

Appendix 2. HBC antibiotic resistance determinant groupings

Table A2.1. The genetic determinants of antibiotic resistance predicted in the HBC genomes, as described in CARD, were grouped by the antibiotic to which they are described as conferring resistance. If more than one antibiotic class was included for a single determinant, these determinants were grouped as “non-specific”. The exception is for resistances to Macrolide, Lincosamide, Pleuromutilin and Streptogramin (MLPS) antibiotics, as resistance determinants against these antibiotics can have cross-resistance to each other.

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Acridine dye	Acridine dye	<i>emeA</i>	Antibiotic efflux
Aminocoumarin	Aminocoumarin antibiotic	<i>mdtA</i>	Antibiotic efflux
Aminocoumarin	Aminocoumarin antibiotic	<i>mdtB</i>	Antibiotic efflux
Aminocoumarin	Aminocoumarin antibiotic	<i>mdtC</i>	Antibiotic efflux
Aminoglycoside	Aminoglycoside	<i>aac(6')-le-aph(2")-la</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aac(6')-li</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aac(6')-lih</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aadA</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aadK</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>ant(6)-la</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>Ant(6)-lb</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(2")</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(2")-lf</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(2")-lla</i>	Antibiotic inactivation

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Aminoglycoside	Aminoglycoside	<i>aph(3'')-Ib</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(3')-Ia</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(3')-IIIa</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>aph(6')-Id</i>	Antibiotic inactivation
Aminoglycoside	Aminoglycoside	<i>kdpE</i>	Antibiotic efflux
Aminoglycoside	Aminoglycoside antibiotic	<i>acrD</i>	Antibiotic efflux
Beta-lactam	Carbapenem, cephalosporin, penam	<i>shv</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin	<i>cblA_1</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin	<i>cepA</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin, monobactam, penam	<i>oxy_2</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin, penam	<i>bcl</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin, penam	<i>bcll</i>	Antibiotic inactivation
Beta-lactam	Cephalosporin, penam	<i>oxa_114a</i>	Antibiotic inactivation
Beta-lactam	Cephamycin	<i>cfxA</i>	Antibiotic inactivation
Beta-lactam	Cephamycin	<i>cmy_101</i>	Antibiotic inactivation
Beta-lactam	Monobactam, cephalosporin, penam, penem	<i>tem</i>	Antibiotic inactivation
Beta-lactam	Monobactam, cephamycin, cephalosporin, penam, carbapenem, penem	<i>K. pneumoniae ompK35</i>	Resistance by absence or reduced permeability to antibiotic
Beta-lactam	Penam	<i>blaZ</i>	Antibiotic inactivation
Beta-lactam	Penam, carbapenem, cephamycin, cephalosporin	<i>act</i>	Antibiotic inactivation
Beta-lactam	Penam carbapenem, cephamycin, cephalosporin	<i>act_1</i>	Antibiotic inactivation
Beta-lactam	Penam, carbapenem, cephamycin, cephalosporin, penem, monobactam	<i>K. pneumoniae ompK36</i>	Resistance by absence or reduced permeability to antibiotic
Beta-lactam	Penam carbapenem, cephamycin, cephalosporin, penem, monobactam	<i>ompC</i>	Resistance by absence or reduced permeability to antibiotic
Beta-lactam	Penam, cephalosporin	<i>ampC_2</i>	Antibiotic inactivation

