*International Journal of Scientific Research and Engineering Development-– Volume 9 Issue 5, Sep-Oct 2026*
*Available at www.ijsred.com*

RESEARCH ARTICLE OPEN ACCESS

# A Six-Stage Computational Framework for Translating Gut Resistome Determinants into Antibiotic-Class Guidance: Architecture, Reference Panels and Decision Logic

Seshu Kumari K[*1], Dr. Munesh Kumar Sharma[*2]

[*1] Phd Scholar, Department of Microbiology (Under Faculty of Medicine), Amaltas University, Dewas, Madhya Pradesh, India

[*2] Professor and Guide, Department of Microbiology (Under Faculty of Medicine), Amaltas University, Dewas, Madhya Pradesh, India

**Abstract:**

Resistome profiling can establish, with reasonable confidence, that a resistance determinant is present in a bacterial genome; converting that observation into a statement about which antibiotic a clinician should prefer is a distinct and largely unsolved engineering problem. This paper specifies and describes the architecture of a six-stage computational framework that maps gut-bacterial resistance determinants onto the drug classes of the Antibiotic Resistance Ontology and thence onto sixteen clinically prescribed antimicrobial classes, before applying an explicit guidance rule. The framework was exercised on a deliberately small, exhaustively inspectable reference panel of ten gut-relevant bacterial strains and six well-characterised resistance determinants, with determinant calls curated from the primary literature rather than generated by sequence annotation. We describe the rationale for a reference-panel design, the provenance of every determinant call, the two-step ontology-to-clinical-class mapping, and a revised three-state decision rule — avoid on positive determinant evidence, avoid on recorded intrinsic resistance, or no evidence — that replaces an original binary rule shown elsewhere to generate clinically unsound recommendations. The architecture is designed so that every stage can be inspected, re-run and corrected independently, a property we argue is a precondition for any resistome-based decision aid intended for eventual clinical use. Companion evaluation results are reported separately.

**Keywords —** antimicrobial resistance; gut microbiota; resistome; Antibiotic Resistance Ontology; Comprehensive Antibiotic Resistance Database; clinical decision support; antibiotic stewardship; intrinsic resistance.

## 1. Introduction

### 1.1 The Gut as a Reservoir of Resistance

The human gastrointestinal tract harbours a dense and taxonomically diverse bacterial community that, independently of any individual's history of antibiotic exposure, carries a substantial repertoire of antimicrobial resistance genes [1]. This collection of determinants, commonly termed the resistome, includes genes that confer clinically significant resistance in recognised pathogens as well as determinants native to commensal organisms that have no history of being clinically resistant themselves but that constitute a mobilisable reservoir [2]. Global estimates attribute more than a million deaths annually to bacterial antimicrobial resistance, with several hundred thousand further deaths associated with it [3], and the European regional burden alone has been estimated at tens of thousands of attributable deaths per year [4]. The economic and clinical costs of resistance are well documented [5], and low- and middle-income settings with high antibiotic consumption, including much of South Asia, are disproportionately exposed to this burden.

Sequence-based annotation against curated reference databases, most prominently the Comprehensive Antibiotic Resistance Database (CARD) and its associated Antibiotic Resistance Ontology (ARO), has made resistome characterisation routine [1]. Tools such as the Resistance Gene Identifier and comparable annotation pipelines can

now return, for a given genome or metagenome, the set of resistance determinants it carries and the ontology class to which each belongs [6]. Deep-learning determinant classifiers offer a complementary route to the same output for metagenomic data of uncertain provenance [7].

### 1.2 From Determinant Detection to a Prescribing Decision: The Translational Gap

Detecting a determinant is not the same task as deciding what to prescribe. Ontology drug classes are curated on a molecular and evolutionary basis; the classes in which antibiotics are actually prescribed are clinical categories defined by route, spectrum and formulary convention. No published, publicly specified procedure converts a determinant panel, expressed in ontology terms, into a decision expressed in the sixteen or so classes a prescriber recognises. Country-specific studies of gut resistome content confirm that the determinants present in a population's gut microbiota track antibiotic use patterns closely enough to be informative [8], and community-level studies show that antimicrobial peptide and antibiotic resistance determinants are not distributed at random across host phylogeny [9], which is precisely the kind of structure a translation framework must respect rather than discard.

