Prediction of antibiotic resistance in *Escherichia coli* from resistance genes

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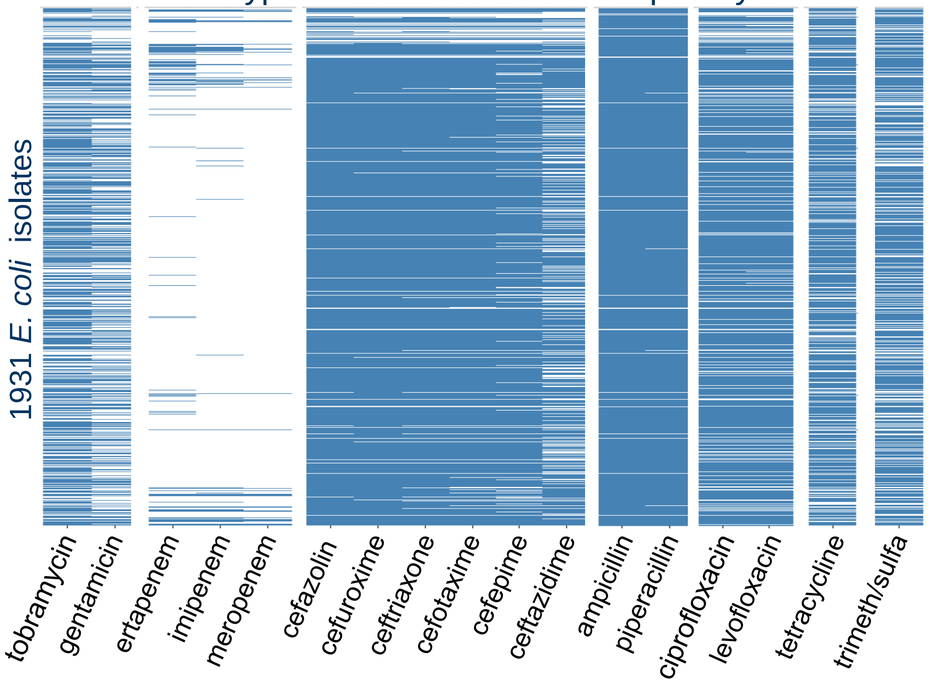
Background: Phenotypic antimicrobial susceptibility testing (AST) is the standard guide for antibiotic use, but it takes days to perform. Molecular tests can rapidly detect resistance genes within hours of specimen collection, but they have not demonstrated comprehensive prediction of phenotypic antibiotic resistance.

Material/Methods: We compared PCR results for 126 resistance genes with phenotypic AST results across 1931 highly resistant clinical isolates of *E. coli* including 1366 ESBLs collected at the Intermountain Medical Center over 2008 to 2015 plus 565 *E. coli* isolates from Merck's SMART Surveillance Network as supplied by International Health Management Associates. Statistical models were used to predict antibiotic resistance from resistance genes.

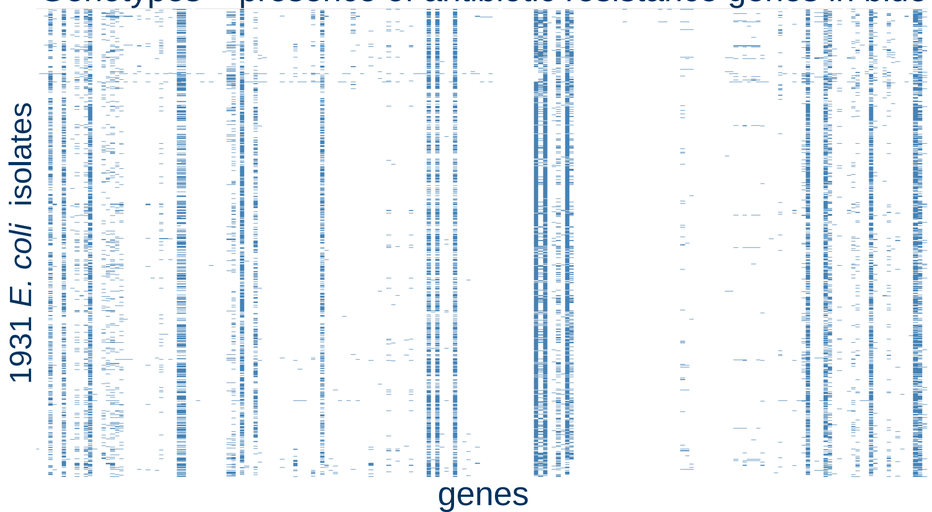
Genotypic prediction of phenotypic non-susceptibility for 1931 *E. coli* isolates

Antibiotic Class	Antibiotic	Accuracy %	Sensitivity %	Specificity %	PPV %	NPV %
Aminoglycosides	Tobramycin	90	91	88	90	90
	Gentamicin	91	87	94	89	92
Carbapenems	Ertapenem	90	52	94	45	95
	Imipenem	94	55	96	46	97
	Meropenem	97	58	98	49	99
Cephalosporins	Cefazolin	88	90	73	97	44
	Cefuroxime	90	91	76	97	52
	Ceftriaxone	92	94	79	97	66
	Cefotaxime	89	91	79	96	61
	Cefepime	88	92	72	92	70
	Ceftazidime	77	81	73	81	73
Penicillins	Ampicillin	95	96	71	99	43
	Piperacillin	94	95	76	99	48
Fluroquinolones	Ciprofloxacin	93	95	85	96	83
	Levofloxacin	93	95	87	96	85
Macrolides	Tetracycline	92	94	89	95	87
Co-trimoxazoles	Trimeth/Sulfa	89	93	83	91	86

Phenotypes – antibiotic non-susceptibility in blue



Genotypes – presence of antibiotic resistance genes in blue



Results: We identified a panel of critical resistance genes and developed statistical algorithms to accurately predict phenotypic resistance for several antibiotics across 1931 highly resistant clinical isolates of *E. coli.* The study demonstrates rapid genotypic prediction of resistance for 17 antibiotics representing 7 antibiotic classes as comprehensive information toward antibiotic options against a spectrum of resistance. Future studies will improve prediction of carbapenem resistance through evaluation of more *E. coli* isolates.

Conclusions: Molecular detection of resistance genes offers the potential to predict antibiotic resistance days ahead of phenotypic AST for Gram-negative bacteria toward better patient and hospital management.