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Genomic and Bioinformatics Perspectives on Multidrug Resistant *Escherichia coli*

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ABSTRACT

Antimicrobial resistance (AMR) is a critical global health crisis that undermines the efficacy of standard infectious disease treatments. Within this landscape, multidrug-resistant (MDR) *Escherichia coli* is especially formidable due to its high genetic plasticity and its capacity for both intestinal and extraintestinal pathogenesis. The proliferation of these MDR strains is fueled by horizontal gene transfer and mobile genetic elements, which allow resistance determinants to bridge human, animal and environmental reservoirs. Fortunately, recent breakthroughs in genomics and bioinformatics, specifically Whole Genome Sequencing (WGS) now allow for the comprehensive mapping of resistomes and virulence factors. By identifying globally disseminated 'high-risk' clones, these computational tools have become indispensable for tracing transmission pathways and predicting resistance phenotypes in real time. This review summarizes current genomic insights into MDR *E. coli*, with emphasis on resistance mechanisms, mobile genetic elements, phylogenetic diversity, and bioinformatics resources for surveillance and analysis. It also discusses the public health implications of rising resistance, including limited therapeutic options and increased risk of treatment failure. Integrating genomic surveillance with advanced analytical approaches will be essential for early detection, effective control strategies, and the development of novel interventions to combat the growing threat of antimicrobial resistance.

Keywords: Multidrug resistant *Escherichia coli*, Antimicrobial resistance, Whole genome sequencing, Resistome, Bioinformatics, Genomic surveillance

INTRODUCTION

Antimicrobial resistance has become a key worldwide health concern, as it has negatively affected many decades of advances in the treatment of infectious diseases. The extensive and frequently inappropriate use of antibiotics in human medicine, veterinary medicine, and agriculture has accelerated the selection of resistant microorganisms, causing infections that are increasingly hard to treat (Salam et al., 2023). AMR contributes significantly to the burden of prolonged illness, increased healthcare expenditure, and mortality across the world. Low and middle income countries are especially vulnerable because of limited diagnostic capacity, uncontrolled antibiotic access, and inadequate infection control measures (Aslam et al., 2024). As resistant pathogens persist in crossing borders through different conduits such as travel, trade, and environmental pathways, AMR has become a transnational threat that requires coordinated global action (Coque et al., 2023).

Among the various strains of antibiotic-resistant bacteria, multidrug-resistant *Escherichia coli* represents one of the most significant clinical concerns, as it holds special importance considering its dual role as a common gut commensal and a versatile opportunistic pathogen (Ding et al., 2025). MDR strains cause a wide range of infections, including urinary tract infections, sepsis, neonatal meningitis, and foodborne diarrheal disease (Priyanka et al., 2023). Moreover, *E. coli* represents one of the foremost reservoirs of resistance genes that might be transferred to other pathogenic bacteria. Its presence in humans, livestock, wildlife, water systems, and food chains underscores the interconnected nature of resistance dissemination within a One Health framework (Naidoo & Zishiri, 2025). Environmental contamination with antibiotic residues and antibiotic resistant bacteria further boosts the survival and dissemination of MDR strains outside healthcare settings. Traditional microbiological methods, such as culture based identification and phenotypic susceptibility testing, are still very important in routine diagnostics but present some

notable limitations (Yakobi & Nwodo, 2025). These approaches are time consuming, may not detect emerging or unusual resistance mechanisms, and provide little insight into the genetic relationships between strains. As a consequence, they are frequently inadequate for rapid outbreak investigations or for understanding the evolutionary dynamics of resistance (Hossain & Chowdhury, 2024).

Advances in genomic technologies have revolutionized the study of MDR pathogens by enabling whole genome analysis. High throughput sequencing allows the identification of resistance determinants, virulence factors, plasmids, and clonal lineages simultaneously, and bioinformatics approaches help analyze large scale datasets and conduct global surveillance (Matsumura et al., 2025). Genomics driven approaches not only improve diagnostic accuracy but also provide valuable insights into transmission pathways, evolutionary trends, and the emergence of high risk clones (Telekes & Horváth, 2022). This review focuses on summarizing available information on the genomic and bioinformatics aspects of MDR *E. coli*, especially the genomic mechanisms of resistance, mobile genetic elements, population structure, and analytical tools used for the detection and surveillance of MDR *E. coli*. By combining findings from clinical, environmental, and computational studies, the review highlights the importance of genomics guided approaches for understanding, monitoring, and ultimately controlling the spread of multidrug resistant *E. coli*.

Biology and Pathogenic Diversity of *Escherichia coli*

Escherichia coli is a gram negative, facultative anaerobic, rod shaped bacterium that belongs to the family Enterobacteriaceae. It has high metabolic versatility, can survive in both aerobic and anaerobic environments, and grows rapidly under favorable conditions (Moxley, 2022). Genetically, *E. coli* has a highly dynamic genome consisting of a conserved core genome and a flexible accessory genome composed of plasmids, transposons, integrons, and pathogenicity regions. It is well adapted to diverse environments as a consequence of this genomic plasticity, which allows it to develop antimicrobial resistance and virulence attributes (Moxley, 2022).

Most types of *E. coli* are benign commensals that colonize the gastrointestinal tract of warm blooded animals and humans soon after birth. In this role, they contribute to gut homeostasis, vitamin synthesis, and colonization resistance against pathogens (Hira Hameed, 2024). However, some strains have developed specific virulence factors that make them capable of causing disease. The distinction between commensal and pathogenic strains is less based on species identity and more on the presence or absence of particular virulence genes (Mendes et al., 2023). Transmission mainly occurs through the fecal oral route, contaminated food and water, direct contact with infected individuals or animals, and healthcare associated spread. The environment further aids dissemination across ecological niches through environmental reservoirs such as wastewater, soil, and surface waters (Dang et al., 2022).

The strains of *E. coli* that cause disease are generally classified as intestinal pathogenic *E. coli* (IPEC) and extraintestinal pathogenic *E. coli* (ExPEC), depending on the site and mechanisms of pathogenicity (Hu et al., 2022). IPEC strains primarily infect the gastrointestinal tract and include pathotypes characterized by toxin production, adherence to epithelial cells, and epithelial invasion. These strains are major causes of diarrheal diseases globally, especially in children in low resource settings (Alhadlaq et al., 2024). Clinical manifestations range from mild, self-limiting diarrhea to severe complications, such as hemorrhagic colitis and hemolytic uremic syndrome, depending on the virulence profile and host susceptibility (Ghazy et al., 2025).

In contrast, ExPEC strains are adapted to survive outside the intestinal tract and cause localized or systemic infections. They are commonly associated with urinary tract infections, bloodstream infections, neonatal meningitis, and intra-abdominal infections (Munhoz et al., 2023). ExPEC strains possess a variety of virulence determinants involved in colonization, immune evasion, and tissue damage, including adhesins, iron acquisition systems, capsules, and toxins. The synergy between virulence and multidrug resistant traits in some high risk lineages has intensified challenges for healthcare professionals, as these strains combine increased virulence potential with limited therapeutic options (Azam et al., 2023; Qiu et al., 2024). Therefore, understanding the biological diversity of *E. coli* through integrated genomic data, epidemiological trends, and targeted prevention strategies is of vital importance.

Table 1 provides a structured overview of the key *E. coli* pathotypes responsible for various clinical conditions, such as diarrhea and urinary tract infections (UTIs). It lists the virulence factors and primary infection sites associated with each pathotype which helps in understanding the diverse pathogenic profiles of *E. coli*, making it easier for clinicians and researchers to diagnose infections based on the pathotype present.

Table 1: Summary of Major E. coli Pathotypes and Clinical Manifestations

Pathotype	Virulence Factors	Primary Infection Site	Clinical Manifestations	References
EPEC	intimin, bundle forming pilus	Small intestine	Infantile diarrhea	(Malesa et al., 2025)
ETEC	Heat labile and heat stable toxins	Small intestine	Traveler's diarrhea, watery diarrhea	(Lee et al., 2023)
EHEC/STEC	Shiga toxins (Stx1, Stx2), intimin	Colon	Hemorrhagic colitis, hemolytic uremic syndrome	(Fernández Fellenz et al., 2025)
EAEC	Aggregative adherence fimbriae, toxins	Colon	Persistent diarrhea	(Moazeni et al., 2024)
EIEC	Invasion plasmid antigens	Colon	Dysentery like diarrhea	(Ghosh et al., 2025)
ExPEC	Adhesins, siderophores, capsules	Urinary tract, bloodstream, CNS	UTIs, sepsis, neonatal meningitis	(Munhoz et al., 2023)

Mechanisms of Antimicrobial Resistance

The origin and spread of antimicrobial resistance in *Escherichia coli* have been explained by various biological mechanisms through which the bacterium survives antibiotic exposure (Endale et al., 2023). Resistance can be categorized as intrinsic or acquired and may involve genetic mutations, horizontal gene transfer, or the expression of specific resistance determinants (Hossain & Chowdhury, 2024). Understanding these mechanisms is critical for the development of effective diagnostics, surveillance strategies, and appropriate treatment approaches.