A second, more fundamental problem sits beneath the translation problem: the treatment of absence. A determinant panel of any realistic size is incomplete, and a genome or a patient's resistome returning zero hits against a given drug class is not thereby shown to be susceptible to that class. Intrinsic resistance — resistance that arises from structural or physiological properties of an organism rather than from an identifiable acquired gene — is common and clinically decisive, and no determinant-counting procedure can detect it unless it is represented as an independent input [2]. Any framework that silently equates "no determinant found" with "safe to use" risks manufacturing confident, wrong recommendations at exactly the point where a clinician is relying on it most.

### 1.3 Aim and Objectives

The aim of the work reported here was to develop a computational framework that converts gut-bacterial resistome content into structured antibiotic-class guidance, and to specify that framework in enough detail that every stage can be inspected and, where necessary, corrected. Framed as objectives, this paper addresses: (i) the specification and implementation of a staged mapping from resistance determinant to ontology drug class to clinical antimicrobial class to guidance decision; and (ii) the assembly of a reference panel of gut-bacterial strains and characterised resistance determinants sufficient to exercise every branch of that mapping, including the branch in which no determinant is present. A companion paper reports the quantitative behaviour of the framework when executed over this panel, the errors this exposed in an initial binary decision rule, and the revised rule and intrinsic-resistance register that removed them.

## 2. Related Work

### 2.1 Resistome Databases, Ontologies and Annotation Tools

CARD is the most widely used curated resource for resistance determinant sequences and detection models, organised under the Antibiotic Resistance Ontology, a controlled vocabulary that groups determinants by mechanism and drug class [1]. Complementary resources include deep-learning classifiers trained to predict resistance genes directly from metagenomic reads without requiring an exact match to a curated reference [7], and country-scale resistome surveys that quantify determinant abundance across sixty or more antibiotic classes and subclasses in faecal metagenomes [8]. None of these resources outputs a prescribing recommendation; each stops at the point of determinant detection and ontology classification, leaving the translation to clinical categories, and the handling of determinant absence, unspecified.

### 2.2 Classification of Resistance Mechanisms and Clinical Classes

The functional classification of β-lactamases by mechanism and inhibitor profile [10] illustrates the kind of structured, mechanism-based classification on which an ontology-to-clinical mapping stage can be built; a determinant assigned to a molecular class under such a scheme can be related, with appropriate care, to the clinical drug classes it is known to inactivate. Standardised definitions of multidrug, extensive drug and pandrug resistance [11] provide the vocabulary in which the clinical consequences of a resistome-derived decision must

ultimately be expressed, even though the present framework operates at the level of individual antimicrobial classes rather than composite resistance phenotypes. Reviews of resistance dissemination in the environment [12] and of gut-specific determinant transfer [9] together motivate treating the gut as a distinct compartment requiring its own reference panel rather than reusing panels assembled for clinical or environmental surveillance.

### 2.3 Gaps Addressed by the Present Framework

Three gaps in the published literature motivate the design reported here. First, existing resistome pipelines characterise determinant content but do not specify a decision procedure that outputs class-level guidance; the translation step, where it appears at all, is described narratively rather than as an inspectable rule. Second, published resistome studies rarely state explicitly how the absence of a determinant is to be interpreted, an omission that becomes consequential the moment resistome data are used to inform, rather than merely describe, antimicrobial choice. Third, no small, fully specified reference panel exists against which a translation framework of this kind can be exhaustively checked by hand before it is applied to real sequencing data; large real-world panels make errors easy to miss precisely because every branch of the logic cannot be inspected. The framework described in Section 3 was designed specifically to close these three gaps.

## 3. Framework Architecture and Materials

### 3.1 Study Design and Scope

This is a methodological study. Its object is an analytical framework, not a human population: no participants were recruited, no biological specimens were collected, and no laboratory procedure was performed. The strains and determinants used to exercise the framework were drawn entirely from published literature and public sequence resources. Three considerations motivated a reference-panel design in preference to an immediate application to real gut metagenomes. First, the translation problem this framework addresses is unsolved independently of any particular dataset, so its logic can and should be validated before it is pointed at real data. Second, a small panel of well-characterised strains allows the behaviour of every stage to be inspected exhaustively — with ten strains and six determinants the entire output can be checked by hand, which is not true of a metagenomic cohort. Third, the framework was developed without reliable, continuous access to the computational infrastructure required to execute sequence annotation tools against a pinned CARD release, so a literature-curated panel was substituted deliberately and is reported as such throughout.

