extra pair of β-strands in the αβ loop and much shortened loops in the D region compared with Tcp pilin, the only Type IVb pilin with known structure. Sequence alignment shows that there is only 16% sequence identity between S. typhi PilS and Tcp, whereas there is close to 50% identity between PilS and the Type IVb pilin from R. typhi pilus, which is required for bacterial mating (Fig. 1) (10). We propose to classify the Type IVb pilin from S. typhi and R. typhi as a distinct subclass of Type IVb pilin having significantly shortened loops in the D region from those in Tcp and...
bundle-forming pilus. Differences between the αβ loop and D region of the two subclasses of Type IVb pilins affected not just the assembly of the pilus but also the availability of exposed residues in the vicinity of the D region for receptor binding.

Although the structures of both Type IVb pilins belong to the same αβ roll class as Type IVa pilins, the addition of extra α-helices at both ends of the β-sheet in Type IVb pilin generates a unique pattern of pilus assembly. Type IVa pilin forms either a right-handed (MS11 and PAK) or left-handed (K122) 1-start helix with five subunits/helical turn. The Type IVb pilus is relatively thick and fragile with a helical pitch of around 40 Å and a diameter of 80 Å (Tcp).

The proposed model shows that S. typhi PilS can also be assembled into a left-handed three-start helix with six subunits/helical turn. Despite the difference in the orientation of α4 relative to the helical axis, the helical pitch (30 Å) and diameter (100 Å) of the PilS pilus model are comparable with those, 37.5 and 100 Å, respectively, obtained for the crystallographic fibers of N-terminal-truncated Tcp. The helical pitch and diameter of the PilS model, however, differ from the intact Tcp filaments, which have a 45-Å pitch and a diameter of ~80 Å (19). Addition of extra pulling forces from the N-terminal helices is expected to increase the helical pitch and reduce the diameter of the intact S. typhi pilus. This speculation also agrees with the measured diameter of intact S. typhi pilus by electron microscopy, which is around 6–8 nm (data not shown).

CFTR has long been recognized as the cellular receptor for S. typhi type pilus. Human cells expressing wild-type CFTR ingested significantly more S. typhi than cells expressing ΔF508 CFTR (5). This entry can be inhibited either with a peptide derived from the first extracellular domain of CFTR (5) or with soluble recombinant protein of PilS (3). The CFTR peptide, but not a scrambled one, can effectively neutralize the cell entry inhibition afforded by the PilS protein and vice versa (4). Because the proposed receptor of PilS on CFTR carry mostly charged residues, we have generated mutants for most of the exposed and charged residues on PilS according to the model to pinpoint its receptor binding site. Based on data from inhibition of bacterial entry by full-length PilS protein, the binding site for CFTR on PilS pilus might be at the interface between adjacent subunits with charged residues not only from the D region but also from the αβ loop. Depending on the conformation of the bound CFTR peptide, the binding site could be between adjacent subunits on the same helical strand or even between subunits on different helical strands (Fig. 5B). In Tcp, functional charged residues that extend outward to the surface of the Tcp filament for interaction with other pili, bacteriophage, or host cells are found exclusively on or adjacent to helix α4 in the D region (19).

This finding also explains why the monomeric t-PilS is unable to bind CFTR, because the complete binding site could be comprised of charged residues from different subunits. CFTR binding is strictly dependent on the assembly of PilS pilus into pilus and might be for improved specificity and cooperativity of binding. This is the first report on structural study of PilS from S. typhi. Identification of the structure of t-PilS and its pattern of pilus assembly, as well as candidate residues that are essential for receptor binding, not only provides the basis for other structural studies but also opens the possibility of rational drug or vaccine design against this adhesin that is commonly used by S. typhi for host invasion.

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REFERENCES