Intrinsic and Acquired Resistance

Intrinsic resistance refers to the inherent capability of *Escherichia coli* to survive exposure to specific antibiotics without prior contact or selective pressure. This phenomenon is encoded within the bacterium's core genome and is mainly due to inherent structural or physiological characteristics (Balachandran et al., 2025). For example, the outer membrane of *E. coli* presents a selective barrier that inhibits the entry of large or hydrophobic antimicrobial agents. In addition, constitutively expressed efflux pumps, such as the AcrAB-TolC efflux pump, actively expel a wide range of antimicrobial compounds from the cytoplasm, further decreasing intracellular drug accumulation (Mahmud & Wakeman, 2024). Other intrinsic mechanisms include the lack or alteration of particular antibiotic targets. For instance, an appropriate binding site for certain macrolides does not exist in *E. coli*, rendering these drugs ineffective. Intrinsic resistance also explains why some antibiotics, such as polymyxins, need to be administered at high concentrations to achieve bactericidal activity, as the cell envelope and membrane charge of the bacterium provide partial protection (Nasrollahian et al., 2024). Although these features are not acquired due to environmental pressure, they define the baseline susceptibility profile of *E. coli* and influence clinical treatment and future resistance evolution.

Acquired resistance, on the other hand, is the ability of previously sensitive strains of *E. coli* to withstand antibiotic exposure due to genetic modifications. Mutation driven resistance is one of the best known mechanisms, whereby spontaneous point mutations, insertions, or deletions in chromosomal genes alter the antibiotic target, affect drug uptake, or modify metabolic pathways (Harris et al., 2023). For example, mutations in the quinolone resistance determining regions (QRDR) of DNA gyrase (gyrA) or topoisomerase IV (parC) decrease fluoroquinolone binding, resulting in high-level resistance (Rezaei et al., 2024). Similarly, changes in penicillin binding proteins (PBPs) can reduce their affinity for β-lactam antibiotics, thereby allowing cell wall synthesis to continue despite the presence of the drug (Dabhi et al., 2024). In addition to structural changes, mutations in regulatory genes can lead to overexpression of efflux pumps or downregulation of porins, contributing to multidrug resistant phenotypes. These genetic alterations typically occur under selective pressure from antibiotic exposure in clinical, agricultural, or environmental settings. Once established, such mutations may persist within populations and, in certain cases, combine with horizontally acquired resistance determinants, giving rise to complex resistance profiles that are increasingly difficult to control (De Gaetano et al., 2023).

Horizontal Gene Transfer

Horizontal gene transfer (HGT) is essential in the high rate of transmitting antimicrobial resistance among *Escherichia coli* populations. HGT in contrast to intrinsic or mutation driven resistance enables bacteria to obtain fully active resistance genes in other organisms, sometimes across species or even genera, and lead to sudden radically large scale changes in differential patterns of resistance (Vinayamohan et al., 2022). Plasmids are one of the most important vectors of this process. These extrachromosomal nutrients of DNA may contain multiple resistance genes which sometimes provide resistance to different classes of antibiotics at the same time. Conjugative plasmids, which have the ability to transfer themselves by directly cell to cell contact, are especially significant in the transmission of the extended spectrum beta-lactamases (ESBLs) and carbapenems, which have caused resistance to last line beta-lactams (Castañeda-Barba et al., 2024; Meng et al., 2022).

The acquisition and rearrangement of the resistance genes by transposons and integrons also contribute to acquisition and rearrangement. Integrons represent an example of gene capturing systems, whereby several gene cassettes can be integrated into the bacterial genome and coordinate the expression of resistance determinants (Bhat et al., 2023). Transposons or jumping genes allow for the transposition of such gene cassettes between plasmids and chromosome giving rise to complicated multidrug resistant strains. Besides plasmids and mobile genetic factors, bacteriophages also play a role in transfer of genes through the process of transduction whereby they package the resistance genes in the hosts of the bacterium and transfer them to the receiver cells (Karampatakis et al., 2025). Environmental reservoirs, like wastewater, soil and animal gut microbiota, offer a plethora of opportunities for HGT which boosted the development of high risk MDR E. coli lineages. This interaction of mechanisms also has a key role in making horizontal gene transfer a key factor in the promotion of worldwide distribution of multidrug resistance, creating severe challenges to the domestic and infection control approaches (De Gaetano et al., 2023).

Major Resistance Mechanisms

One of the most clinically important resistance determinants is β-lactamases, which are often combined by *Escherichia coli* to form complex multidrug-resistant phenotypes (Maveke et al., 2024). Extended spectrum β-lactamases (ESBLs) catalyze the hydrolysis of penicillins, cephalosporins, and monobactams, whereas carbapenemases inactivate carbapenems, one of the last-resort classes of antibiotics. The spread of ESBL and

carbapenemase producing *E. coli* strains has greatly restricted therapeutic options and is linked to increased morbidity and mortality in both community and hospital settings (Aurilio et al., 2022).

Another major mechanism of resistance is efflux pumps. These membrane bound proteins expel a wide range of antimicrobial agents and decrease intracellular drug concentrations to sub inhibitory levels (De Gaetano et al., 2023). The AcrAB-TolC efflux system has the capability to target multiple antibiotic classes simultaneously, making it a key contributor to broad spectrum resistance and treatment failure. Target modification is equally important; mutations or enzymatic modifications alter antibiotic binding sites and lessen drug efficacy (Alenazy, 2022). These include point mutations in DNA gyrase responsible for fluoroquinolone resistance and methylation of 23S rRNA, which confers resistance to macrolides (Maveke et al., 2024).

Figure 1 provides a necessary visual synthesis of the multifaceted resistance landscape in *Escherichia coli* which is critical for bridging the gap between abstract genetic determinants and their functional clinical impact. Finally, low membrane permeability also contributes to resistance. Loss or structural alteration of porin proteins in the outer membrane reduces antibiotic entry, especially for β-lactams and carbapenems (Ghai, 2023). These mechanisms often act synergistically. For example, a strain may produce a β-lactamase while simultaneously decreasing membrane permeability and increasing efflux pump expression, resulting in high level multidrug resistance (Hussein et al., 2024). Knowledge of these molecular mechanisms is critical for interpreting genomic data, predicting resistance patterns, and developing effective treatment and prevention strategies. With genomic and bioinformatics tools, comprehensive mapping of these mechanisms has become possible, providing insight into their distribution, evolution, and clinical consequences.

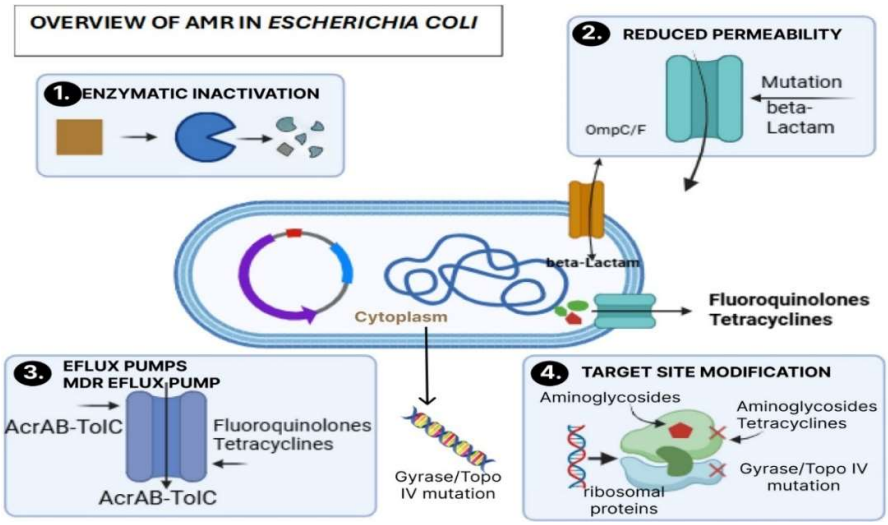

Fig 1: Principal molecular mechanisms of antimicrobial resistance in Escherichia coli (Coque et al., 2023; Matsumura et al., 2025)

Table 2 outlines the primary mechanisms by which *E. coli* develops resistance to antibiotics. By categorizing mechanisms such as β-lactamase production, efflux pump activity, target modification, and membrane permeability changes, this table provides a clear link between molecular mechanisms and their clinical impacts. It also highlights specific genes involved in each mechanism, giving insight into how resistance can be genetically mapped and targeted in therapeutic strategies. Understanding these mechanisms is essential for developing new antibiotics and resistance management strategies.

Table 2: Mechanisms of Antimicrobial Resistance in E. coli

Mechanism	Description	Example Genes/Proteins	Impact on Therapy	References
β-lactamases	Enzymatic hydrolysis of β-lactams	TEM, SHV, CTX-M, NDM	Resistance to penicillins, cephalosporins, carbapenems	(Belay et al., 2024)
Efflux pumps	Active expulsion of antibiotics	AcrAB-TolC, MdfA	Reduced intracellular drug levels; multidrug resistance	(Lorusso et al., 2022)
Target modification	Mutation or modification of antibiotic binding sites	gyrA, parC, rpoB, 23S rRNA methylation	Resistance to fluoroquinolones, rifampicin, macrolides	(Rezaei et al., 2024)
Reduced permeability	Porin loss or modification limiting drug entry	OmpF, OmpC	Reduced susceptibility to β-lactams, carbapenems	(Hussein et al., 2024)

Genomic Insights into MDR *Escherichia coli*

Genomic technologies have radically changed the study of multidrug-resistant *Escherichia coli*, providing deeper insight into its genetic composition and mechanisms of resistance, virulence potential, and evolutionary dynamics (Jhalora & Bist, 2025). Whole genome sequencing and bioinformatics analyses now allow comprehensive profiling

of the bacterial genome, enabling the simultaneous assessment of resistomes, virulomes, plasmids, and clonal relationships (Wareth et al., 2022). These insights play an important role in surveillance, outbreak investigations, and the design of targeted antimicrobial strategies.