### 3.2 Computing Environment

The framework was implemented in Python using the pandas, NumPy, SciPy, scikit-learn, NetworkX, Matplotlib and seaborn libraries. All analyses were executed in a single reproducible run; the strain panel, determinant panel, both mapping tables, the intrinsic resistance register and the guidance rule are fully specified so that the run can be repeated exactly from the tables given in this paper.

### 3.3 The Reference Strain Panel

Ten strains were selected to represent the principal functional and taxonomic groups of the human colonic microbiota together with organisms of established clinical relevance (Table I). The panel comprises four Gram-negative and six Gram-positive organisms and spans the dominant obligate anaerobes, mucin-degrading specialists, facultative Enterobacterales, an enterococcal reference strain and two reference probiotic organisms. Faecalibacterium prausnitzii is classified here as Gram-positive on phylogenetic grounds, as a member of the phylum Bacillota, although it stains Gram-negative in practice.

*Table I. Composition of the reference strain panel.*

| Strain | Gram | Oxygen requirement | Rationale for inclusion |
|---|---|---|---|
| Escherichia coli Nissle 1917 | − | Facultative anaerobe | Commensal / probiotic Enterobacterales reference |
| Klebsiella pneumoniae MGH78578 | − | Facultative anaerobe | Clinically important Enterobacterales, intestinal reservoir |
| Bacteroides fragilis NCTC9343 | − | Obligate anaerobe | Dominant colonic anaerobe, |

| | | | |
|---|---|---|---|
| | | | opportunistic pathogen |
| Bacteroides thetaiotaomicron VPI5482 | − | Obligate anaerobe | Dominant colonic anaerobe, polysaccharide utilisation |
| Enterococcus faecalis V583 | + | Facultative anaerobe | Reference vancomycin-resistant enterococcus |
| Clostridioides difficile 630 | + | Obligate anaerobe | Reference enteric pathogen of antimicrobial exposure |
| Faecalibacterium prausnitzii A2165 | + | Obligate anaerobe | Major butyrate producer, healthy-community marker |
| Bifidobacterium longum NCC2705 | + | Obligate anaerobe | Reference infant and adult commensal |
| Lactobacillus rhamnosus GG | + | Facultative anaerobe | Reference probiotic organism |
| Akkermansia muciniphila BAA835 | − | Obligate anaerobe | Mucin-degrading specialist, metabolic-health marker |

### 3.4 The Resistance Determinant Panel and Its Provenance

Six resistance determinants were included (Table II), selected as the minimum set sufficient to exercise every branch of the mapping and guidance logic: a determinant-present branch for several drug classes, and a determinant-absent branch for the remainder. The panel is deliberately not a survey of the gut resistome and does not attempt to be. This limitation is stated at the outset rather than qualified afterwards, because it governs the interpretation of every downstream result: the panel omits carbapenemases, extended-spectrum β-lactamases, plasmid-mediated quinolone determinants and mobile colistin-resistance genes, and the framework is accordingly untested against the determinant classes of greatest current clinical concern.

*Table II. The resistance determinant panel.*

| Determinant | Mechanism | ARO drug class | Classification |
|---|---|---|---|
| AmpC β-lactamase (blaEC family) | Enzymatic hydrolysis of β-lactams | Cephalosporin, penam | Intrinsic chromosomal |
| SHV β-lactamase | Enzymatic hydrolysis of β-lactams | Cephalosporin, penam | Intrinsic chromosomal |
| cepA cephalosporinase | Enzymatic hydrolysis of cephalosporins | Cephalosporin | Intrinsic chromosomal |
| tetW ribosomal protection protein | Protection of the ribosomal target | Tetracycline | Acquired, mobile-associated |
| aac(6′)-Ii acetyltransferase | Enzymatic modification of aminoglycosides | Aminoglycoside | Intrinsic chromosomal |
| vanB glycopeptide operon | Alteration of the peptidoglycan precursor | Glycopeptide | Acquired, transposon-associated |