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Beta-lactam	Penam, cephalosporin	<i>oxa_347</i>	Antibiotic inactivation
Beta-lactam	Penam,cephalosporin	<i>oxa_4</i>	Antibiotic inactivation
Beta-lactam	Penam,cephalosporin, monobactam	<i>acc</i>	Antibiotic inactivation
Beta-lactam	Penam, cephalosporin, monobactam	<i>oxy</i>	Antibiotic inactivation
Beta-lactam	Penam, monobactam, penam, carbapenem, cephamicin, cephalosporin	<i>K. pneumoniae ompK37</i>	Resistance by absence or reduced permeability to antibiotic
Beta-lactam	Penem, penam	<i>len_1</i>	Antibiotic inactivation
Chloramphenicol	Phenicol antibiotic	<i>cat</i>	Antibiotic inactivation
Chloramphenicol	Phenicol antibiotic	<i>E. faecalis chloramphenicol+</i>	Antibiotic inactivation
Diaminopyrimidine	Diaminopyrimidine antibiotic	<i>dfrA14</i>	Antibiotic target replacement
Diaminopyrimidine	Diaminopyrimidine antibiotic	<i>dfrC</i>	Antibiotic target replacement
Diaminopyrimidine	Diaminopyrimidine antibiotic	<i>dfrE</i>	Antibiotic target replacement
Diaminopyrimidine	Diaminopyrimidine antibiotic	<i>dfrF</i>	Antibiotic target replacement
Diaminopyrimidine	Diaminopyrimidine antibiotic	<i>dfrG</i>	Antibiotic target replacement
Elfamycin	Elfamycin	<i>E. coli ef-tu</i>	Antibiotic target alteration
Fluoroquinolone	Fluoroquinolone antibiotic	<i>emrA</i>	Antibiotic efflux
Fluoroquinolone	Fluoroquinolone antibiotic	<i>emrB</i>	Antibiotic efflux
Fluoroquinolone	Fluoroquinolone antibiotic	<i>emrR</i>	Antibiotic efflux
Fluoroquinolone	Fluoroquinolone antibiotic	<i>mdtH</i>	Antibiotic efflux
Fluoroquinolone	Fluoroquinolone antibiotic	<i>patA</i>	Antibiotic efflux
Fosfomycin	Fosfomycin	<i>E. coli cyaA</i>	Antibiotic target alteration
Fosfomycin	Fosfomycin	<i>E. coli glpT</i>	Antibiotic target alteration
Fosfomycin	Fosfomycin	<i>E. coli uhpA</i>	Antibiotic target alteration
Fosfomycin	Fosfomycin	<i>E. coli uhpT</i>	Antibiotic target alteration
Fosfomycin	Fosfomycin	<i>fosA2</i>	Antibiotic inactivation

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Fosfomycin	Fosfomycin	<i>fosA5</i>	Antibiotic inactivation
Fosfomycin	Fosfomycin	<i>fosA7</i>	Antibiotic inactivation
Fosfomycin	Fosfomycin	<i>fosB</i>	Antibiotic inactivation
Fosfomycin	Fosfomycin	<i>mdtG</i>	Antibiotic efflux
Glycopeptide	Glycopeptide antibiotic	<i>vanA</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanC</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanD</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanHA</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanHD</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanRA</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanRC</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanRD</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanSA</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanSC</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanTC</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanXA</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanXD</i>	Antibiotic target alteration
Glycopeptide	Glycopeptide antibiotic	<i>vanXYC</i>	Antibiotic target alteration
MLPS	Lincosamide antibiotic	<i>lmrB</i>	Antibiotic efflux
MLPS	Lincosamide antibiotic	<i>InuC</i>	Antibiotic inactivation
MLPS	Lincosamide antibiotic	<i>InuG</i>	Antibiotic inactivation
MLPS	Lincosamide antibiotic macrolide antibiotic, streptogramin antibiotic	<i>ermB</i>	Antibiotic target alteration
MLPS	Lincosamide antibiotic, streptogramin antibiotic, macrolide antibiotic	<i>ermG</i>	Antibiotic target alteration
MLPS	Macrolide antibiotic	<i>mefA</i>	antibiotic efflux
MLPS	Macrolide antibiotic, lincosamide antibiotic, streptogramin antibiotic	<i>ermF</i>	Antibiotic target alteration