Whole Genome Sequencing (WGS)

Whole genome sequencing has become the gold standard for detailed genetic analysis in MDR *Escherichia coli*, with the ability to study determinants of resistance, virulence factors and evolutionary patterns of MDR E. coli at single nucleotide resolution. WGS is feasible using short read sequencing technologies such as Illumina's, which offer high accuracy, low error rates, and yield deep coverage which can be used to identify single nucleotide polymorphisms (SNPs), small insertions or deletion, and gene presence or absence (Chekole et al., 2025; Matsumura et al., 2025). However, short reads frequently have difficulties resolving repetitive sequences, structural variations and complete assemblies of plasmids, which are important in understanding multidrug resistance. The concomitant nature of short read and long read sequencing technologies has allowed crafting hybrid assemblies using short reads with high accuracy and similarly long reads with continuity to create vastly complete and perfect assemblies of genomes that can be used in subsequent genomic research (Rose et al., 2023; Zhao et al., 2023).

After sequencing, bioinformatics pipelines are used to achieve many steps such as quality control, genome assembly, error correction and functional annotation (Abdi et al., 2024). These annotated genomes include comprehensive information on coding sequences, regulatory features, non-coding RNAs, plasmids and mobile genetic elements coding sequences, regulative elements, non-coding RNAs, plasmids and mobile genetic elements, like integrons, transposons as well as prophages (Lamping & Krebber, 2025). The resulting genomic maps enable the researchers to determine antimicrobial resistance genes, future resistance phenotypic prediction, and determine the interaction between virulence and resistance determinants. Also, WGS can be used to do comparative genomics, where the formation of the clonal relationships, evolutionary patterns and the occurrence of a horizontal transfer of genes leading to the rise of high risk lineages with MDR can be detected (Matsumura et al., 2025). WGS has therefore emerged as an invaluable resource at both fundamental research level and even for a clinical or epidemiological purpose, such as researching outbreaks, surveillance of susceptible clones, and ensuring the formulation of targeted response antimicrobial plans (Struelens et al., 2024).

Resistome Analysis

Resistome analysis provides a comprehensive overview of all antimicrobial resistance genes present in *Escherichia coli*, thereby improving the understanding of multidrug resistance at the genomic level (Peng et al., 2022). From whole genome sequences, researchers can identify resistance determinants associated with different classes of antibiotics, including β-lactams, aminoglycosides, tetracyclines, fluoroquinolones, and others. Systematic detection, classification, and annotation of resistance genes are supported by bioinformatics tools and databases such as Comprehensive Antibiotic Resistance Database (CARD), ResFinder, and ARG-ANNOT (Manzoor et al., 2025). This analysis not only identifies the presence of individual resistance genes but also maps their genomic context, such as their location on plasmids, integrons, transposons, or chromosomal islands. This information is essential for understanding the potential for horizontal gene transfer, resistance evolution, and the identification of high risk clones capable of disseminating resistance within populations (Vinayamohan et al., 2022). Resistome profiling also reveals co-resistance, where multiple resistance genes are co-located on the same mobile genetic element, potentially conferring multidrug resistance even in strains previously considered susceptible (Wareth et al., 2022).

Mobile genetic elements, including plasmids, transposons, and integrons, play a crucial role in shaping the resistome of *E. coli*. Plasmids can harbor multiple resistance genes simultaneously and are capable of transferring these genes between bacterial strains and even across species through conjugation (Rezaei et al., 2024). Resistance determinants are frequently organized into gene cassettes captured and expressed by integrons, contributing to rapid adaptation under antibiotic pressure. Transposons facilitate the movement of resistance genes between plasmids and the chromosome, adding to the dynamic architecture of the resistome (Karampatakis et al., 2025). Furthermore, co-resistance and cross resistance patterns may complicate treatment planning, as a single resistance determinant can confer reduced susceptibility to multiple antibiotic classes due to genetic linkage or shared efflux mechanisms (Rose et al., 2023). Population scale mapping of the resistome enables researchers and clinicians to monitor emerging resistance trends, anticipate potential treatment failures, and design targeted antimicrobial stewardship interventions to reduce the prevalence of multidrug resistant *E. coli* in clinical, environmental, and agricultural settings (Ding et al., 2025).

Virulome and Pathogenicity Factors

Virulome of *Escherichia coli* is the totality of the genes that led the bacterium to have the power to colonize hosts, avoid immune responses and disease. High pathogenicity is due to adhesins, invasins, toxins, iron acquisition systems, capsules, and secretion systems, which are encoded by these genes (Manzoor et al., 2025). Whole genome sequencing and bioinformatics databases such as Virulence Factor Database (VFDB) are referred to as the virulence gene profiling which enables the categorization of strains into certain pathotypes, such as intestinal pathogenic E. coli (IPEC) and extraintestinal pathogenic E. coli (ExPEC) (AlJindan et al., 2023). Virulence determinants identification allows critically important understanding of the molecular pathogenesis of an illness, including adherence to epithelial

cells, toxin induced injury, and immunomodulatory effects. These virulence factors usually work together in pathogenic strains to enhance their capacity to cause serious infections including diarrheal diseases to sepsis and magnitude (Land, 2023).

The relationship between virulence and antimicrobial resistance is growing in the MDR E. coli. There are also cases of high risk lineages that possess virulence determinants and several resistance genes that result in strains of increased pathogenicity and very few treatment options (Qin et al., 2022). This intersection complicates the clinical care and adds to the increased morbidity and mortality rates. Knowing the association between the virulome and resistome creates the opportunity to forecast the behavior of the strain, the probability of outbreak, and the possibility of failure in treatment (Interrante et al., 2022). Combining virulence profiling with resistome and genomic data base informs efficiency in public health, led to specific surveillance, vaccine building and risk evaluation. It is through a virulome mapped together with well-established resistance determinants that researchers are able to determine emergent high risk clones, monitor their distribution via human, animal and environmental reservoirs and establish biointerventions to counter their effect (Hasan et al., 2025; Sherry et al., 2025).

Phylogenomics and Population Structure

Phylogenomic analyses provide high resolution information about evolutionary relationships, clonal dynamics, and the global dissemination of multidrug resistant *Escherichia coli*. By comparing whole genome sequences, researchers can construct phylogenetic trees that illustrate lineage diversification, population structure, and the emergence of high risk clones (Siddique et al., 2025). Sequence typing approaches used to identify sequence types (STs) and clonal complexes associated with specific resistance or virulence phenotypes include multilocus sequence typing (MLST) and core genome MLST (cgMLST) (Kalizang'oma et al., 2023). Certain lineages, such as *Escherichia coli* ST131, *Escherichia coli* ST69, and *Escherichia coli* ST405, have become globally disseminated due to their combined virulence and multidrug resistance and represent significant clinical challenges. Phylogenomic approaches also assist in tracing the sources and transmission routes of MDR strains among clinical, animal, and environmental reservoirs, providing valuable insights for outbreak investigations and infection control (Ding et al., 2025; Siddique et al., 2025).

Population structure analysis reveals the genetic diversity within and between *E. coli* populations and explains how horizontal gene transfer, recombination, and selective pressures drive the emergence of resistant and virulent clones (Han et al., 2024). Clonal expansions are often associated with the acquisition of key resistance determinants, plasmids, and pathogenicity islands, leading to the dominance of certain lineages within specific ecological niches or geographical regions (Domingues et al., 2025). By integrating phylogenomic data with resistome and virulome profiles, it becomes possible to identify high risk MDR clones, monitor their dissemination, and predict their potential evolutionary trajectories. These insights are fundamental for global surveillance initiatives, the formulation of antimicrobial stewardship policies, and the development of strategies aimed at preventing the widespread transmission of MDR *E. coli* across human, animal, and environmental interfaces (Dabhi et al., 2024).

Table 3 identifies the most concerning multidrug resistant *E. coli* clonal lineages (e.g., ST131, ST69, and ST405). It details their global distribution, associated resistance profiles, and virulence traits. Table 3 is crucial for epidemiological surveillance as it allows researchers and public health authorities to identify high risk clones that might be spreading globally. It also helps in monitoring the evolution and transmission dynamics of these strains across regions, which is essential for targeted control measures.

Table 3: High-Risk MDR E. coli Clonal Lineages

Clonal Lineage (ST)	Global Distribution	Associated Resistance	Virulence Traits	References
ST131	Worldwide	ESBLs (CTX-M), fluoroquinolone resistance	Adhesins, siderophores	(Pitout et al., 2023)
ST69	Europe, North America	Multidrug resistant plasmids	Toxins, adhesins	(Benlabidi et al., 2023)
ST405	Asia, Europe	Carbapenemases, ESBLs	Capsule, siderophores	(Kocsis et al., 2022)
ST38	Global, sporadic	ESBLs, aminoglycoside resistance	Adhesins, iron uptake	(Kocsis et al., 2022)

Bioinformatics Tools and Databases

Bioinformatics tools and databases have played an important role in the study of multidrug resistant *Escherichia coli* by enabling researchers to process and interpret large volumes of genomic data efficiently. Through these platforms, it is possible to rapidly identify resistance genes, virulence determinants, plasmids, and mobile genetic elements, as well as to perform comparative genomics and predictive modeling (Subramanian & Natarajan, 2023). The integration of bioinformatics with whole genome sequencing and metagenomic approaches has revolutionized the surveillance, outbreak investigation, and epidemiological analysis of MDR pathogens (Ding et al., 2025).

