(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
05 March 2020 (05.03.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/046801 A9

(51) International Patent Classification:
C12Q 1/04 (2006.01) *G01N 33/15* (2006.01)
C12Q 1/68 (2018.01)

(21) International Application Number:
PCT/US2019/048114

(22) International Filing Date:
26 August 2019 (26.08.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/723,417 27 August 2018 (27.08.2018) US
62/834,786 16 April 2019 (16.04.2019) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(48) Date of publication of this corrected version:
16 April 2020 (16.04.2020)

(54) Title: COMPOSITIONS AND METHODS FOR DETECTING ANTIBIOTIC RESPONSIVE mRNA EXPRESSION SIGNATURES AND USES THEREOF

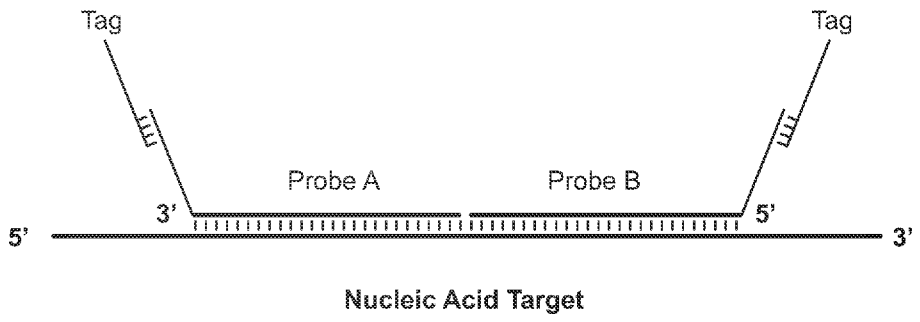


FIG. 1C

(57) Abstract: The present disclosure relates to compositions, methods, and kits for rapid phenotypic detection of antibiotic resistance/susceptibility.

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(15) Information about Correction:
see Notice of 16 April 2020 (16.04.2020)

COMPOSITIONS AND METHODS FOR DETECTING ANTIBIOTIC RESPONSIVE mRNA EXPRESSION SIGNATURES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is an International Patent Application which claims the benefit of priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No: 62/723,417, filed on August 27, 2018, entitled, "Compositions and Methods for Detecting Antibiotic Responsive mRNA Expression Signatures and Uses Thereof"; and to U.S. Provisional Application No: 62/834,786, filed on April 16, 2019, entitled, "Compositions and Methods for Detecting Antibiotic Responsive mRNA Expression Signatures and Uses Thereof." The entire contents of these patent applications are hereby incorporated by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

The invention was made with government support under Grant Nos. AI117043 and AI119157, awarded by the National Institutes of Health, and by contract No. HHSN272200900018C. The government has certain rights in the invention.

FIELD OF THE DISCLOSURE

The present disclosure relates to compositions, methods, and kits for rapid phenotypic detection of antibiotic resistance/susceptibility.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been filed electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 19, 2019, is named 52199_534001WO_BI10397_SL.txt and is 800 kB in size.

BACKGROUND OF THE DISCLOSURE

Antimicrobial agents such as antibiotics have been used successfully for many decades treat patients who have infectious diseases related to microbial pathogens. Unfortunately, these antimicrobial agents have been broadly used for such a long period of time that many microbial pathogens have become resistant to the antibiotics that are designed to kill them, which greatly reduces the efficacy of the antimicrobial agents that are currently available. This creates a significant

healthcare issue. For example, each year in the United States at least 2 million people become infected with antibiotic resistant bacteria, which results in the death of at least 23,000 people each year. Accordingly, there is an urgent need for compositions and methods that enable rapid and accurate detection of antibiotic resistance in microbial pathogens.

