



Draft Genome of Carbapenemases and Extended-Spectrum β -Lactamase (ESBL) Producing Extraintestinal *Escherichia coli* (ExPEC) ST410 from a Chicken Farm in Malaysia

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ABSTRACT

Food animals have been implicated as potential sources of common multidrug-resistant bacteria. We report the draft genome of an extended-spectrum β -lactamase (ESBL)-producing and carbapenem-resistant *Escherichia coli* ST410 isolated from a chicken. Identification of the *E. coli* isolate was done using both phenotypic and genotypic methods. Genomic DNA from the isolate was extracted and sequenced using the Illumina HiSeq 2000 platform. The draft genome was annotated, and AMR and virulence genes were identified. The assembled genome comprised 181 contigs, with a total length of 5,212,201 bp and an average GC content of 50.39%. The N50 length and L50 count were 109,990 bp and 15, respectively. Several genes conferring resistance to carbapenems, β -lactam antibiotics, and other major antibiotic classes were detected. The isolate was assigned to the globally prevalent *E. coli* ST410, which carries the β -lactamase-encoding genes CTX-55 and TEM-176. Various virulence-encoding genes, including *fim*, *ompF*, *SbcD*, and *recD*, were identified. The genome sequence helps in understanding AMR and virulence in *E. coli* from food animals, particularly chickens.

Keywords: *Escherichia coli*; ESBL; CRE; whole-genome sequencing; antimicrobial resistance

INTRODUCTION

Carbapenems are broad-spectrum beta (β)-lactam antimicrobials that are considered last-resort agents for the treatment of severe infections caused by multidrug-resistant Gram-negative bacteria. The expanded use of carbapenems in clinical settings has contributed to the global emergence of carbapenem-resistant Enterobacteriaceae, which pose a major public health challenge due to limited therapeutic options and high associated morbidity and mortality (Paul *et al.*, 2022). Although carbapenem resistance has traditionally been linked to healthcare environments, increasing evidence indicates that resistant bacteria and resistance determinants are now disseminated across diverse ecological niches beyond hospitals.

Food-producing animals have gained attention as potential reservoirs and transmission pathways for clinically relevant antimicrobial-resistant bacteria. Carbapenem-resistant and extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* have been detected in livestock, companion animals, wildlife, and food products, raising concerns regarding zoonotic

transmission and environmental dissemination (Köck *et al.*, 2018). Given that carbapenems are not approved for use in animal agriculture, carbapenem resistance in food animals is thought to result from indirect selection pressure, co-selection with other antimicrobials, and horizontal gene transfer mediated by mobile genetic elements (EFSA & ECDC, 2023).

Among antimicrobial-resistant organisms, ESBL-producing *E. coli* has been designated by the World Health Organization as a critical priority pathogen due to its widespread distribution, genetic plasticity, and ability to cause both intestinal and extraintestinal infections. ESBL-producing *E. coli* are commonly reported in food-animal reservoirs and retail meat products, and several studies have demonstrated genetic relatedness between animal-derived isolates and human clinical strains, underscoring the public health importance of the food chain as a potential route of transmission (Kanokudom *et al.*, 2021).

In Malaysia, antimicrobial-resistant *E. coli* in poultry has been documented, including reports of carbapenem-resistant *E. coli* in live chickens and ESBL-producing strains in poultry products (Aklilu

et al., 2021; Aklilu *et al.*, 2018). However, information remains limited regarding isolates that simultaneously exhibit carbapenem resistance and ESBL production, particularly those characterized using whole-genome sequencing. Moreover, data on the genetic backgrounds, resistance gene profiles, and virulence potential of such isolates from food animals in Malaysia are scarce.

Within a One Health framework that recognizes the interconnectedness of human, animal, and environmental health, genomic surveillance of antimicrobial-resistant bacteria in food-animal production systems is essential for early detection of high-risk lineages and mitigation of their spread. Whole-genome sequencing enables comprehensive characterization of resistance and virulence determinants and supports high-resolution tracking of globally disseminated clones. This study aimed to characterize the genome, antimicrobial resistance determinants, and virulence-associated genes of a novel carbapenem-resistant ESBL-producing *E. coli* ST410 isolate from poultry in Malaysia.