Every determinant call was curated by the investigator from the primary literature describing the corresponding strain (Table III), rather than generated by executing an annotation tool against a genome sequence. Two consequences of this design decision constrain the interpretation of the framework throughout this paper and its companion. First, the results reported describe the behaviour of the mapping and guidance logic when supplied with correct determinant calls; they do not demonstrate that the framework correctly calls determinants from raw sequence, because no sequence annotation step was executed. Second, any comparison of framework output against the published phenotype of a strain compares the output against the literature from which its own input was drawn, and is therefore a consistency check on transmission of input to output rather than an external validation of predictive accuracy.

*Table III. Representative sources of the curated determinant calls (selected entries).*

| Strain | Source publication | Determinant attribute drawn from source |
|---|---|---|
| Enterococcus faecalis V583 | Paulsen et al. (2003) [13] | vanB operon and intrinsic aac(6′)-Ii |
| Bifidobacterium longum NCC2705 | Schell et al. (2002) | tetW determinant |
| Klebsiella pneumoniae MGH78578 | McClelland et al. (2008) | Chromosomal SHV β-lactamase |
| Escherichia coli Nissle 1917 | Patzer et al. (2003); Donelli et al. (2014) | AmpC cephalosporinase |
| Bacteroides fragilis / B. thetaiotaomicron | Frydrich (1992) | cepA / cepA-family cephalosporinase |
| Lactobacillus rhamnosus GG | Kankainen et al. (2009) | Absence of acquired determinants |
| Akkermansia muciniphila BAA835 | Derrien et al. (2004); Guo et al. (2017) | Absence of acquired determinants |

### 3.5 Stage 1–2: Determinant Detection and Strain Assignment

The first two stages of the framework fix, for each of the ten strains, the subset of the six-determinant panel it carries, as tabulated in Table III. The product is a ten-by-six binary strain-by-determinant matrix that forms the input to every subsequent stage.

### 3.6 Stage 3: Mapping Determinants to Ontology Drug Classes

Each determinant was assigned to one or more Antibiotic Resistance Ontology drug classes following the classification used by CARD [1]. Because a single enzyme can hydrolyse substrates from more than one clinical family, both panel β-lactamases (AmpC and SHV) were assigned to two ontology classes each — cephalosporin and penam — reflecting their established substrate range [10]. The product of this stage is a strain-by-ontology-class matrix.

### 3.7 Stage 4: Mapping Ontology Classes to Clinical Antimicrobial Classes

Ontology drug classes are not the categories in which prescribing decisions are made, so a second mapping table converts each ontology class into one or more of sixteen clinical antimicrobial classes covering the antibacterial agents in common therapeutic use (cephalosporins, penicillins, tetracyclines, aminoglycosides, glycopeptides, carbapenems, monobactams, fluoroquinolones, macrolides, lincosamides, sulfonamides, folate inhibitors, polymyxins, nitroimidazoles, rifamycins and oxazolidinones). Classes for which the six-determinant panel contains no representative at all are retained in the mapping rather than omitted, deliberately, because their retention is what allows the framework's central limitation — an empty column is not evidence of susceptibility — to be seen rather than hidden by the table's own construction.

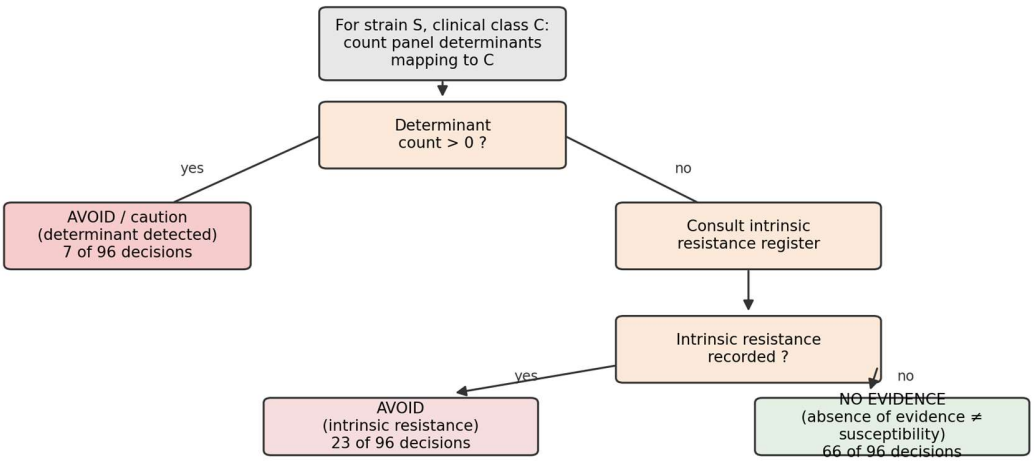
### 3.8 Stage 5: The Guidance Rule and the Intrinsic Resistance Register

