Complete Genome Sequence of the Neonatal-Meningitis-Associated
Escherichia coli Strain CE10

Shuting Lu,¹ Xiaobing Zhang,¹ Yafang Zhu,¹ Kwang Sik Kim,² Jian Yang,¹* and Qi Jin¹*

State Key Laboratory for Molecular Virology and Genetic Engineering, Institute of Pathogen Biology, Chinese Academy Medical
Sciences & Peking Union Medical College, Beijing 100017, China,¹ and Department of Pediatrics, Division of
Pediatric Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287²

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Neonatal bacterial meningitis continues to be an important cause of mortality and morbidity worldwide. Escherichia coli possessing the K1 capsular polysaccharide is the most common Gram-negative pathogen causing neonatal meningitis. Here we present the complete genome sequence of neonatal meningitis-associated E. coli strain CE10, a unique K1 strain with a functional type III secretion system. Functional analysis of the genome should enhance our knowledge of the pathogenesis of neonatal E. coli K1 meningitis.

Despite advances in antibiotics, neonatal bacterial meningitis remains a significant threat to the health of newborns worldwide (3, 4). Neonatal meningitis-associated Escherichia coli (NMEC) is one of the leading causative agents of neonatal meningitis (4). E. coli strains possessing the K1 capsular polysaccharide are predominant among NMEC isolates, and the K1 strains isolated from cerebrospinal fluid (CSF) can be categorized into two distinct groups in terms of genomic background, which are likely to utilize different pathogenic mechanisms to cause meningitis (7). E. coli O7:K1 strain CE10 (previously named strain EC10), which was isolated from the CSF of a neonate with meningitis, is a representative of group 2 isolates from CSF (7). Strain CE10 was found to carry a complete gene set encoding the type III secretion system (T3SS), which was recently demonstrated to be involved in the invasion and intracellular survival of the bacterium in human brain microvascular endothelial cells (8). Most of the K1 isolates from CSF belong to phylogenetic group B2 and, to a less extent, to group D (7). Strain CE10 belongs to group D, and the unique characteristics of the strain make it an interesting focus for pathogenesis and evolution studies of E. coli K1 strains.

The whole genome was sequenced using a Roche/454 FLX genome sequencer system, and the raw data set contains 503,963 reads, totaling 204 Mbp (~38-fold coverage). The initial assembly, performed using Newbler software, yielded 144 large (~500-bp) contigs. Gaps were then closed on the Consed workbench, using genomic PCR and primer walking with conventional Sanger sequencing (2). Glimmer3 and tRNAscan-SE were used to predict protein-coding sequences (CDS) and tRNA genes, respectively (1, 5). Functional annotation of CDS was performed by BLAST searches of the GenBank nonredundant protein database followed by manual curation.

The whole genome of CE10 is composed of a 5,313,531-bp chromosome and four plasmids. The chromosome (50.6% GC content) is predicted to possess 5,009 CDS, 76 pseudogenes, 91 tRNAs, and 7 rRNA operons. It shares a colinear backbone of ~4.1 Mb with the chromosome of strain S88, another E. coli K1 strain (O45:K1; B2 group). However, the results of genome-based phylogenetic analysis indicated that CE10 is closely related to uropathogenic E. coli (UPEC) strain IA139 (O7:K1) rather than to other K1 strains. Indeed, a total of about 5.0 Mb (93.4%) of the CE10 chromosome is highly conserved with respect to the IA139 chromosome, with identity > 99%, but the collinearity between them is severely interrupted by genomic translocations and inversions, which are probably recent events due to niche-specific adaptations.

Genome sequencing of CE10 confirmed the presence of epr-epa-eiv operons encoding the T3SS apparatus. Furthermore, we also identified genes scattered throughout the CE10 genome that encode putative T3SS effectors, including homologues of EspL, EspR, EspX, and EspY, which are experimentally confirmed T3SS effectors in enterohemorrhagic E. coli (6). Functional studies of the T3SS effectors may shed light on the pathogenic mechanism of the T3SS in strain CE10 that is employed for traversal of the blood-brain barrier and penetration into the central nervous system.

Nucleotide sequence accession numbers. Complete sequences of E. coli CE10 have been deposited in GenBank under accession no. CP003034 to CP003038.

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REFERENCES