MATERIALS AND METHODS

Ethical Approval

This study was approved by the Institutional Animal Care and Use Committee of University Malaysia Kelantan (Approval code: UMK/FPV/ACUE/PG/2/2019, Approval Date: February 2019). The animal subjects (chickens from commercial poultry farms) were used only for cloacal swab collection, and no invasive or harmful procedures were performed during handling.

Bacterial Isolation and Antimicrobial Susceptibility Testing

Escherichia coli strain PR24.ERK-UMK was isolated from a cloacal swab collected in January 2019 from a four-week-old broiler chicken sampled at a commercial poultry farm in Kelantan, Malaysia. Isolation and species identification were performed using routine microbiological methods, followed by PCR amplification of the species-specific *phoA* gene and selected antimicrobial resistance genes, including *bla*CTX, *bla*TEM, *bla*OXA-48, *bla*IMP, and *bla*NDM. Antimicrobial susceptibility was determined by disk diffusion, and minimum inhibitory concentrations (MICs) of selected antibiotics were assessed using E-test strips (bioMérieux, France). Phenotypic confirmation of carbapenem resistance was performed using the carbapenem inactivation method in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2021). Interpretation of susceptibility results followed CLSI breakpoints.

Genomic DNA Extraction, Sequencing, and Assembly

Genomic DNA was extracted from overnight cultures grown on Brain Heart Infusion agar using a commercial DNA, RNA, and protein purification kit (Macherey-Nagel, Germany) according to

the manufacturer's instructions. DNA quality and purity were assessed using a NanoDrop 2000 spectrophotometer (Thermo Scientific), and concentrations were measured using a Qubit 2.0 Fluorometer (Life Technologies). Whole-genome sequencing libraries were prepared from 50 ng of genomic DNA and sequenced using the Illumina HiSeq 2000 platform (Illumina Inc., San Diego, CA, USA). Raw sequencing reads were quality-checked with FastQC, then de novo genome assembly was performed using the CGE Assembler pipeline after adapter trimming.

Genome Annotation and Bioinformatics Analysis

The assembled draft genome was annotated using the NCBI prokaryotic genome annotation pipeline and the RASTtk annotation system (Olson *et al.*, 2023). Comprehensive genome analysis, including identification of antimicrobial resistance genes, virulence factors, protein families, and metabolic pathways, was performed using the PATRIC bioinformatics platform (Wattam *et al.*, 2017). Functional annotation included assignment of Gene Ontology terms (The Gene Ontology Consortium, 2023), KEGG pathway mapping (Kanehisa *et al.*, 2023), and classification into protein families using PATtyFams and subsystem-based approaches (Davis *et al.*, 2016; Overbeek *et al.*, 2005). Virulence-associated genes were identified using curated virulence factor databases integrated into PATRIC (Liu *et al.*, 2022; Sayers *et al.*, 2022). Antimicrobial resistance determinants and potential drug targets were annotated using established resistance and pharmacological databases (Alcock *et al.*, 2023; Wang *et al.*, 2020; Wishart *et al.*, 2018). Multilocus sequence typing (MLST) was performed *in silico* using the MLST 2.0 tool from the Center for Genomic Epidemiology to determine the isolate's sequence type.

RESULTS

The genome annotation service in PATRIC uses a k-mer-based AMR gene detection method that leverages PATRIC's curated collection of representative AMR gene sequence variants and assigns functional annotations, broad mechanisms of antibiotic resistance, drug classes, and, in some cases, the specific antibiotic to which each AMR confers resistance. A summary of the AMR and virulence genes annotated in this genome, along with the corresponding AMR mechanisms, is shown in Tables 1 and 2. Multilocus sequence typing (MLST) of the isolate, performed using MLST 2.0 (<https://cge.cbs.dtu.dk/services/MLST/>), showed that PR24.ERK-UMK belongs to a globally disseminated antimicrobial-resistant *E. coli*, ST410.