For every strain and every one of the sixteen clinical classes, the framework counts the panel determinants mapping to that class and emits a decision. An original, binary implementation of this rule treated a non-zero count as grounds to avoid the class and a zero count as grounds to recommend it as a preferred candidate. This second limb is unsound: a count of zero is evidence only that the six-determinant panel contains nothing mapping to that class, not evidence that the strain is susceptible to it. The rule was therefore revised to the three-state form illustrated in Fig. 2: (a) a positive determinant count is evidence to avoid or use the class with caution; (b) a zero count consulted against an independently compiled intrinsic resistance register that documents non-susceptibilities arising from structural or physiological properties rather than identifiable genes is, where a record exists, also grounds to avoid; and (c) a zero count with no intrinsic-resistance record is reported as absence of evidence and generates no positive therapeutic claim. Critically, the revised rule never asserts that an agent is a preferred candidate under any circumstance, because the panel is not, and does not claim

to be, a complete description of any strain's resistance phenotype. The intrinsic resistance register is consulted at the guidance stage as an input independent of the determinant panel; that it had to be compiled separately, and that its entries contradict the original rule's output at several points, is itself among the principal findings reported in the companion evaluation paper.

*Figure 2. Revised three-state guidance rule replacing the original binary (present / preferred-candidate) rule of Section 3.10.*



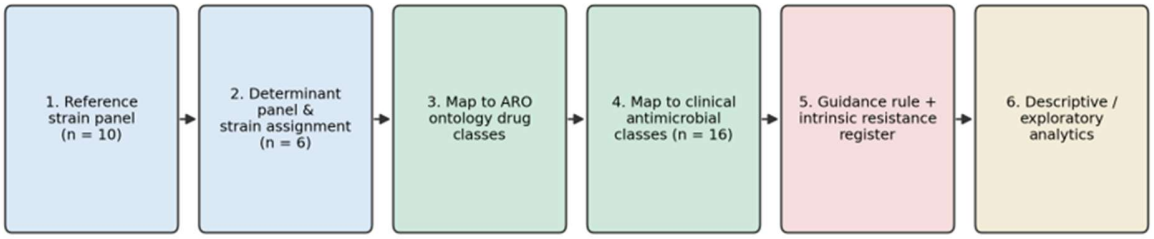

### 3.9 Stage 6: Descriptive and Exploratory Analytics

The final stage computes, from the strain-by-determinant matrix, three per-strain descriptive measures (resistome burden, richness and coverage-weighted Shannon diversity), an ordination by principal component analysis with average-linkage hierarchical clustering, a pairwise determinant co-occurrence network based on the phi coefficient, an association test between each determinant and Gram reaction by Fisher's exact test with Benjamini–Hochberg correction [14], and an exploratory random forest classifier of Gram reaction from determinant profile with permutation feature importance. These analyses are included in the architecture because a framework intended for eventual application to real metagenomic cohorts must offer more than a per-class decision; but at the panel size used here several of these measures are, by construction, at or beyond the limit of their statistical applicability, a point developed quantitatively in the companion paper.

### 3.10 Overall Architecture

Fig. 1 summarises the six stages end to end. Each stage writes an intermediate table that can be inspected independently of the stages before and after it, a design choice motivated directly by the implementation defect described in the companion evaluation paper, in which an error in stage 4 was traced to a specific collapse of the ontology mapping only because the intermediate output at that stage could be examined in isolation.