BRIEF SUMMARY OF THE DISCLOSURE

The current disclosure relates, at least in part, to compositions, methods, and kits for rapid phenotypic detection of antibiotic resistance. The techniques herein provide compositions and methods that provide rapid phenotypic detection of antibiotic resistance/susceptibility in microbial pathogens, and are faster than the prior art growth-based phenotypic assays that currently comprise the gold standard for such detection (e.g., antibiotic susceptibility testing (AST)). The techniques herein also provide compositions and methods that enable simultaneous detection of multiple resistance genes in the same assay. In this manner, the techniques herein enable more accurate determination of antibiotic resistance, as well as provide: 1) mechanistic explanations for key antibiotic resistant strains, 2) epidemiologic tracking of known resistance mechanisms, and 3) immediate identification of unknown or potentially novel resistance mechanisms (such as, e.g., discordant cases when a resistant organism does not display a known resistance phenotype). Currently, detection of antibiotic resistance genes typically requires separate PCR or sequencing assays, which require different assay infrastructure and often necessitate sending samples out to reference laboratories.

In one aspect, the disclosure provides a method that includes the following steps: obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a patient or an environmental source; processing the sample to enrich the one or more bacterial cells; contacting the sample with one or more antibiotic compounds; lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; hybridizing the released mRNA to at least one set of two nucleic acid probes, wherein each nucleic acid probe includes a unique barcode or tag; detecting the hybridized nucleic acid probes; identifying one or more genetic resistance determinants; and determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells.

In embodiments, the at least one set of two nucleic acid probes includes one or more probes from **Table 3** and one or more probes from **Table 4**.

In embodiments, the at least one set of two nucleic acid probes includes one or more probes from **Table 5** and one or more probes from **Table 6**.

In some embodiments, the at least one set of two nucleic acid probes includes a first probe that possesses a sequence of SEQ ID NOs: 1877-2762 and a second probe that possesses a sequence of SEQ ID NOs: 2763-3648. Optionally, the first probe possesses a sequence of SED ID NO: (1877+n) and the second probe possesses a sequence of SEQ ID NO: (2763+n), where n = an integer ranging from 0 to 885 in value. Optionally, one or both probes further includes a tag sequence.

In embodiments, the at least one set of two nucleic acid probes binds to one or more Cre2 target sequences listed in **Table 1**.

In embodiments, the at least one set of two nucleic acid probes binds to one or more KpMero4 target sequences listed in **Table 2**.

In embodiments, the hybridizing may occur at a temperature between about 64°C and about 69°C. The hybridizing may occur at a temperature between about 65°C and about 67°C. The hybridizing may also occur at a temperature of about 65°C or about 66°C or about 67°C. The hybridizing may occur at a temperature of about 65.0°C, 65.1°C, 65.2°C, 65.3°C, 65.4°C, 65.5°C, 65.6°C, 65.7°C, 65.8°C, 65.9°C, 66.0°C, 66.1°C, 66.2°C, 66.3°C, 66.4°C, 66.5°C, 66.6°C, 66.7°C, 66.8°C, 66.9°C, 67.0°C, 67.1°C, 67.2°C, 67.3°C, 67.4°C, 67.5°C, 67.6°C, 67.7°C, 67.8°C, or 67.9°C.

In one aspect, the disclosure provides a composition comprising a set of nucleic acid probes corresponding to the probes listed in **Table 3** and **Table 4**.

In one aspect, the disclosure provides a composition comprising a set of nucleic acid probes corresponding to the probes listed in **Table 5** and **Table 6**.

In an aspect, the disclosure provides a composition that includes at least one set of two nucleic acid probes including a first probe that possesses a sequence of SEQ ID NOs: 1877-2762 and a second probe that possesses a sequence of SEQ ID NOs: 2763-3648. Optionally, the first probe possesses a sequence of SED ID NO: (1877+n) and the second probe possesses a sequence of SEQ ID NO: (2763+n), where n = an integer ranging from 0 to 885 in value. Optionally, one or both probes further includes a tag sequence.

In one aspect, the disclosure provides a method of treating a patient that includes the steps of: obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a

patient or an environmental source; processing the sample to enrich the one or more bacterial cells; contacting the sample with one or more antibiotic compounds;

lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; hybridizing the released mRNA to at least one set of two nucleic acid probes at 65-67°C, wherein each nucleic acid probe includes a unique barcode or tag; detecting the hybridized nucleic acid probes; identifying one or more genetic resistance determinants; determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; and administering to the patient an appropriate antibiotic based on the determination of the identity and the antibiotic susceptibility of the one or more bacterial cells.