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
MLPS	Pleuromutilin antibiotic, lincosamide antibiotic	<i>IsaE</i>	Antibiotic efflux
MLPS	Pleuromutilin antibiotic, lincosamide antibiotic, streptogramin antibiotic	<i>eatAv</i>	Antibiotic efflux
MLPS	Streptogramin antibiotic, lincosamide antibiotic, macrolide antibiotic	<i>ermQ</i>	Antibiotic target alteration
MLPS	Streptogramin antibiotic, lincosamide antibiotic, pleuromutilin antibiotic	<i>IsaA</i>	Antibiotic efflux
MLPS	Streptogramin antibiotic, macrolide antibiotic	<i>mel</i>	Antibiotic efflux
MLPS	Streptogramin antibiotic, macrolide antibiotic	<i>msrC</i>	Antibiotic efflux
MLPS	Streptogramin antibiotic, macrolide antibiotic, lincosamide antibiotic	<i>ermD</i>	Antibiotic efflux
MLPS	Streptogramin antibiotic, pleuromutilin antibiotic	<i>vgaC</i>	Antibiotic efflux
Mupirocin	Mupirocin	<i>ileS</i>	antibiotic target alteration
Nitrofuran	Nitrofuran antibiotic	<i>nfsA</i>	antibiotic target alteration
Nitroimidazole	Nitroimidazole antibiotic	<i>msbA</i>	Antibiotic efflux
Non-specific	Acridine dye, fluoroquinolone antibiotic	<i>blt</i>	Antibiotic efflux
Non-specific	Acridine dye, fluoroquinolone antibiotic	<i>cdeA</i>	Antibiotic efflux
Non-specific	Aminocoumarin antibiotic, aminoglycoside antibiotic	<i>baeR</i>	Antibiotic efflux
Non-specific	Aminocoumarin antibiotic, aminoglycoside antibiotic	<i>baeS</i>	Antibiotic efflux
Non-specific	Aminocoumarin antibiotic, aminoglycoside antibiotic	<i>cpxA</i>	Antibiotic efflux
Non-specific	Aminoglycoside antibiotic, fluoroquinolone antibiotic	<i>mipA</i>	Resistance by absence or reduced permeability to antibiotic
Non-specific	Aminoglycoside antibiotic, tetracycline antibiotic, phenicol antibiotic	<i>ykkC</i>	Antibiotic efflux
Non-specific	Cephalosporin, macrolide antibiotic, aminoglycoside antibiotic, fluoroquinolone antibiotic	<i>axyX</i>	Antibiotic efflux
Non-specific	Cephalosporin, macrolide antibiotic, aminoglycoside antibiotic, fluoroquinolone antibiotic	<i>axyZ</i>	Antibiotic efflux
Non-specific	Fluoroquinolone antibiotic, acridine dye	<i>norA</i>	Antibiotic efflux
Non-specific	Fluoroquinolone antibiotic, macrolide antibiotic, penam, cephamycin, cephalosporin, tetracycline antibiotic	<i>h_ns</i>	Antibiotic efflux