*Figure 1. The six-stage architecture of the resistome-to-guidance framework.*



## 4. Illustrative Execution of the Framework

Executed end to end over the ten-strain, six-determinant panel, the six stages of Section 3 ran to completion without manual intervention, producing seven determinant-present calls, a nine-cell strain-by-ontology-class matrix, and 96 guidance decisions (six determinant-carrying strains, all ten strains evaluated, across sixteen clinical classes). All seven decisions in which the framework recommended avoidance corresponded to an established resistance of the organism concerned; every case in which the original binary rule instead asserted that an agent was a preferred candidate in the absence of a panel determinant was subsequently checked against standard clinical microbiological references, and several were found to contradict established fact — most conspicuously, cephalosporins recommended for an intrinsically cephalosporin-resistant enterococcus, and aminoglycosides recommended for obligate anaerobes that cannot take up the drug class at all. Applying the revised three-state rule together with the intrinsic resistance register of Section 3.8 removed every such error, at the cost of no longer asserting suitability for any class under any circumstance. A full, quantitative account of this execution — including the descriptive analytics of Section 3.9, a forty-community synthetic simulation, and an internal consistency check against the source literature — is given in the companion evaluation paper, which this design paper is intended to be read alongside.

## 5. Discussion

### 5.1 Design Rationale

The architecture reported here separates four logically distinct operations — determinant detection, ontology assignment, clinical-class assignment and therapeutic decision — into stages that can be run, inspected and corrected independently. This separation has demonstrable practical value: two defects of different kinds, one conceptual (treating absence of evidence as evidence of susceptibility) and one an implementation error (loss of an ontology assignment before the clinical-class count was taken), were each traced to a specific stage only because that stage's output could be examined on its own. A framework that instead computed a single end-to-end score from determinant panel to recommendation would have obscured both defects behind a plausible-looking output.

### 5.2 Why a Small, Curated Panel Rather Than a Real Metagenomic Cohort

The decision to exercise the framework on a literature-curated panel of ten strains, rather than a real gut metagenomic cohort annotated by a sequence-analysis tool, is the central methodological choice of this study and warrants explicit defence. A framework whose translation logic has not first been checked exhaustively by hand is a poor candidate for application to data whose ground truth is unknown; the panel reported here makes every stage checkable, at the acknowledged cost that no claim is made, or should be inferred, about the framework's behaviour when supplied with tool-generated determinant calls from raw sequence data. Execution against determinant calls generated by the Resistance Gene Identifier or an equivalent tool against a pinned CARD release is accordingly identified as the first and most important extension of this work.

### 5.3 Limitations

Four limitations follow directly from the design just defended. First, the determinant panel is small by construction and omits several classes of determinant of major current clinical concern, so the framework is untested against carbapenemases, extended-spectrum β-lactamases, plasmid-mediated quinolone resistance and mobile colistin resistance. Second, the determinant calls were curated rather than computed, so no claim is made about the framework's behaviour on tool-generated input. Third, the intrinsic resistance register compiled for this work covers only the ten panel species and would need substantial extension before the framework could be applied to an unconstrained clinical isolate. Fourth, several of the Stage 6 descriptive analyses are, at this panel size, mathematically constrained to particular outcomes regardless of the underlying biology, a point quantified in the companion evaluation paper rather than here.

### 5.4 Relationship to the Companion Evaluation Paper

This paper specifies what the framework is and why it is built the way it is; it reports execution only illustratively. The companion paper reports, with full quantitative detail, how the framework behaved when run over the panel described here: the resistome burden and diversity of each strain, the descriptive analytics of Stage 6 and the statistical conditions under which they are and are not informative, the guidance decisions generated by the original and revised rules and the errors the revision removed, an internal consistency check against the source literature, and a forty-community synthetic simulation used to confirm that the burden and diversity measures respond

in the expected direction to constructed differences in community composition. Readers seeking the numerical results of applying this architecture are referred there.

