# Analysis of Beta-lactam Resistance Mechanisms in Clinical E. coli Isolates

## Introduction:

The increasing prevalence of antimicrobial resistance (AMR) in Escherichia coli poses a significant challenge in clinical settings. This study aimed to analyze the resistance mechanisms in five E. coli isolates, focusing on penicillin-binding proteins (PBPs), β-lactamase genes, and efflux-mediated resistance. Notably, NDM-5 indicates high-level resistance to carbapenems, a class of last-resort antibiotics. The findings help understand the genetic basis of resistance, particularly to beta-lactams, aiding in clinical decision-making for effective treatment strategies.

## Methods:

- **Genome Annotation:** The genomes were annotated using Prokka.
- **PBP Gene Extraction:** Key penicillin-binding protein genes (PBP1a, PBP1b, PBP2, PBP3, PBP4, PBP5, PBP6, PBP7) were extracted using Biopython.
- **Multiple Sequence Alignment (MSA):** PBP sequences were aligned against the wild-type reference to identify mutations.
- **ResFinder & RGI (CARD) Analysis:** AMR gene detection and phenotypic resistance prediction were performed.
- **Antibiotic Sensitivity Testing (AST):** Resistance profiles were analyzed for β-lactams and other antibiotic classes.

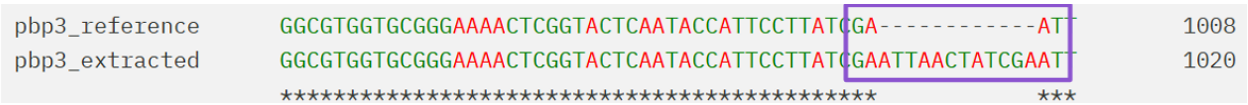
## Results:

### Isolate Description

All five isolates were Escherichia coli, exhibiting multidrug resistance, with a strong focus on β-lactam resistance.

### Key Findings from PBP Analysis

- In all isolates, an insertion mutation **(ATTAACTATCGA)** was identified in **PBP3**, correlating with resistance to **aztreonam and avibactam**.
- Other mutations in PBPs were also observed, potentially contributing to altered β-lactam binding.



## β-lactamase Enzymes Identified (ResFinder & CARD RGI Results):

| Gene | Resistance to | Mechanism |
|---|---|---|
| blaNDM-5 | Carbapenems, cephalosporins, penicillins | Metallo-Beta-Lactamase (MBL) hydrolyses Beta lactams |
| blaCMY-42 | Extended-spectrum cephalosporins, penicillins | AmpC beta-lactamase production |
| blaTEM-1B | Penicillins, aminopenicillins | Hydrolyzes narrow spectrum beta-lactams but not ESBL |
| blaCTX-M-15 | Cephalosporins | Extended-spectrum Beta-lactamase (ESBL) |

## Cultural Sensitivity Report & Resistance Profile:

| | sample_id | Zone | Specimen_coll | Ertapenem | Imipenem | Meropenem | Ceftazidime | Ceftriaxone | Cefepime | Aztreonam | icillin.Clavulani | azidime.Avibac | racillin.Tazobactam | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | EC031 | Northern | blood | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | |
| 3 | EC040 | Northern | blood | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | |
| 4 | ECBN29 | Western | blood | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | | Resistant | |
| 5 | ECBN31 | Western | blood | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | | Resistant | |
| 6 | ECBN32 | Western | blood | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | Resistant | | Resistant | |

## Conclusion:

This study confirms the presence of CTX-M, TEM β-lactamases, NDM-5, CMY-42 β-lactamases, PBP3 mutations, and efflux-mediated resistance as primary drivers of β-lactam resistance in these E. coli isolates. The findings suggest that standard β-lactam treatments may be ineffective, necessitating alternative therapeutic strategies. Further clinical correlation is advised to optimize treatment outcomes.