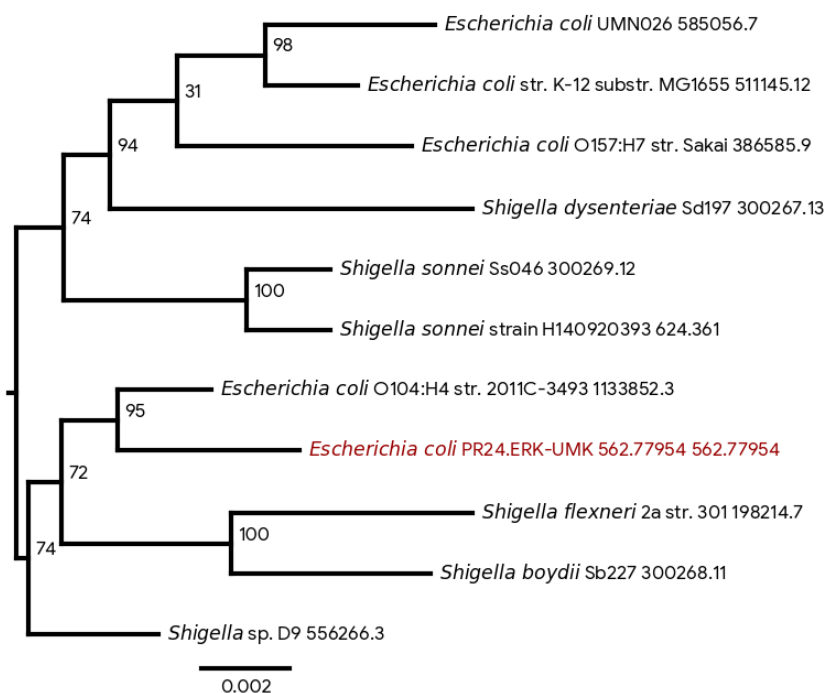
Phylogenetic analyses showed that *E. coli* PR24.ERK-UMK was closely related to *E. coli* O104:H4 str.2011-3493. The isolate also shares about 72% similarity with *Shigella* sp. (*Shigella flexneri* 2a str. 301 and *Shigella boydii* sb227) based on whole-genome single-nucleotide polymorphism (SNP) analysis (Figure 1). Several antibiotic resistance-conferring genes were identified, providing resistance against extended-

Table 1. Antimicrobial resistance genes and the respective mechanisms of action of carbapenem-resistant *Escherichia coli* and extended-spectrum beta-lactamases producing *E. coli* isolates from chicken

AMR mechanism	Genes
Antibiotic activation enzyme	KatG
Antibiotic inactivation enzyme	APH (3'')-1, APH (3')-1, APH(6)-Ic/APH(6)-Id, BlaEC family, CTX-M family, Mph(A) family, TEM family
Antibiotic resistance gene cluster, cassette, or operon	MarA, MarB, MarR
Antibiotic target in susceptible species	Alr, Ddl, dxr, EF-G, EF-Tu, folA, Dfr, folP, gyrA, gyrB, inhA, fabI, Iso-tRNA, kasA, MurA, rho, rpoB, rpoC, SLOp, S12p
Antibiotic target modifying enzyme	Erm (42)
Antibiotic target protection protein	BcrC
Efflux pump conferring antibiotic resistance	AcrAB-TolC, AcrAD-TolC, AcrEF-TolC, AcrZ, EmrAB-TolC, EmrD, EmrE, EmrKY-TolC, FloR family, MacA, MacB, MdfA/Cmr, MdtABC-TolC, MdtEF-TolC, MdtL, MdtM, QacE, SugE, Tet(A), TolC/OpmH
Gene conferring resistance via absence	gidB
Protein altering cell wall charge conferring antibiotic resistance	GdpD, PgsA
Regulator modulating expression of antibiotic resistance genes	AcrAB-TolC, EmrAB-TolC, GadE, H-NS, OxyR