## 6. Conclusion

We have specified a six-stage computational framework that converts gut-bacterial resistance determinant content into structured, class-level antibiotic guidance, and described the reference strain panel, determinant panel, ontology-to-clinical mapping and three-state decision rule that implement it. The central design principle is separability: each stage can be inspected, checked and corrected on its own, a property that allowed two distinct defects — one conceptual, one an implementation error — to be located and removed in this study, and that we argue should be regarded as a precondition, not an optional feature, of any computational framework intended to translate resistome data into a form that could plausibly inform antibiotic selection. The framework performs the mapping it was designed to perform, and where a resistance determinant is present its guidance is correct; where no determinant is present, the revised rule reports absence of evidence rather than asserting suitability, which we consider the only defensible position available to a framework built on a necessarily incomplete determinant panel. Quantitative evaluation of this architecture, including its guidance output, error modes and descriptive analytics, is reported in a companion paper.

## References

[1] B. P. Alcock et al., "CARD 2020: antibiotic resistome surveillance with the Comprehensive Antibiotic Resistance Database," Nucleic Acids Research, vol. 48, no. D1, pp. D517–D525, 2020. https://doi.org/10.1093/nar/gkz935

[2] W. E. Anthony, C. A. D. Burnham, G. Dantas, and J. H. Kwon, "The gut microbiome as a reservoir for antimicrobial resistance," The Journal of Infectious Diseases, vol. 223, no. Suppl. 3, pp. S209–S213, 2021. https://doi.org/10.1093/infdis/jiaa528

[3] C. J. L. Murray et al., "Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis," The Lancet, vol. 399, no. 10325, pp. 629–655, 2022. https://doi.org/10.1016/S0140-6736(21)02724-0

[4] A. Cassini et al., "Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015," The Lancet Infectious Diseases, vol. 19, no. 1, pp. 56–66, 2019. https://doi.org/10.1016/S1473-3099(18)30605-4

[5] P. Dadgostar, "Antimicrobial resistance: implications and costs," Infection and Drug Resistance, vol. 13, pp. 3903–3910, 2020. https://doi.org/10.2147/IDR.S234610

[6] D. G. J. Larsson and C. F. Flach, "Antibiotic resistance in the environment," Nature Reviews Microbiology, vol. 20, no. 5, pp. 257–269, 2022. https://doi.org/10.1038/s41579-021-00649-x

[7] G. Arango-Argoty, E. Garner, A. Pruden, L. S. Heath, P. Vikesland, and L. Zhang, "DeepARG: a deep learning approach for predicting antibiotic resistance genes from metagenomic data," Microbiome, vol. 6, no. 1, p. 23, 2018. https://doi.org/10.1186/s40168-018-0401-z

[8] K. Forslund, S. Sunagawa, J. R. Kultima, D. R. Mende, M. Arumugam, A. Typas, and P. Bork, "Country-specific antibiotic use practices impact the human gut resistome," Genome Research, vol. 23, no. 7, pp. 1163–1169, 2013. https://doi.org/10.1101/gr.155465.113

[9] B. Kintses et al., "Phylogenetic barriers to horizontal transfer of antimicrobial peptide resistance genes in the human gut microbiota," Nature Microbiology, vol. 4, no. 3, pp. 447–458, 2018. https://doi.org/10.1038/s41564-018-0313-5

[10] K. Bush and G. A. Jacoby, "Updated functional classification of β-lactamases," Antimicrobial Agents and Chemotherapy, vol. 54, no. 3, pp. 969–976, 2010. https://doi.org/10.1128/AAC.01009-09

[11] A. P. Magiorakos et al., "Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions," Clinical Microbiology and Infection, vol. 18, no. 3, pp. 268–281, 2012. https://doi.org/10.1111/j.1469-0691.2011.03570.x

[12] V. M. D'Costa, K. M. McGrann, D. W. Hughes, and G. D. Wright, "Sampling the antibiotic resistome," Science, vol. 311, no. 5759, pp. 374–377, 2006. https://doi.org/10.1126/science.1120800

[13] I. T. Paulsen et al., "Role of mobile DNA in the evolution of vancomycin-resistant Enterococcus faecalis," Science, vol. 299, no. 5615, pp. 2071–2074, 2003. https://doi.org/10.1126/science.1080613

[14] Y. Benjamini and Y. Hochberg, "Controlling the false discovery rate: a practical and powerful approach to multiple testing," Journal of the Royal Statistical Society: Series B, vol. 57, no. 1, pp. 289–300, 1995. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x