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Non-specific	Fluoroquinolone antibiotic, penam, cephamycin, cephalosporin	<i>acrF</i>	Antibiotic efflux
Non-specific	Fluoroquinolone antibiotic, penam, macrolide antibiotic	<i>crp</i>	Antibiotic efflux
Non-specific	Fluoroquinolone antibiotic, penam, macrolide antibiotic	<i>mdtE</i>	Antibiotic efflux
Non-specific	Fluoroquinolone antibiotic, penam, tetracycline antibiotic, macrolide antibiotic	<i>evgA</i>	Antibiotic efflux
Non-specific	Glycopeptide antibiotic, streptogramin antibiotic, lincosamide antibiotic, macrolide antibiotic, phenicol antibiotic, pleuromutilin antibiotic	<i>Propionibacterium 23S rRNA</i>	Antibiotic target alteration
Non-specific	Glycopeptide antibiotic, streptogramin antibiotic, lincosamide antibiotic, macrolide antibiotic, phenicol antibiotic, pleuromutilin antibiotic	<i>S. pneumoniae 23S rRNA</i>	Antibiotic target alteration
Non-specific	Glycopeptide antibiotic, streptogramin antibiotic, macrolide antibiotic, phenicol antibiotic, lincosamide antibiotic, pleuromutilin antibiotic	<i>E. coli 23S rRNA</i>	Antibiotic target alteration
Non-specific	Glycopeptide antibiotic, streptogramin antibiotic, macrolide antibiotic, phenicol antibiotic, lincosamide antibiotic, pleuromutilin antibiotic, oxazolidinone antibiotic	<i>S. aureus 23S rRNA</i>	Antibiotic target alteration
Non-specific	Glycopeptide antibiotic, tetracycline antibiotic, glycylcycline, nucleoside antibiotic, aminoglycoside antibiotic, peptide antibiotic	<i>rrsB</i>	Antibiotic target alteration
Non-specific	Glycopeptide antibiotic, tetracycline antibiotic, peptide antibiotic, aminoglycoside antibiotic, nucleoside antibiotic, glycylcycline	<i>M. abscessus 16S rRNA</i>	Antibiotic target alteration
Non-specific	Macrolide antibiotic, cephalosporin, aminoglycoside antibiotic, fluoroquinolone antibiotic	<i>axyY</i>	Antibiotic efflux
Non-specific	Macrolide antibiotic, cephalosporin, aminoglycoside antibiotic, fluoroquinolone antibiotic	<i>oprZ</i>	Antibiotic efflux
Non-specific	Macrolide antibiotic, fluoroquinolone antibiotic	<i>efmA</i>	Antibiotic efflux
Non-specific	Macrolide antibiotic, penam, fluoroquinolone antibiotic	<i>gadW</i>	Antibiotic efflux
Non-specific	Macrolide antibiotic, penam, fluoroquinolone antibiotic	<i>gadX</i>	Antibiotic efflux
Non-specific	Nucleoside antibiotic, acridine dye	<i>mdtN</i>	Antibiotic efflux
Non-specific	Nucleoside antibiotic, acridine dye	<i>mdtO</i>	Antibiotic efflux
Non-specific	Nucleoside antibiotic, acridine dye	<i>mdtP</i>	Antibiotic efflux
Non-specific	Nucleoside antibiotic, phenicol antibiotic, acridine dye, fluoroquinolone antibiotic	<i>bmr</i>	Antibiotic efflux

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Non-specific	Nucleoside antibiotic, phenicol antibiotic, lincosamide antibiotic, fluoroquinolone antibiotic, acridine dye	<i>mdtM</i>	Antibiotic efflux
Non-specific	Penam, cephamycin, cephalosporin, fluoroquinolone antibiotic	<i>acrE</i>	Antibiotic efflux
Non-specific	Penam, macrolide antibiotic, fluoroquinolone antibiotic	<i>mdtF</i>	Antibiotic efflux
Non-specific	Peptide antibiotic, macrolide antibiotic	<i>mgrB</i>	Resistance by absence, antibiotic efflux and antibiotic target alteration
Non-specific	Tetracycline antibiotic, benzalkonium chloride, rhodamine	<i>mdfA</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, cephalosporin, rifamycin antibiotic, phenicol antibiotic, glycyclcline, penam, fluoroquinolone antibiotic, triclosan	<i>acrA1</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, diaminopyrimidine antibiotic, glycyclcline, nitrofuran antibiotic, fluoroquinolone antibiotic	<i>oqxA</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, fluoroquinolone antibiotic	<i>E. coli lamB</i>	Resistance by absence or reduced permeability to antibiotic
Non-specific	Tetracycline antibiotic, glycyclcline, rifamycin antibiotic, phenicol antibiotic, fluoroquinolone antibiotic, penam, cephamycin, cephalosporin, triclosan	<i>acrS</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, macrolide antibiotic, fluoroquinolone antibiotic, penam	<i>evgS</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, nitrofuran antibiotic, fluoroquinolone antibiotic, glycyclcline, diaminopyrimidine antibiotic	<i>oqxB</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, penam, cephalosporin, glycyclcline, rifamycin antibiotic, phenicol antibiotic, triclosan, fluoroquinolone antibiotic	<i>acrB</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, penam, cephalosporin, rifamycin antibiotic, phenicol antibiotic, glycyclcline, fluoroquinolone antibiotic, triclosan	<i>acrA</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, penam, cephalosporin, rifamycin antibiotic, phenicol antibiotic, glycyclcline, fluoroquinolone antibiotic, triclosan	<i>marR</i>	Antibiotic efflux and antibiotic target alteration
Non-specific	Tetracycline antibiotic, penem, penam, carbapenem, cephamycin, cephalosporin, rifamycin antibiotic, phenicol antibiotic, monobactam, glycyclcline, fluoroquinolone antibiotic, triclosan	<i>marA</i>	Antibiotic efflux and reduced permeability to beta-lactams