Table 2. Virulence genes of *Escherichia coli* PR24.UMK-ERK isolated from chicken

Virulence factor	Identity	Query / Template length	Position in contig	Protein function	Accession number
<i>cib</i>	100	1881 / 1881	601..2481	Colicin ib	KP198616
<i>fyuA</i>	100	2022 / 2022	40177..42198	Siderophore receptor	ADTR01000532
<i>gad</i>	100	1401 / 1401	8694..10094	Glutamate decarboxylase	CP004009
<i>hra</i>	89.54	784 / 792	1840..2607	Heat-resistant agglutinin	CP043942
<i>irp2</i>	100	6108 / 6108	20881..26988	High molecular weight protein 2 non-ribosomal peptide synthetase	NZ_UEMO01000028
<i>iss</i>	98.64	294 / 294	36461..36754	Increased serum survival	CP004009
<i>lpfA</i>	100	573 / 573	80837..81409	Long polar fimbriae	AY646923
<i>terC</i>	100	714 / 714	83275..83988	Tellurium ion resistance protein	CP007491
<i>terC</i>	100	966 / 966	29194..130159	Tellurium ion resistance protein	MG591698

Figure 1. Phylogenetic analyses of *Escherichia coli* PR24.ERK-UMK shows close similarity to *E. coli* O104:H4 str. 20113493 and to *Shigella* species based on Single Nucleotide Polymorphism (SNP) analysis.

spectrum β -lactams, carbapenems, fluoroquinolones, macrolides, and tetracyclines (Table 1).

Among the several resistance encoding genes identified are *fim* (Fimbrin-like protein FimI), *ompF* (Outer membrane porin OmpF), *SbcD* (Exonuclease SbcD), *recD* (Exodeoxyribonuclease V alpha chain (EC 3.1.11.5)), *fur* (Ferric uptake regulation protein), *soxS* (DNA-binding transcriptional dual regulator SoxS), *cadB* (Lysine/cadaverine antiporter membrane protein CadB), *fimB* (Type 1 fimbriae regulatory protein FimB), *hrpA* (ATP-dependent helicase HrpA) and *speA* (Biosynthetic arginine decarboxylase (EC 4.1.1.19)) (Figure 2).

Comparative structural analyses of the Class A beta-lactamase (EC 3.5.2.6), CTX-M family, and extended-spectrum beta-lactamase show the unique features of the isolate, implying the possible novelty

of the beta-lactamase gene in this isolate (Figure 3). The whole-genome sequence was submitted to GenBank. Biosample metadata are available in the NCBI BioSample database (<http://www.ncbi.nlm.nih.gov/biosample/>) under accession number SAMN22160936.

DISCUSSION

Extended-spectrum β -lactamase-producing and carbapenem-resistant *E. coli* have become emerging problems in food animals and are a potential source of human infection and/or colonization. Although extended-spectrum β -lactam antibiotics and carbapenems are not used in poultry production in Malaysia, reports have documented the prevalence of these pathogens in chickens (Aklilu *et al.*, 2021). This