In embodiments, the processing includes subjecting the sample to centrifugation or differential centrifugation.

In embodiments, the one or more antibiotic compounds are at a clinical breakpoint concentration.

In embodiments, lysing occurs by a method selected from the group consisting of mechanical lysis, liquid homogenization lysis, sonication, freeze-thaw lysis, and manual grinding.

In embodiments, the at least one set of two nucleic acid probes includes one control set and one responsive set, 3-5 control sets and 3-5 responsive sets, or 8-10 control sets and 8-10 responsive sets.

In embodiments, the hybridizing may occur at a temperature between about 64°C and about 69°C. The hybridizing may occur at a temperature between about 65°C and about 67°C. The hybridizing may also occur at a temperature of about 65°C or about 66°C or about 67°C. The hybridizing may occur at a temperature of about 65.0°C, 65.1°C, 65.2°C, 65.3°C, 65.4°C, 65.5°C, 65.6°C, 65.7°C, 65.8°C, 65.9°C, 66.0°C, 66.1°C, 66.2°C, 66.3°C, 66.4°C, 66.5°C, 66.6°C, 66.7°C, 66.8°C, 66.9°C, 67.0°C, 67.1°C, 67.2°C, 67.3°C, 67.4°C, 67.5°C, 67.6°C, 67.7°C, 67.8°C, or 67.9°C.

In one aspect, the disclosure provides a kit, including a set of nucleic acid probes corresponding to the probes listed in **Table 3** and **Table 4**.

In one aspect, the disclosure provides a kit, comprising a set of nucleic acid probes corresponding to the probes listed in **Table 5** and **Table 6**.

Another aspect of the instant disclosure provides a kit, including at least one set of two nucleic acid probes including a first probe that possesses a sequence of SEQ ID NOs: 1877-2762

and a second probe that possesses a sequence of SEQ ID NOs: 2763-3648, and instructions for its use.

Definitions

Unless specifically stated or obvious from context, as used herein, the term "about" is understood as within a range of normal tolerance in the art, for example within 2 standard deviations of the mean. "About" can be understood as within 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1%, 0.05%, or 0.01% of the stated value. In certain embodiments, the term "approximately" or "about" refers to a range of values that fall within 25%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less in either direction (greater than or less than) of the stated reference value unless otherwise stated or otherwise evident from the context (except where such number would exceed 100% of a possible value). Unless otherwise clear from context, all numerical values provided herein are modified by the term "about."

The term "administration" refers to introducing a substance into a subject. In general, any route of administration applicable to antimicrobial agents (e.g., an antibiotic) may be utilized including, for example, parenteral (e.g., intravenous), oral, topical, subcutaneous, peritoneal, intra-arterial, inhalation, vaginal, rectal, nasal, introduction into the cerebrospinal fluid, or instillation into body compartments. In some embodiments, administration is oral. Additionally or alternatively, in some embodiments, administration is parenteral. In some embodiments, administration is intravenous.

By "agent" is meant any small compound (e.g., small molecule), antibody, nucleic acid molecule, or polypeptide, or fragments thereof or cellular therapeutics such as allogeneic transplantation and/or CART-cell therapy.

As herein, the term "algorithm" refers to any formula, model, mathematical equation, algorithmic, analytical or programmed process, or statistical technique or classification analysis that takes one or more inputs or parameters, whether continuous or categorical, and calculates an output value, index, index value or score. Examples of algorithms include but are not limited to ratios, sums, regression operators such as exponents or coefficients, biomarker value transformations and normalizations (including, without limitation, normalization schemes that are based on clinical parameters such as age, gender, ethnicity, etc.), rules and guidelines, statistical classification models, statistical weights, and neural networks trained on populations or datasets.

By "alteration" is meant a change (increase or decrease) in the expression levels or activity of a gene or polypeptide as detected by standard art known methods such as those described herein. As used herein, an alteration includes a 10% change in expression levels, preferably a 25% change, more preferably a 40% change, and most preferably a 50% or greater change in expression levels.

The transitional term "comprising," which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. By contrast, the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed disclosure.