AMR Gene Identification Tools

Accurate identification of antimicrobial resistance genes is crucial in understanding the resistome of E. coli and also to predict therapeutic outcome. Tools like ResFinder, CARD (Comprehensive Antibiotic Resistance Database) and ARG-ANNOT contain curated databases of known resistance determinants, and as a result, genome sequences can be

screened in a widely available and systematic manner for the presence of the above mentioned resistance mechanisms, such as v-lactamases, aminoglycoside modifying enzymes, efflux pumps and other resistance genes (Ali et al., 2023; Jhalora & Bist, 2025). These even assign genes the antibiotic class and mechanism of action that help to interpret patterns of multidrug resistance (Jhalora & Bist, 2025). Integration with the analysis of mobile genetic elements enables determination of whether resistance genes are located on plasmids, integrons, or chromosomes, providing insight into their potential for horizontal transfer and dissemination among bacterial strains (Siddique et al., 2025).

The problem of AMR gene identification tools is limited to single isolates. Population genomics media allow researchers to monitor the distribution and most commonness of resistance genes worldwide since it is an enormous examination of the constitutionery data (Shaik et al., 2022). Comparative studies based on these tools can show emergence of high risk MDR lineages, track evolutionary changes and provide information supporting interventions in public health. With gathering information from genome wide resistance profiling and metadata, are be combined to help predict resistance profiles and prioritize strategies for antimicrobial stewardship, such as clinical outcomes, environmental sources, or geographic distribution (Malesa et al., 2025).

Genome Analysis Platforms

Genome analysis platforms play a crucial role in processing raw sequencing data, performing data assembly, annotation, and comparative genomics to understand the genomic context of resistance and virulence (Vashisht et al., 2023). Tools such as SPAdes, Velvet, and Canu are used for de novo genome assembly, producing high quality draft or complete genomes. Annotation pipelines, including Prokka and RAST, assign functional roles to coding sequences and regulatory elements, while specialized tools are available to detect plasmids, integrons, and prophages (Çabuk & Ünlü, 2022). Comparative genomics platforms, such as Roary and Panaroo, can be used to analyze pangenomes, revealing the core and accessory gene content across different *E. coli* strains and lineage specific genomic adaptations linked to multidrug resistance (Çabuk & Ünlü, 2022).

Processing Whole Genome Sequencing (WGS) data involves a complex, multi-stage pipeline; including assembly, annotation, and resistome mapping which is follow through by Figure 2. Figure 2 clarifies how specific bioinformatics tools like SPAdes and Prokka are integrated to facilitate real time surveillance and the identification of high-risk clones. Phylogenomic analyses, single nucleotide polymorphism studies, and clonal relationship assessments are also performed using these platforms, which are valuable for monitoring MDR lineages in clinical, agricultural, and environmental settings (Ramaloko & Osei Sekyere, 2022). By integrating genome assembly, annotation, and comparative analysis, researchers can elucidate the composition and evolution of resistance and virulence, identify emerging high risk clones, and investigate the interplay of horizontal gene transfer and selective pressure. These integrated approaches are essential for effective surveillance, outbreak investigation, and informed decision making in public health.

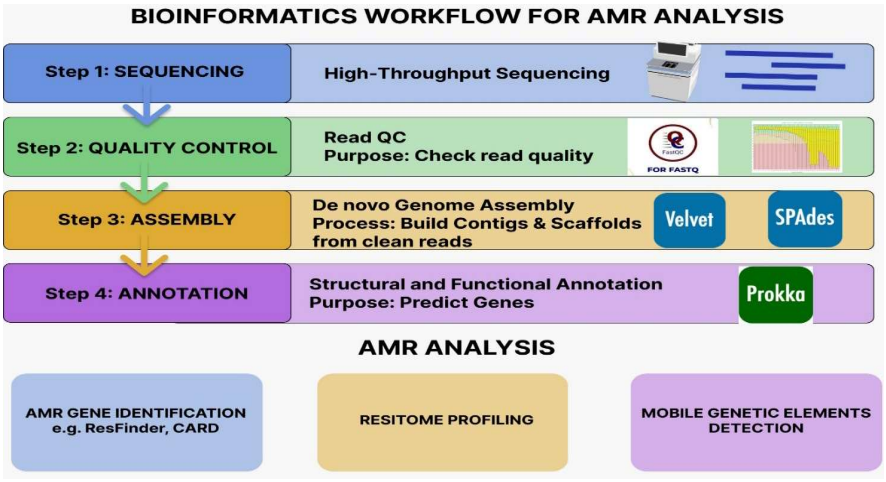

Fig. 2: Integrated bioinformatics pipeline for genomic AMR surveillance (Sader de Azevedo et al., 2026; Subramanian & Natarajan, 2023)

Table 4 systematically outlines key bioinformatics tools and databases that are indispensable for the identification and characterization of antimicrobial resistance genes in *Escherichia coli*. The tools presented, such as ResFinder, CARD, ARG-ANNOT, Prokka, and Roary/Panaroo are central to the high throughput analysis of *E. coli* genomes, enabling the rapid detection of resistance determinants across diverse strains. These tools facilitate the annotation of genomic sequences, the classification of AMR genes, and the prediction of phenotypic resistance profiles, providing essential data for understanding the genetic basis of multidrug resistance.

Metagenomic Approaches

Metagenomics can be used to culture independently detect and characterize *Escherichia coli* and other antimicrobial resistant bacteria in complex ecosystems such as the human gut, wastewater, soil, and livestock

(Barcenilla Canduela, 2024). Shotgun metagenomics enables sequencing of all microbial DNA within a sample, providing a comprehensive understanding of the resistome, including non-cultivable or rare strains. This approach can identify resistance genes, mobile genetic elements, and patterns of community level co-resistance, offering a global perspective on resistance dynamics within microbiomes (Nogueira & Botelho, 2021).

Table 4: Bioinformatics Tools and Databases for MDR E. coli

Tool/Database	Purpose	Key Features	References
ResFinder	AMR gene identification	Antibiotic class classification; plasmid detection	(Saleem et al., 2026)
CARD	Comprehensive AMR database	Resistance gene curation; mechanism annotation	(Edalatmand & McArthur, 2023)
ARG-ANNOT	AMR gene detection	Integron and gene cassette analysis	(Gupta & Rolain, 2014)
Prokka	Genome annotation	Coding sequences, rRNAs, tRNAs	(Sader de Azevedo et al., 2026)
Roary / Panaroo	Pangenome analysis	Core and accessory gene comparison	(Dimonaco, 2026)

Metagenomic studies of environmental and gut microbial communities have revealed extensive reservoirs of resistance genes that may contribute to the emergence and dissemination of MDR *E. coli (Munhoz et al., 2023)*. These studies identify hotspots of horizontal gene transfer and demonstrate links between human, animal, and environmental resistomes, supporting One Health approaches to antimicrobial resistance management (Hossain & Chowdhury, 2024). Integration of metagenomic data with bioinformatics pipelines allows researchers to track trends in resistance determinants, evaluate the impact of antibiotic use, and develop targeted strategies to control infections (Bhat et al., 2023).

Epidemiology and Global Surveillance

The genomic epidemiology of multidrug resistant *Escherichia coli* has provided unprecedented insights into the origin, evolution, and global dissemination of high risk clones. Whole genome sequencing and phylogenomic analyses have enabled the identification of globally dominant lineages, such as *Escherichia coli* ST131, *Escherichia coli* ST69, and *Escherichia coli* ST405, which combine enhanced virulence with multidrug resistance (Arcari & Carattoli, 2023; Shaik et al., 2022). These approaches allow high resolution profiling of resistance determinants, plasmid types, and mobile genetic elements, providing a detailed understanding of the evolutionary dynamics driving the proliferation of MDR *E. coli (Ding et al., 2025)*. By integrating genomic data with metadata, including temporal and geographical information, researchers can identify transmission patterns, detect the emergence of high risk clones, and track the spread of resistance across healthcare, community, and environmental contexts (Belay et al., 2024). Such genomic surveillance forms the foundation for informing public health policies and guiding antimicrobial stewardship strategies at regional and global levels.

Transmission of MDR *E. coli* occurs across interconnected human, animal, and environmental networks, highlighting the importance of a One Health approach. Humans acquire resistant strains through contaminated food and water, direct contact with animals, or exposure to healthcare settings, while livestock, wildlife, and companion animals serve as reservoirs and amplifiers of resistance (Han et al., 2024). Environmental contamination from wastewater, agricultural runoff, and hospital effluents facilitates horizontal gene transfer between bacterial populations. Hospital acquired organisms are often associated with high risk clones carrying multiple resistance determinants, whereas foodborne or environmental exposures may contribute to the emergence of community acquired strains (Hutinel et al., 2021). Genomic tools have greatly enhanced outbreak investigations by enabling rapid identification of sources, transmission pathways, and relatedness of isolates in both hospital and community settings. This large scale genomic approach allows public health authorities to implement targeted infection control measures, monitor their effectiveness, and anticipate the emergence of MDR lineages, thereby mitigating the global impact on human and animal health (Manzoor et al., 2025).

Clinical and Public Health Implications

The emergence of multidrug resistant *Escherichia coli* has severe implications for clinical care and public health worldwide. Infections caused by these strains often compromise the effectiveness of first line antibiotics, necessitating the use of last resort drugs such as carbapenems or combination therapies, which may be costly, toxic, or less accessible in low income countries (Kumar et al., 2024; Shoaib et al., 2023). Treatment failure due to resistance is associated with prolonged hospitalization, increased morbidity and mortality, and higher healthcare costs. MDR *E. coli* further complicates the management of both community acquired and hospital acquired infections, including urinary tract infections, bloodstream infections, and neonatal sepsis (Ding et al., 2025; Kumar et al., 2024). Therefore, understanding the resistome and virulome of circulating strains is critical for selecting effective therapeutics and predicting emerging resistance trends (Shoaib et al., 2023).