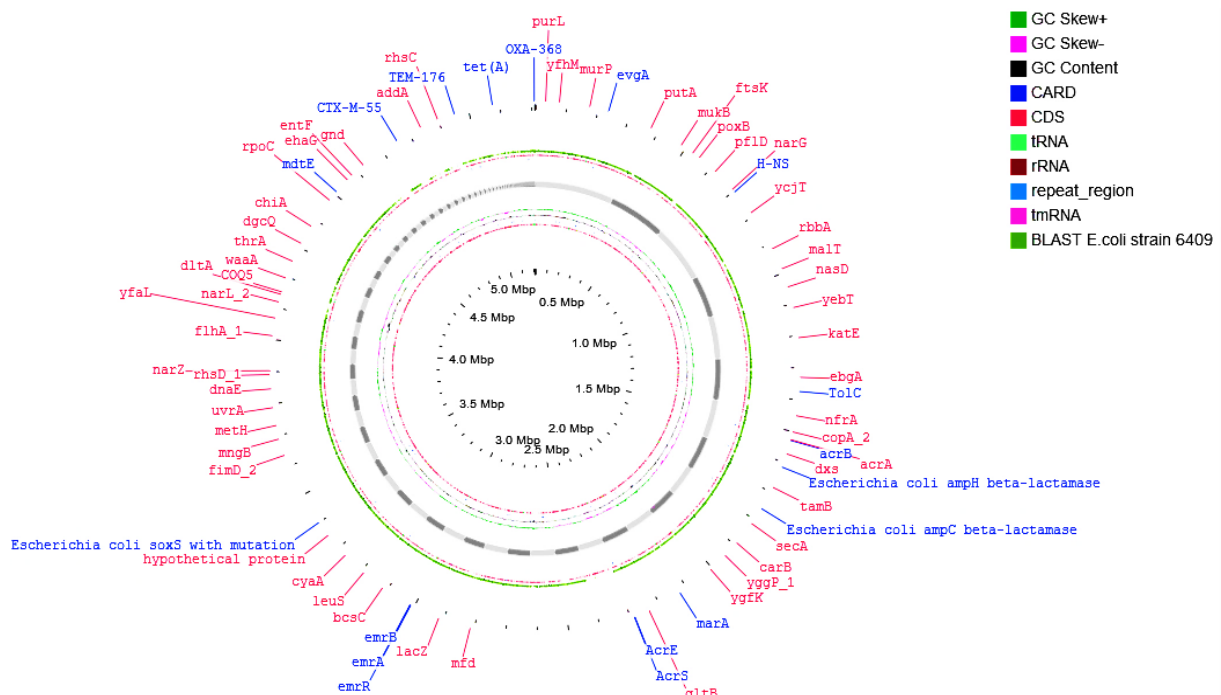


Figure 2. Genome structure of *Escherichia coli* PR24.ERK-UMK showing selected and major antimicrobial resistance and virulence genes

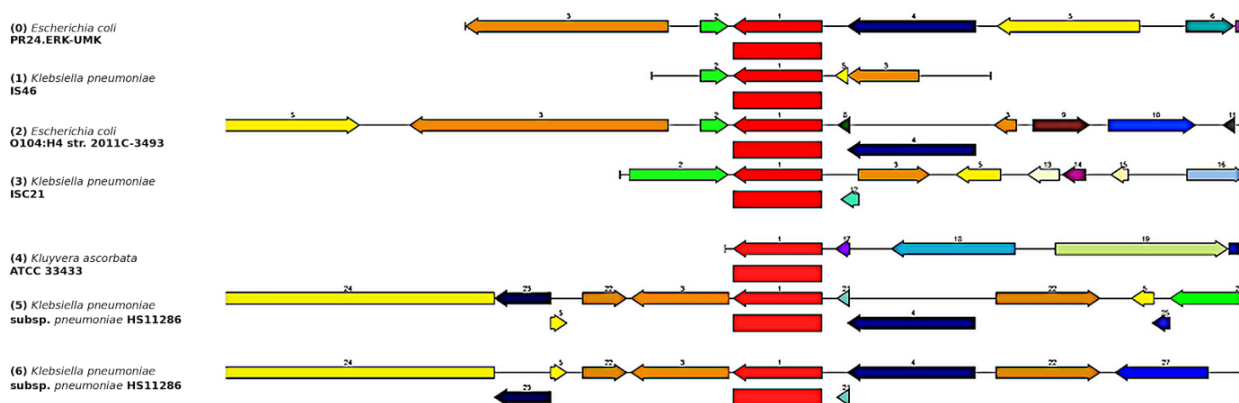


Figure 3. Comparison of Class A beta-lactamase (EC 3.5.2.6), CTX-M family, and extended-spectrum beta-lactamase genes of *Escherichia coli* PR24.ERK-UMK with other isolates based on PATRIC cross-genus families (PGfams). Key: 1) Class A beta-lactamase (EC 3.5.2.6), CTX-M family and extended-spectrum, 2) Tryptophan synthase (indole-salvaging) (EC 4.2.1.122), 3) Mobile element protein, 4) Mobile element protein, 5) FIG00639819: hypothetical protein, 6) Hypothetical protein.

might be attributed to the fact that genes encoding carbapenemases and extended-spectrum β -lactamases are mostly plasmid-mediated, and that co-resistance may play a role in the spread of such plasmid-mediated resistance mechanisms (EFSA & ECDC, 2023).