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Non-specific	Tetracycline antibiotic, phenicol antibiotic, aminoglycoside antibiotic	<i>ykkD</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, phenicol antibiotic, glycylcycline, penam, cephalosporin, rifamycin antibiotic, fluoroquinolone antibiotic, triclosan	<i>acrA2</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, rifamycin antibiotic, phenicol antibiotic, aminocoumarin antibiotic, fluoroquinolone antibiotic, penam, cephemycin, cephalosporin, glycylcycline, macrolide antibiotic, triclosan	<i>tolC</i>	Antibiotic efflux
Non-specific	Tetracycline antibiotic, rifamycin antibiotic, phenicol antibiotic, glycylcycline, penam, cephalosporin, triclosan, fluoroquinolone antibiotic	<i>ramR</i>	Antibiotic efflux
Non-specific		<i>emrD</i>	Antibiotic efflux
Non-specific		<i>emrE</i>	Antibiotic efflux
Nucleoside	Nucleoside antibiotic	<i>sat2</i>	Antibiotic inactivation
Nucleoside	Nucleoside antibiotic	<i>sat4</i>	Antibiotic inactivation
Nucleoside	Nucleoside antibiotic	<i>tmrB</i>	Reduced permeability to antibiotic
Peptide	Peptide antibiotic	<i>bacA</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>bcrA</i>	Antibiotic efflux
Peptide	Peptide antibiotic	<i>bcrB</i>	Antibiotic efflux
Peptide	Peptide antibiotic	<i>bcrC</i>	Antibiotic efflux
Peptide	Peptide antibiotic	<i>eptA</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>mprF</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>mprF3</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>mprF4</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>pmrF</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>ugd</i>	Antibiotic target alteration
Peptide	Peptide antibiotic	<i>yojI</i>	Antibiotic efflux

Custom Group	CARD antibiotic classes	Antibiotic resistance gene/determinant	Mechanism
Sulphonamide	Sulfonamide antibiotic, sulfone antibiotic	<i>sul2</i>	Antibiotic target replacement
Tetracycline	Tetracycline antibiotic	<i>emrK</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>emrY</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>P. acnes 16S rRNA</i>	Antibiotic target alteration
Tetracycline	Tetracycline antibiotic	<i>tet_40</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>tet_J</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>tet_K</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>tet44</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic	<i>tetA_46</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>tetA_P</i>	Antibiotic efflux
Tetracycline	Tetracycline antibiotic	<i>tetB_P</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic	<i>tetM</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic	<i>tetO</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic	<i>tetQ</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic	<i>tetS</i>	Antibiotic target protection
Tetracycline	Tetracycline antibiotic, glycylcycline	<i>tetA</i>	Antibiotic efflux

Table A2.2. A complete list of HBC isolates and the antibiotic resistance genes and mutations identified in their genomes. The genetic determinants of antibiotic resistance predicted in the HBC genomes, as described in CARD, were grouped by the antibiotic to which they are described as conferring resistance. If more than one antibiotic class was included for a single determinant, these determinants were grouped as “non-specific”. The exception is for resistances to Macrolide, Lincosamide, Pleuromutilin and Streptogramin (MLPS) antibiotics, as resistance determinants against these antibiotics can have cross-resistance to each other. The table can be viewed here:

https://docs.google.com/spreadsheets/d/1zwmhUicOW3JVW_9y6P6LssbavW47EFiRq4_wwnS9CMg/edit?usp=sharing

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