Genomic tools have revolutionized diagnostics, infection control, and individualized antimicrobial therapy. Whole genome sequencing and bioinformatics analyses enable rapid detection of resistance genes, virulence determinants, and clonal relationships, supporting precise diagnosis of infectious diseases. Integrating genomic data with patient history and antimicrobial susceptibility profiles can inform personalized therapy, optimizing drug selection and minimizing the development of further resistance (Abdi et al., 2024). At the public health level,

genomics aids in outbreak investigations, surveillance, and risk assessment by identifying high risk clones and monitoring their spread across hospitals, communities, and environmental reservoirs (Hill et al., 2023). These insights guide infection control measures, including isolation policies, antibiotic stewardship programs, and targeted hygiene interventions. Collectively, genomic surveillance combined with informed clinical management maximizes control of MDR *E. coli*, reduces the burden of antimicrobial resistance, and supports evidence based policy decisions for global health (Siddique et al., 2025).

Emerging Technologies and Future Directions

Advances in genomic technologies have revolutionized the surveillance, diagnosis, and management of multidrug resistant *Escherichia coli*. Real time sequencing platforms, such as portable Oxford Nanopore devices, facilitate genomic profiling in clinical and field settings, allowing rapid identification of resistance genes, virulence factors, and outbreak associated strains (Zhao et al., 2023). These approaches enable timely infection control measures and dynamic surveillance of high risk clones across hospitals, communities, and environmental reservoirs (Barcenilla Canduela, 2024). When coupled with automated bioinformatics pipelines, real time sequencing provides actionable data that can guide both individual patient management and public health interventions, significantly reducing the time delays associated with traditional culture based methods (Hossain & Chowdhury, 2024).

Beyond surveillance, innovative therapeutic and diagnostic strategies are emerging. CRISPR based systems offer precise genome editing capabilities, enabling rapid detection of resistance genes or targeted elimination of specific MDR strains (Allemailem, 2024). Phage therapy, which employs bacteriophages to lyse resistant *E. coli*, provides an alternative to conventional antibiotics, circumventing multidrug resistance (Eid et al., 2022). Additionally, integrative multi-omics approaches; combining genomics, transcriptomics, proteomics, and metabolomics; provide a holistic understanding of bacterial physiology, resistance mechanisms, and host pathogen interactions (Lv & Fan, 2026). These methods facilitate the identification of novel drug targets, resistance pathways, and virulence factors, supporting precision medicine strategies. Collectively, the integration of real time sequencing, CRISPR technologies, phage therapy, and multi-omics analyses holds great promise for improving our ability to predict, prevent, and treat infections caused by MDR *E. coli*, representing a paradigm shift in clinical management and public health response (Wang et al., 2024).

Challenges and Limitations

Despite the transformative potential of applying genomic and bioinformatics approaches to the study of multidrug resistant *Escherichia coli*, several challenges remain. A major limitation is the complexity of data interpretation. Whole genome sequencing generates vast amounts of information, including resistance genes, mobile genetic elements, virulence determinants, and phylogenetic relationships. Distinguishing clinically relevant resistance from incidental genomic findings, predicting phenotypes from genotypes, and integrating genomic data with epidemiological and clinical metadata require advanced bioinformatics expertise and robust analytical pipelines. Misinterpretation of data can lead to incorrect conclusions about resistance patterns, clonal relationships, or transmission dynamics.

Additional challenges include the high cost of sequencing, infrastructure requirements, and the lack of standardized analytical protocols. Implementing genomic surveillance in low resource settings is particularly difficult due to limited access to sequencing platforms, computational resources, and trained personnel. Furthermore, variability in genome assembly, annotation methods, and resistance gene detection between laboratories complicates comparisons across studies and hinders global surveillance efforts. Ethical concerns and restrictions on data sharing, especially regarding patient genomic information, further limit the utility of these technologies.

To overcome these obstacles, it is essential to adopt standardized genetic workflows, implement cost effective sequencing technologies, provide proper training, and establish ethical frameworks for data sharing. Balancing privacy with the need for open access databases will enable global collaboration, facilitate comparative studies, and ultimately advance efforts to control and prevent MDR *E. coli* infections.

Conclusions

Multidrug resistant *Escherichia coli* represents a major global health threat due to the combined presence of virulence factors, antimicrobial resistance determinants, and its capacity for rapid dissemination across human, animal, and environmental reservoirs. The emergence of high risk clones and the widespread distribution of mobile genetic elements have further accelerated the global spread of resistance. This review highlights the critical role of genomic and bioinformatics approaches in advancing the understanding of MDR *E. coli*, including comprehensive characterization of resistomes, virulomes, plasmids, integrons, transposons, and population structure. Whole genome sequencing, combined with advanced bioinformatics pipelines, provides high resolution insights for outbreak investigations, surveillance, evolutionary analysis, and epidemiological mapping. These approaches enable precise identification of high risk clones and elucidate the molecular mechanisms driving multidrug resistance at local and global levels.

Genomics guided strategies have significant implications for clinical management, antimicrobial stewardship, and public health interventions. Integration of resistome and virulome data supports prediction of resistance

phenotypes, optimization of antimicrobial therapy, and implementation of targeted infection control measures. Rapid sequencing platforms and user friendly bioinformatics tools facilitate timely detection of resistance genes and transmission pathways, improving real time surveillance capabilities. In addition, emerging technologies such as CRISPR based diagnostics, bacteriophage therapy, antimicrobial peptides, and multi-omics approaches offer promising alternatives for the detection, prevention, and management of MDR strains.

Future research should prioritize the standardization of genomic data interpretation, development of globally harmonized analytical pipelines, and expansion of international surveillance networks within a One Health framework. Integrative strategies that combine genomic, phenotypic, clinical, and environmental data will be essential for understanding transmission dynamics and resistance evolution. Collectively, these efforts will enhance the capacity to prevent, monitor, and control MDR *E. coli*, ultimately supporting more effective treatment strategies and safeguarding global public health.

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REFERENCES

Abdi, G., Jain, M., Barwant, M., Tendulkar, R., Tendulkar, M., Tariq, M., & Amir, A. (2024). Unveiling the Dynamic Role of Bioinformatics in Automation for Efficient and Accurate Data Processing and Interpretation. In V. Singh & A. Kumar (Eds.), *Advances in Bioinformatics* (pp. 279-319). Springer Nature Singapore. https://doi.org/10.1007/978-981-99-8401-5_15

Alenazy, R. (2022). Drug Efflux Pump Inhibitors: A Promising Approach to Counter Multidrug Resistance in Gram-Negative Pathogens by Targeting AcrB Protein from AcrAB-TolC Multidrug Efflux Pump from Escherichia coli. *Biology*, *11*(9), 1328. https://www.mdpi.com/2079-7737/11/9/1328

Alhadlaq, M. A., Aljurayyad, O. I., Almansour, A., Al-Akeel, S. I., Alzahrani, K. O., Alsalman, S. A., Yahya, R., Al-Hindi, R. R., Hakami, M. A., Alshahrani, S. D., Alhumeed, N. A., Al Moneea, A. M., Al-Seghayer, M. S., AlHarbi, A. L., Al-Reshoodi, F. M., & Alajel, S. (2024). Overview of pathogenic Escherichia coli, with a focus on Shiga toxin-producing serotypes, global outbreaks (1982–2024) and food safety criteria. *Gut Pathogens*, *16*(1), 57. https://doi.org/10.1186/s13099-024-00641-9

Ali, T., Ahmed, S., & Aslam, M. (2023). Artificial Intelligence for Antimicrobial Resistance Prediction: Challenges and Opportunities towards Practical Implementation. *Antibiotics*, *12*(3), 523. https://www.mdpi.com/2079-6382/12/3/523

AlJindan, R., AlEraky, D. M., Farhat, M., Almandil, N. B., AbdulAzeez, S., & Borgio, J. F. (2023). Genomic Insights into Virulence Factors and Multi-Drug Resistance in Clostridium perfringens IRMC2505A. *Toxins*, *15*(6), 359. https://www.mdpi.com/2072-6651/15/6/359

Allemailem, K. S. (2024). Recent Advances in Understanding the Molecular Mechanisms of Multidrug Resistance and Novel Approaches of CRISPR/Cas9-Based Genome-Editing to Combat This Health Emergency. *International Journal of Nanomedicine*, *19*(null), 1125-1143. https://doi.org/10.2147/IJN.S453566

Arcari, G., & Carattoli, A. (2023). Global spread and evolutionary convergence of multidrug-resistant and hypervirulent Klebsiella pneumoniae high-risk clones. *Pathogens and Global Health*, *117*(4), 328-341. https://doi.org/10.1080/20477724.2022.2121362

Aslam, B., Asghar, R., Muzammil, S., Shafique, M., Siddique, A. B., Khurshid, M., Ijaz, M., Rasool, M. H., Chaudhry, T. H., Aamir, A., & Baloch, Z. (2024). AMR and Sustainable Development Goals: at a crossroads. *Globalization and Health*, *20*(1), 73. https://doi.org/10.1186/s12992-024-01046-8

