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LETTER TO THE EDITOR

CHTyper, a Web Tool for Subtyping of Extraintestinal Pathogenic *Escherichia coli* Based on the *fumC* and *fimH* Alleles

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Escherichia coli can cause a variety of extraintestinal infections, such as urinary tract infection, meningitis, peritonitis, and septicemia.

In 2012, Weissman et al. developed *fumC fimH* (CH) typing, a two-locus, sequenced-based typing scheme, for a fast determination of sequence types (STs) and sub-ST clonal groups of extraintestinal pathogenic *E. coli* strains according to the multilocus sequence typing (MLST) scheme (1). CH typing is based on *fumC*, one of the household genes used in the seven-locus-based MLST scheme (2), and an internal fragment of the type 1 fimbrial-adhesin-encoding gene *fimH*. In May 2017, we published a Web tool for subtyping *E. coli* based on the *fimH* sequence (3). Here, we present a new Web tool for CH typing (https://cge.cbs.dtu.dk/services/chtyper/) based on both *fumC* and *fimH* which allows users to obtain a CH type from Sanger sequencing-generated sequences and fastq files, as well as assembled whole-genome sequencing (WGS) data.

In the paper by Weissman et al., the results of MLST and CH typing were compared using 191 commensal and pathogenic *E. coli* isolates and 853 clinical *E. coli* isolates (2).

TABLE 1 Numbers of types found and *D* values for individual and combined loci of 35,704 *E. coli* isolates from EnteroBase

Typing method	No. of types found	*D* (95% confidence interval)
Single loci or MLST		
adk	311	0.8762 (0.8740–0.8783)
fumC	428	0.8882 (0.8863–0.8900)
gyrB	318	0.9205 (0.9193–0.9217)
icd	356	0.9107 (0.9095–0.9119)
mdh	275	0.9096 (0.9085–0.9106)
purA	266	0.8646 (0.8627–0.8665)
recA	240	0.8449 (0.8425–0.8474)
ST	2,362	0.9606 (0.9596–0.9616)
fimH + *fimH0*	300	0.9495 (0.9488–0.9502)
Loci or ST paired with *fimH*		
adk + *fimH*	985	0.9704 (0.9698–0.9709)
fumC + *fimH*	1,187	0.9717 (0.9711–0.9723)
gyrB + *fimH*	1,110	0.9720 (0.9714–0.9726)
icd + *fimH*	1,082	0.9714 (0.9707–0.9720)
mdh + *fimH*	984	0.9711 (0.9705–0.9717)
purA + *fimH*	925	0.9705 (0.9699–0.9711)
recA + *fimH*	891	0.9702 (0.9696–0.9708)
ST + *fimH*	3,167	0.9768 (0.9762–0.9774)

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TABLE 2 STs and CH types for 243 third-generation-cephalosporin-resistant *E. coli* isolates obtained from patients with bloodstream infection

ST	CH type(s) (no. of isolates)
12	13-41 (1), 13-106 (4)
23	4-35 (1)
38	26-0 (2), 26-5 (14), 26-54 (1), 26-65 (1)
44	11-54 (2)
58	4-27 (1), 4-30 (2), 4-32 (1)
69	35-27 (10)
73	24-10 (1), 24-30 (1), 24-103 (1)
88	4-39 (1), 4-43 (1)
90	4-142 (1)
93	11-41 (1)
95	38-15 (1), 38-27 (1), 38-41 (2), 38-483 (1)
117	45-97 (1)
127	14-2 (2)
131	40-22 (1), 40-27 (14), 40-30 (95), 40-35 (1), 40-41 (11)
135	39-2 (1)
141	52-5 (1)
167	11-0 (3), 11-215 (1)
205	23-54 (1)
209	11-54 (1)
345	4-31 (1)
349	36-54 (1)
354	88-58 (1)
393	106-54 (1)
405	37-27 (10), 37-29 (3)
410	4-24 (4)
421	38-0 (1)
443	19-24 (1)
450	11-34 (1), 11-54 (2)
453	6-31 (1)
550	14-54 (1)
603	4-517 (1)
617	11-0 (1), 11-29 (1)
624	4-27 (1)
636	108-0 (1)
648	4-0 (4), 4-27 (4)
977	188-25 (1)
1163	45-63 (1)
1177	26-65 (1)
1193	14-64 (2)
1248	29-31 (1)
1706	29-38 (1)
2509	95-60 (1)
2522	29-38 (1)
3014	41-34 (1)
3057	54-445 (1)
3285	6-35 (1)
3666	26-5 (3)
3995	4-27 (1)
5824	11-0 (1)

Here, CH types and MLSTs were compared using assembled WGS data obtained from the EnteroBase database on 3 July 2017 (http://enterobase.warwick.ac.uk). Only *E. coli* genomes meeting the criteria of known MLSTs, according to the MLST scheme (1), and known *fimH* allele or *fimH*-null isolates (isolates without *fimH*) were included in the analysis, resulting in 35,704 *E. coli* genomes from the EnteroBase database. Discriminatory power was analyzed using the Simpsons index of diversity (*D*) (4).

The individual MLST loci exhibited between 240 and 428 alleles, based on the available *E. coli* genomes obtained from EnteroBase, which resulted in 2,362 MLSTs, whereas the combination of *fumC* and *fimH* resulted in 1,187 unique CH types (Table 1). The combination of *fumC* and *fimH* had a slightly higher discriminatory power ($D = 0.9717$ [confidence interval, 0.9711 to 0.9723]) than the discriminatory power of MLST

($D = 0.9606$) (confidence interval, 0.9596 to 0.9616). Similar observations were seen in the paper by Weissman et al. for the 191 commensal and pathogenic *E. coli* isolates (2).

To determine the resolution of CH typing for clinical field application, CHTyper was used to analyze genomic data from 243 *E. coli* isolates that were resistant to third-generation cephalosporins and obtained from patients with bloodstream infection (5). Here, 48 different STs were obtained. ST131 was the most common ($n = 122$), and 18 STs were represented by more than one isolate. Using CHTyper, 70 CH types were obtained for the 243 *E. coli* isolates (Table 2). CH typing further subdivided 12 of the 18 STs represented by more than one isolate; e.g., ST131 was subdivided into 5 CH types (Table 2).

Weissman et al. showed that specific CH types corresponded to specific STs and ST complexes, with 95% accuracy, allowing good prediction of the MLST-based profile. Furthermore, CH typing can detect the ST131 clonal subgroup H30, responsible for the current pandemic of fluoroquinolone- and multidrug-resistant *E. coli* infections around the globe (6). Therefore, CH typing can be used to study sub-ST clonal diversity or as a rapid screening test prior to selection for WGS.

In summary, CHTyper is a highly suitable tool that can act as a rapid alternative to conventional MLST surveillance and for outbreak detection.

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