The identification of a carbapenem-resistant and ESBL-producing *Escherichia coli* ST410 isolate from poultry highlights the expanding ecological distribution of this globally disseminated high-risk clone. Although carbapenems are not used in poultry production, the presence of carbapenem-associated resistance determinants likely reflects indirect selection pressure and horizontal gene transfer mediated by plasmid-encoded co-resistance mechanisms (EFSA & ECDC, 2023; Paul *et al.*, 2022). Similar observations have been reported among livestock-associated Enterobacteriaceae, suggesting that food animals may act as reservoirs for clinically relevant antimicrobial resistance genes (Kanokudom *et al.*, 2021).

The assignment of this isolate to sequence type ST410 is notable, as this lineage has been increasingly associated with multidrug resistance and ESBL production in both human and animal sources worldwide (Paul *et al.*, 2022; Köck *et al.*, 2018). This resistance profile is consistent with previously reported ST410 isolates from human and animal sources, which frequently co-harbor these mechanisms of resistance. The detection of *bla*CTX-M-55 and *bla*TEM-176, together with regulatory and efflux-related genes (*acrAB*-*TolC*, *marA*, *soxS*), supports the classification of this isolate as a multidrug-resistant lineage with enhanced adaptive potential (Alcock *et al.*, 2023).

In addition to antimicrobial resistance, the genome harbored several virulence-associated genes consistent with extraintestinal pathogenic *E. coli*. Genes involved in adhesion, iron acquisition, serum survival, and stress adaptation (*fimB*, *fyuA*, *irp2*, *iss*, *gad*) may enhance colonization and persistence in host environments (Liu *et al.*, 2022; Sayers *et al.*, 2022). The co-occurrence of resistance and virulence determinants raises concerns about zoonotic potential and underscores the value of whole-genome sequencing for the surveillance of food-animal-associated AMR pathogens.

The detection of a multidrug-resistant ExPEC ST410 strain in poultry has important public health implications, as food animals may serve as reservoirs for high-risk *E. coli* lineages that can be transmitted to humans through the food chain or environmental exposure. Genomically similar resistant strains have been reported across animal, food, and clinical sectors, reinforcing the need for integrated One Health surveillance approaches (Paul *et al.*, 2022; Kanokudom *et al.*, 2021). Early genomic detection of such lineages in food production systems may facilitate targeted interventions to limit dissemination.

This study is limited by the analysis of a single isolate, preventing the assessment of prevalence or transmission dynamics within poultry populations. In addition, reliance on short-read sequencing limited our ability to fully resolve plasmid structures and the mobile genetic elements that mediate resistance transfer. Functional validation of resistance and virulence genes

was beyond the scope of this work. Future studies incorporating larger collections of isolates, long-read sequences, and comparative analyses across animal, human, and environmental sources are warranted.

CONCLUSION

This study reports the draft genome of a carbapenem-resistant, ESBL-producing *E. coli* ST410 isolate from poultry in Malaysia, providing genomic evidence for the presence of a globally disseminated high-risk clone in food animal production. Despite methodological limitations, the co-occurrence of multidrug resistance and ExPEC-associated virulence determinants highlights the public health relevance of this finding. These results support the use of whole-genome sequencing as a critical tool for early detection and surveillance of priority antimicrobial-resistant lineages within a One Health framework.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the author(s) used the built-in Microsoft Word Copilot to facilitate formatting and editing. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the publication.

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