Aurilio, C., Sansone, P., Barbarisi, M., Pota, V., Giaccari, L. G., Coppolino, F., Barbarisi, A., Passavanti, M. B., & Pace, M. C. (2022). Mechanisms of Action of Carbapenem Resistance. *Antibiotics*, *11*(3), 421. https://www.mdpi.com/2079-6382/11/3/421

Azam, M. W., Zarrilli, R., & Khan, A. U. (2023). Updates on the Virulence Factors Produced by Multidrug-Resistant Enterobacterales and Strategies to Control Their Infections. *Microorganisms*, *11*(8), 1901. https://www.mdpi.com/2076-2607/11/8/1901

Balachandran, M., Chatterjee, R., Chaudhary, I., Jena, C., & Matange, N. (2025). Impeding pathways of intrinsic resistance in Escherichia coli confers antibiotic sensitization and resistance proofing. *PLoS Biology*, *23*(10), e3003443. https://doi.org/10.1371/journal.pbio.3003443

Barcenilla Canduela, C. (2024). *Microbiome-based analytical approaches and biopreservation agents for improving meat quality and safety* [info:eu-repo/semantics/doctoralThesis, http://hdl.handle.net/10612/21863

Belay, W. Y., Getachew, M., Tegegne, B. A., Teffera, Z. H., Dagne, A., Zeleke, T. K., Abebe, R. B., Gedif, A. A., Fenta, A., Yirdaw, G., Tilahun, A., & Aschale, Y. (2024). Mechanism of antibacterial resistance, strategies and next-generation antimicrobials to contain antimicrobial resistance: a review [Review]. *Frontiers in Pharmacology*, *Volume 15 - 2024*. https://doi.org/10.3389/fphar.2024.1444781

Benlabidi, S., Raddaoui, A., Lengliz, S., Cheriet, S., Hynds, P., Achour, W., Ghrairi, T., & Abbassi, M. S. (2023). Occurrence of High-Risk Clonal Lineages ST58, ST69, ST224, and ST410 among Extended-Spectrum β-Lactamase-Producing Escherichia coli Isolated from Healthy Free-Range Chickens (Gallus gallus domesticus) in a Rural Region in Tunisia. *Genes*, *14*(4), 875. https://www.mdpi.com/2073-4425/14/4/875

Bhat, B. A., Mir, R. A., Qadri, H., Dhiman, R., Almilaibary, A., Alkhanani, M., & Mir, M. A. (2023). Integrons in the development of antimicrobial resistance: critical review and perspectives [Mini Review]. *Frontiers in Microbiology*, *Volume 14 - 2023*. https://doi.org/10.3389/fmicb.2023.1231938

Çabuk, U., & Ünlü, E. S. (2022). A combined de novo assembly approach increases the quality of prokaryotic draft genomes. *Folia Microbiologica*, *67*(5), 801-810. https://doi.org/10.1007/s12223-022-00980-7

Castañeda-Barba, S., Top, E. M., & Stalder, T. (2024). Plasmids, a molecular cornerstone of antimicrobial resistance in the One Health era. *Nature Reviews Microbiology*, *22*(1), 18-32. https://doi.org/10.1038/s41579-023-00926-x

Chekole, W. S., Potgieter, L., Adamu, H., Sternberg-Lewerin, S., Tessema, T. S., & Magnusson, U. (2025). Genomic insights into antimicrobial resistance and virulence of E. coli in central Ethiopia: a one health approach [Original Research]. *Frontiers in Microbiology*, *Volume 16 - 2025*. https://doi.org/10.3389/fmicb.2025.1597580

Coque, T. M., Cantón, R., Pérez-Cobas, A. E., Fernández-de-Bobadilla, M. D., & Baquero, F. (2023). Antimicrobial Resistance in the Global Health Network: Known Unknowns and Challenges for Efficient Responses in the 21st Century. *Microorganisms*, *11*(4), 1050. https://www.mdpi.com/2076-2607/11/4/1050

Dabhi, M., Patel, R., Shah, V., Soni, R., Saraf, M., Rawal, R., & Goswami, D. (2024). Penicillin-binding proteins: the master builders and breakers of bacterial cell walls and its interaction with β-lactam antibiotics. *Journal of Proteins and Proteomics*, *15*(2), 215-232. https://doi.org/10.1007/s42485-024-00135-x

Dang, C., Wang, J., He, Y., Yang, S., Chen, Y., Liu, T., Fu, J., Chen, Q., & Ni, J. (2022). Rare biosphere regulates the planktonic and sedimentary bacteria by disparate ecological processes in a large source water reservoir. *Water Research*, *216*, 118296. https://doi.org/https://doi.org/10.1016/j.watres.2022.118296

De Gaetano, G. V., Lentini, G., Famà, A., Coppolino, F., & Beninati, C. (2023). Antimicrobial Resistance: Two-Component Regulatory Systems and Multidrug Efflux Pumps. *Antibiotics*, *12*(6), 965. https://www.mdpi.com/2079-6382/12/6/965

Dimonaco, N. J. (2026). PyamilySeq: exposing the fragility of conventional gene (re) clustering and prokaryotic pangenomic inference methods. *NAR Genomics and Bioinformatics*, *8*(1), lqaf198.

Ding, W., Cheng, Y., Liu, X., Zhu, Z., Wu, L., Gao, J., Lei, W., Li, Y., Zhou, X., Wu, J., Gao, Y., Ling, Z., & Jiang, R. (2025). Harnessing the human gut microbiota: an emerging frontier in combatting multidrug-resistant bacteria [Review]. *Frontiers in Immunology*, *Volume 16 - 2025*. https://doi.org/10.3389/fimmu.2025.1563450

Domingues, C. P. F., Rebelo, J. S., Dionisio, F., & Nogueira, T. (2025). Plasmid Genomic Dynamics and One Health: Drivers of Antibiotic Resistance and Pathogenicity. *Pathogens*, *14*(10), 1054. https://www.mdpi.com/2076-0817/14/10/1054

Edalatmand, A., & McArthur, A. G. (2023). CARD* Shark: automated prioritization of literature curation for the Comprehensive Antibiotic Resistance Database. *Database*, *2023*, baad023.

Eid, S., Tolba, H. M. N., Hamed, R. I., & Al-Atfeehy, N. M. (2022). Bacteriophage therapy as an alternative biocontrol against emerging multidrug resistant E. coli in broilers. *Saudi Journal of Biological Sciences*, *29*(5), 3380-3389. https://doi.org/https://doi.org/10.1016/j.sjbs.2022.02.015

Endale, H., Mathewos, M., & Abdeta, D. (2023). Potential Causes of Spread of Antimicrobial Resistance and Preventive Measures in One Health Perspective-A Review. *Infection and Drug Resistance*, *16*(null), 7515-7545. https://doi.org/10.2147/IDR.S428837

Fernández Fellenz, D., Ruiz, J. M., Etcheverría, A. I., Colello, R., Velez, M. V., Sanz, M. E., Sparo, M. D., Lissarrague, S., Pereyra, J., Zanelli, G., & Padola, N. L. (2025). Detection of EPEC and STEC strains isolated from children with diarrhea in Argentina. *Revista Argentina de Microbiología*, *57*(1), 59-62. https://doi.org/https://doi.org/10.1016/ j.ram.2024.07.003

Ghai, I. (2023). A Barrier to Entry: Examining the Bacterial Outer Membrane and Antibiotic Resistance. *Applied Sciences*, *13*(7), 4238. https://www.mdpi.com/2076-3417/13/7/4238

Ghazy, R. M., Alshaikhi, S. A., Assiri, H. A. H., Almozaini, A. A., Alhazmi, A. F., Elhasaneen, H. E. M., & Abdo, S. M. (2025). Tropical diseases and the gastrointestinal tract: an overlooked connection [Review]. *Frontiers in Tropical Diseases*, *Volume 6 - 2025*. https://doi.org/10.3389/fitd.2025.1612952

Ghosh, D., Halder, P., Samanta, P., Chowdhury, G., Shaw, S., Bose, P., Roy, D., Roy, N., Kitahara, K., Ramamurthy, T., Koley, H., Miyoshi, S.-i., Dutta, S., & Mukhopadhyay, A. K. (2025). Lactose fermenting enteroinvasive Escherichia coli from diarrhoeal cases confers enhanced virulence. *Scientific Reports*, *15*(1), 24040. https://doi.org/10.1038/s41598-025-07232-x

Gupta, S. K., & Rolain, J.-M. (2014). Reply to "Comparison of the web tools ARG-ANNOT and ResFinder for detection of resistance genes in bacteria". *Antimicrobial Agents and Chemotherapy*, *58*(8), 4987-4987.

Han, D., Ma, S., He, C., Yang, Y., Li, P., & Lu, L. (2024). Unveiling the genetic architecture and transmission dynamics of a novel multidrug-resistant plasmid harboring blaNDM-5 in E. Coli ST167: implications for antibiotic resistance management. *BMC Microbiology*, *24*(1), 178. https://doi.org/10.1186/s12866-024-03333-1

Harris, M., Fasolino, T., Ivankovic, D., Davis, N. J., & Brownlee, N. (2023). Genetic Factors That Contribute to Antibiotic Resistance through Intrinsic and Acquired Bacterial Genes in Urinary Tract Infections. *Microorganisms*, *11*(6), 1407. https://www.mdpi.com/2076-2607/11/6/1407

Hasan, G. M., Mohammad, T., Shamsi, A., Sohal, S. S., & Hassan, M. I. (2025). Applications of Genome Sequencing in Infectious Diseases: From Pathogen Identification to Precision Medicine. *Pharmaceuticals*, *18*(11), 1687. https://www.mdpi.com/1424-8247/18/11/1687

Hill, V., Githinji, G., Vogels, C. B. F., Bento, A. I., Chaguza, C., Carrington, C. V. F., & Grubaugh, N. D. (2023). Toward a global virus genomic surveillance network. *Cell Host & Microbe*, *31*(6), 861-873. https://doi.org/10.1016/j.chom.2023.03.003

Hira Hameed, M. T. S., Ruba Zafar, Qasim Raza, Qurat-ul-Ain, Shahida Younas, Simran Arshad. (2024). E. coli and the Normal Microbiota; Their Interaction and Role in Health and Disease. *Frontiers in Microbiology and Biotechnology*, *2*(01), 1-16. https://doi.org/10.54219/fmb.02.2024.161

Hossain, A. K. M. Z., & Chowdhury, A. M. M. A. (2024). Understanding the Evolution and Transmission Dynamics of Antibiotic Resistance Genes: A Comprehensive Review. *Journal of Basic Microbiology*, *64*(10), e2400259. https://doi.org/https://doi.org/10.1002/jobm.202400259

Hu, J., Afayibo, D. J. A., Zhang, B., Zhu, H., Yao, L., Guo, W., Wang, X., Wang, Z., Wang, D., Peng, H., Tian, M., Qi, J., & Wang, S. (2022). Characteristics, pathogenic mechanism, zoonotic potential, drug resistance, and prevention of avian pathogenic Escherichia coli (APEC) [Review]. *Frontiers in Microbiology*, *Volume 13 - 2022*. https://doi.org/10.3389/fmicb.2022.1049391

Hussein, R. A., Al-Kubaisy, S. H., & Al-Ouqaili, M. T. S. (2024). The influence of efflux pump, outer membrane permeability and β-lactamase production on the resistance profile of multi, extensively and pandrug resistant Klebsiella pneumoniae. *Journal of Infection and Public Health*, *17*(11), 102544. https://doi.org/https://doi.org/10.1016/j.jiph.2024.102544

Hutinel, M., Fick, J., Larsson, D. G. J., & Flach, C.-F. (2021). Investigating the effects of municipal and hospital wastewaters on horizontal gene transfer. *Environmental Pollution*, *276*, 116733. https://doi.org/https://doi.org/10.1016/j.envpol.2021.116733

Interrante, J. D., Tuttle, M. S., Admon, L. K., & Kozhimannil, K. B. (2022). Severe Maternal Morbidity and Mortality Risk at the Intersection of Rurality, Race and Ethnicity, and Medicaid. *Women's Health Issues*, *32*(6), 540-549. https://doi.org/https://doi.org/10.1016/j.whi.2022.05.003

Jhalora, V., & Bist, R. (2025). A Comprehensive Review of Molecular Mechanisms Leading to the Emergence of Multidrug Resistance in Bacteria. *Indian Journal of Microbiology*, *65*(2), 844-865. https://doi.org/10.1007/s12088-024-01384-6

Kalizang'oma, A., Kwambana-Adams, B., Chan, J. M., Viswanath, A., Gori, A., Richard, D., Jolley, K. A., Lees, J., Goldblatt, D., Beleza, S., Bentley, S. D., Heyderman, R. S., & Chaguza, C. (2023). Novel Multilocus Sequence Typing and Global Sequence Clustering Schemes for Characterizing the Population Diversity of Streptococcus mitis. *Journal of Clinical Microbiology*, *61*(1), e00802-00822. https://doi.org/doi:10.1128/jcm.00802-22

Karampatakis, T., Tsergouli, K., & Behzadi, P. (2025). Carbapenem-Resistant Pseudomonas aeruginosa's Resistome: Pan-Genomic Plasticity, the Impact of Transposable Elements and Jumping Genes. *Antibiotics*, *14*(4), 353. https://www.mdpi.com/2079-6382/14/4/353

Kocsis, B., Gulyás, D., & Szabó, D. (2022). Emergence and Dissemination of Extraintestinal Pathogenic High-Risk International Clones of Escherichia coli. *Life*, *12*(12), 2077. https://www.mdpi.com/2075-1729/12/12/2077

Kumar, N. R., Balraj, T. A., Kempegowda, S. N., & Prashant, A. (2024). Multidrug-Resistant Sepsis: A Critical Healthcare Challenge. *Antibiotics*, *13*(1), 46. https://www.mdpi.com/2079-6382/13/1/46

Lamping, J.-P., & Krebber, H. (2025). The hidden power of antisense long non-coding RNAs: a dive into a novel regulatory layer mediated by double-stranded RNA formation. *RNA Biology*, *22*(1), 1-16. https://doi.org/10.1080/15476286.2025.2530797

Land, W. G. (2023). Virulence of Pathogens and the Counteracting Responses of the Host. In *Damage-Associated Molecular Patterns in Human Diseases : Volume 3: Antigen-Related Disorders* (pp. 109-202). Springer International Publishing. https://doi.org/10.1007/978-3-031-21776-0_3

Lee, W., Sung, S., Ha, J., Kim, E., An, E. S., Kim, S. H., Kim, S. H., & Kim, H.-Y. (2023). Molecular and Genomic Analysis of the Virulence Factors and Potential Transmission of Hybrid Enteropathogenic and Enterotoxigenic Escherichia coli (EPEC/ETEC) Strains Isolated in South Korea. *International Journal of Molecular Sciences*, *24*(16), 12729. https://www.mdpi.com/1422-0067/24/16/12729

Lorusso, A. B., Carrara, J. A., Barroso, C. D. N., Tuon, F. F., & Faoro, H. (2022). Role of Efflux Pumps on Antimicrobial Resistance in Pseudomonas aeruginosa. *International Journal of Molecular Sciences*, *23*(24), 15779. https://www.mdpi.com/1422-0067/23/24/15779

Lv, Y., & Fan, G. (2026). Network-Driven Insights into Plant Immunity: Integrating Transcriptomic and Proteomic Approaches in Plant-Pathogen Interactions. *Int J Mol Sci*, *27*(3). https://doi.org/10.3390/ijms27031242

Mahmud, H. A., & Wakeman, C. A. (2024). Navigating collateral sensitivity: insights into the mechanisms and applications of antibiotic resistance trade-offs [Review]. *Frontiers in Microbiology*, *Volume 15 - 2024*. https://doi.org/10.3389/fmicb.2024.1478789

Malesa, R., Pierneef, R., Mafuna, T., Magwedere, K., Seakamela, E., & Matle, I. (2025). Genome-Based In Silico Analysis of the Structural and Functional Characteristics of the Type Three Secretion System (T3SS) and Core Effector Proteins in Enteropathogenic Escherichia coli (EPEC) Strains Isolated from Food-Producing Animals and Products of Animal Origin. *Pathogens*, *14*(11), 1099. https://www.mdpi.com/2076-0817/14/11/1099

Manzoor, H., Li, H., & Kayani, M. U. R. (2025). Identification of antibiotic resistance genes from whole genome and metagenome sequencing datasets. *One Health Advances*, *3*(1), 14. https://doi.org/10.1186/s44280-025-00079-x

Matsumura, Y., Yamamoto, M., Gomi, R., Tsuchido, Y., Shinohara, K., Noguchi, T., & Nagao, M. (2025). Integrating whole-genome sequencing into antimicrobial resistance surveillance: methodologies, challenges, and perspectives. *Clinical Microbiology Reviews*, *38*(4), e00140-00122. https://doi.org/doi:10.1128/cmr.00140-22

Maveke, S. M., Aboge, G. O., Kanja, L. W., Mainga, A. O., Gachau, N., Muchira, B. W., & Moriasi, G. A. (2024). Phenotypic and Genotypic Characterization of Extended Spectrum Beta-Lactamase-Producing Clinical Isolates of Escherichia coli and Klebsiella pneumoniae in Two Kenyan Facilities: A National Referral and a Level Five Hospital. *International Journal of Microbiology*, *2024*(1), 7463899. https://doi.org/https://doi.org/10.1155/2024/7463899

Mendes, G., Santos, M. L., Ramalho, J. F., Duarte, A., & Caneiras, C. (2023). Virulence factors in carbapenem-resistant hypervirulent Klebsiella pneumoniae [Review]. *Frontiers in Microbiology*, *Volume 14 - 2023*. https://doi.org/10.3389/fmicb.2023.1325077

Meng, M., Li, Y., & Yao, H. (2022). Plasmid-Mediated Transfer of Antibiotic Resistance Genes in Soil. *Antibiotics*, *11*(4), 525. https://www.mdpi.com/2079-6382/11/4/525

Moazeni, S., Askari Badouei, M., Hashemitabar, G., Rezatofighi, S. E., & Mahmoodi, F. (2024). Detection and characterization of potentially hybrid enteroaggregative Escherichia coli (EAEC) strains isolated from urinary tract infection. *Brazilian Journal of Microbiology*, *55*(1), 1-9. https://doi.org/10.1007/s42770-023-01195-9

Moxley, R. A. (2022). Family Enterobacteriaceae. In *Veterinary Microbiology* (pp. 41-55). https://doi.org/https://doi.org/10.1002/9781119650836.ch5

Munhoz, D. D., Richards, A. C., Santos, F. F., Mulvey, M. A., & Piazza, R. M. F. (2023). E. coli Common pili promote the fitness and virulence of a hybrid aEPEC/ExPEC strain within diverse host environments. *Gut Microbes*, *15*(1), 2190308. https://doi.org/10.1080/19490976.2023.2190308

Naidoo, N., & Zishiri, O. T. (2025). Presence, Pathogenicity, Antibiotic Resistance, and Virulence Factors of Escherichia coli: A Review. *Bacteria*, *4*(1), 16. https://www.mdpi.com/2674-1334/4/1/16

Nasrollahian, S., Graham, J. P., & Halaji, M. (2024). A review of the mechanisms that confer antibiotic resistance in pathotypes of E. coli [Review]. *Frontiers in Cellular and Infection Microbiology*, *Volume 14 - 2024*. https://doi.org/10.3389/fcimb.2024.1387497

Nogueira, T., & Botelho, A. (2021). Metagenomics and Other Omics Approaches to Bacterial Communities and Antimicrobial Resistance Assessment in Aquacultures. *Antibiotics*, *10*(7), 787. https://www.mdpi.com/2079-6382/10/7/787

Peng, Z., Hu, Z., Li, Z., Zhang, X., Jia, C., Li, T., Dai, M., Tan, C., Xu, Z., Wu, B., Chen, H., & Wang, X. (2022). Antimicrobial resistance and population genomics of multidrug-resistant Escherichia coli in pig farms in mainland China. *Nature Communications*, *13*(1), 1116. https://doi.org/10.1038/s41467-022-28750-6

Pitout, J. D. D., Peirano, G., & DeVinney, R. (2023). The contributions of multidrug resistant clones to the success of pandemic extra-intestinal Pathogenic Escherichia coli. *Expert Review of Anti-infective Therapy*, *21*(4), 343-353. https://doi.org/10.1080/14787210.2023.2184348

Priyanka, P., Meena, P. R., Raj, D., Rana, A., Dhanokar, A., Duggirala, K. S., & Singh, A. P. (2023). Urinary tract infection and sepsis causing potential of multidrug-resistant Extraintestinal pathogenic E. coli isolated from plant-origin foods. *International Journal of Food Microbiology*, *386*, 110048. https://doi.org/https://doi.org/10.1016/j.ijfoodmicro.2022.110048

Qin, S., Xiao, W., Zhou, C., Pu, Q., Deng, X., Lan, L., Liang, H., Song, X., & Wu, M. (2022). Pseudomonas aeruginosa: pathogenesis, virulence factors, antibiotic resistance, interaction with host, technology advances and emerging therapeutics. *Signal Transduction and Targeted Therapy*, *7*(1), 199. https://doi.org/10.1038/s41392-022-01056-1

Qiu, L., Chirman, D., Clark, J. R., Xing, Y., Hernandez Santos, H., Vaughan, E. E., & Maresso, A. W. (2024). Vaccines against extraintestinal pathogenic Escherichia coli (ExPEC): progress and challenges. *Gut Microbes*, *16*(1), 2359691. https://doi.org/10.1080/19490976.2024.2359691

Ramaloko, W. T., & Osei Sekyere, J. (2022). Phylogenomics, epigenomics, virulome and mobilome of Gram-negative bacteria co-resistant to carbapenems and polymyxins: a One Health systematic review and meta-analyses. *Environmental Microbiology*, *24*(3), 1518-1542. https://doi.org/https://doi.org/10.1111/1462-2920.15930

Rezaei, S., Tajbakhsh, S., Naeimi, B., & Yousefi, F. (2024). Investigation of gyrA and parC mutations and the prevalence of plasmid-mediated quinolone resistance genes in Klebsiella pneumoniae clinical isolates. *BMC Microbiology*, *24*(1), 265. https://doi.org/10.1186/s12866-024-03383-5

Rose, R., Nolan, D. J., Ashcraft, D., Feehan, A. K., Velez-Climent, L., Huston, C., Lain, B., Rosenthal, S., Miele, L., Fogel, G. B., Pankey, G., Garcia-Diaz, J., & Lamers, S. L. (2023). Comparing antimicrobial resistant genes and phenotypes across multiple sequencing platforms and assays for Enterobacterales clinical isolates. *BMC Microbiology*, *23*(1), 225. https://doi.org/10.1186/s12866-023-02975-x

Sader de Azevedo, P., Vedovatto, M. M., Gimenes de Freitas, P. C., Luz, R. B. S., Streit, R. S. A., & Persinoti, G. F. (2026). parsomics: a data-driven framework for metagenomics data integration powered by a local relational database. *Bioinformatics Advances*, vbag049.

Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., & Alqumber, M. A. A. (2023). Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare*, *11*(13), 1946. https://www.mdpi.com/2227-9032/11/13/1946

Saleem, S., Raza, F., Akbar, A., Firdous, Z., Noman, H., & Fatima, M. (2026). Computational Analysis of Acquired Antimicrobial Resistance Genes in Mycobacterium Plasmid. *Journal of Health, Wellness and Community Research*, e1256-e1256.

Shaik, S., Singh, A., Suresh, A., & Ahmed, N. (2022). Genome Informatics and Machine Learning-Based Identification of Antimicrobial Resistance-Encoding Features and Virulence Attributes in Escherichia coli Genomes Representing Globally Prevalent Lineages, Including High-Risk Clonal Complexes. *mBio*, *13*(1), e03796-03721. https://doi.org/doi:10.1128/mbio.03796-21

Sherry, N. L., Lee, J. Y. H., Giulieri, S. G., Connor, C. H., Horan, K., Lacey, J. A., Lane, C. R., Carter, G. P., Seemann, T., Egli, A., Stinear, T. P., & Howden, B. P. (2025). Genomics for antimicrobial resistance—progress and future directions. *Antimicrobial Agents and Chemotherapy*, *69*(5), e01082-01024. https://doi.org/doi:10.1128/aac.01082-24

Shoaib, M., He, Z., Geng, X., Tang, M., Hao, R., Wang, S., Shang, R., Wang, X., Zhang, H., & Pu, W. (2023). The emergence of multi-drug resistant and virulence gene carrying Escherichia coli strains in the dairy environment: a rising threat to the environment, animal, and public health [Original Research]. *Frontiers in Microbiology*, *Volume 14 - 2023*. https://doi.org/10.3389/fmicb.2023.1197579

Siddique, N., Arafat, K. Y., Gilman, M. A. A., Rahman, M. M., Das, Z. C., Islam, T., & Hoque, M. N. (2025). Genomic insights into multidrug resistant Escherichia coli from bovine mastitis in Bangladesh. *BMC Microbiology*, *25*(1), 788. https://doi.org/10.1186/s12866-025-04514-2

Struelens, M. J., Ludden, C., Werner, G., Sintchenko, V., Jokelainen, P., & Ip, M. (2024). Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance [Frontiers in Science Lead Article]. *Frontiers in Science*, *Volume 2 - 2024*. https://doi.org/10.3389/fsci.2024.1298248

Subramanian, D., & Natarajan, J. (2023). Leveraging big data bioinformatics approaches to extract knowledge from Staphylococcus aureus public omics data. *Critical Reviews in Microbiology*, *49*(3), 391-413. https://doi.org/10.1080/1040841X.2022.2065905

Telekes, A., & Horváth, A. (2022). The Role of Cell-Free DNA in Cancer Treatment Decision Making. *Cancers*, *14*(24), 6115. https://www.mdpi.com/2072-6694/14/24/6115

Vashisht, V., Vashisht, A., Mondal, A. K., Farmaha, J., Alptekin, A., Singh, H., Ahluwalia, P., Srinivas, A., & Kolhe, R. (2023). Genomics for Emerging Pathogen Identification and Monitoring: Prospects and Obstacles. *BioMedInformatics*, *3*(4), 1145-1177. https://www.mdpi.com/2673-7426/3/4/69

Vinayamohan, P. G., Pellissery, A. J., & Venkitanarayanan, K. (2022). Role of horizontal gene transfer in the dissemination of antimicrobial resistance in food animal production. *Current Opinion in Food Science*, *47*, 100882. https://doi.org/https://doi.org/10.1016/j.cofs.2022.100882

Wang, Z., Xie, W., Luo, D., Wang, L., Xu, Y., Rosenn, E. H., & Soni, V. (2024). Omics-Based Approaches in Developing Treatments Against Antimicrobial Resistance. In V. Soni & A. S. Akhade (Eds.), *Antimicrobial Resistance: Factors to Findings: Omics and Systems Biology Approaches* (pp. 387-413). Springer International Publishing. https://doi.org/10.1007/978-3-031-65986-7_12

Wareth, G., Linde, J., Hammer, P., Pletz, M. W., Neubauer, H., & Sprague, L. D. (2022). WGS-Based Phenotyping and Molecular Characterization of the Resistome, Virulome and Plasmid Replicons in Klebsiella pneumoniae Isolates from Powdered Milk Produced in Germany. *Microorganisms*, *10*(3), 564. https://www.mdpi.com/2076-2607/10/3/564

Yakobi, S. H., & Nwodo, U. U. (2025). Microbiological methodologies: Comparative evaluation of microbial community and enhanced antibiotic susceptibility testing. *Electronic Journal of Biotechnology*, *74*, 29-40. https://doi.org/https://doi.org/10.1016/j.ejbt.2025.01.001

Zhao, W., Zeng, W., Pang, B., Luo, M., Peng, Y., Xu, J., Kan, B., Li, Z., & Lu, X. (2023). Oxford nanopore long-read sequencing enables the generation of complete bacterial and plasmid genomes without short-read sequencing [Original Research]. *Frontiers in Microbiology*, *Volume 14 - 2023*. https://doi.org/10.3389/fmicb.2023.1179966