By "control" or "reference" is meant a standard of comparison. In one aspect, as used herein, "changed as compared to a control" sample or subject is understood as having a level that is statistically different than a sample from a normal, untreated, or control sample. Control samples include, for example, cells in culture, one or more laboratory test animals, or one or more human subjects. Methods to select and test control samples are within the ability of those in the art. Determination of statistical significance is within the ability of those skilled in the art, e.g., the number of standard deviations from the mean that constitute a positive result.

"Detect" refers to identifying the presence, absence or amount of the analyte (e.g., rRNA, mRNA, and the like) to be detected.

By "detectable label" is meant a composition that when linked to a molecule of interest (e.g., a nucleic acid probe) renders the latter detectable, via spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include radioactive isotopes, magnetic beads, metallic beads, colloidal particles, fluorescent dyes, electron-dense reagents, enzymes (for example, as commonly used in an ELISA), biotin, digoxigenin, or haptens. As used herein, the term "gene" refers to a DNA sequence in a chromosome that codes for a product (either RNA or its translation product, a polypeptide). A gene contains a coding region and includes regions preceding and following the coding region (termed respectively "leader" and "trailer"). The coding region is comprised of a plurality of coding segments ("exons") and intervening sequences ("introns") between individual coding segments.

The disclosure provides a number of specific nucleic acid targets (e.g., mRNA transcripts) or sets of nucleic acid targets that are useful for the identifying microbial pathogens (e.g., bacteria)

that are susceptible or resistant to treatment with specific antibiotics. In addition, the methods of the disclosure provide a facile means to identify therapies that are safe and efficacious for use in subjects that have acquired bacterial infections involving antibiotic resistant strains of bacteria. In addition, the methods of the disclosure provide a route for analyzing virtually any number of bacterial strains via antibiotic susceptibility testing (AST) to identify mRNA signature patterns indicative of antibiotic susceptibility or resistance, which may then be used to rapidly identify such traits in the clinic, and direct appropriate therapeutic intervention.

By "fragment" is meant a portion of a polypeptide or nucleic acid molecule. This portion contains, preferably, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of the entire length of the reference nucleic acid molecule or polypeptide. A fragment may contain 10, 20, 30, 40, 50, 60, 70, 80, 90, or 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 nucleotides or amino acids.

"Hybridization" means hydrogen bonding, which may be Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding, between complementary nucleobases. For example, adenine and thymine are complementary nucleobases that pair through the formation of hydrogen bonds.

"Infectious diseases," also known as communicable diseases or transmissible diseases, comprise clinically evident illness (i.e., characteristic medical signs and/or symptoms of disease) resulting from the infection, presence, and growth of pathogenic biological agents (e.g., bacteria) in a subject (Ryan and Ray (eds.) (2004). Sherris Medical Microbiology (4th ed.). McGraw Hill). A diagnosis of an infectious disease can confirmed by a physician through, e.g., diagnostic tests (e.g., blood tests), chart review, and a review of clinical history. In certain cases, infectious diseases may be asymptomatic for some or all of their course. Infectious pathogens can include viruses, bacteria, fungi, protozoa, multicellular parasites, and prions. One of skill in the art would recognize that transmission of a pathogen can occur through different routes, including without exception physical contact, contaminated food, body fluids, objects, airborne inhalation, and through vector organisms. Infectious diseases that are especially infective are sometimes referred to as contagious and can be transmitted by contact with an ill person or their secretions.

The terms "isolated," "purified, " or "biologically pure" refer to material that is free to varying degrees from components which normally accompany it as found in its native state.

"Isolate" denotes a degree of separation from original source or surroundings. "Purify" denotes a degree of separation that is higher than isolation.

By "isolated polynucleotide" is meant a nucleic acid (e.g., a DNA) that is free of the genes which, in the naturally-occurring genome of the organism from which the nucleic acid molecule of the disclosure is derived, flank the gene. The term therefore includes, for example, a recombinant DNA that is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote; or that exists as a separate molecule (for example, a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences. In addition, the term includes an RNA molecule that is transcribed from a DNA molecule, as well as a recombinant DNA that is part of a hybrid gene encoding additional polypeptide sequence.

By "marker" is meant any protein or polynucleotide having an alteration in expression level or activity that is associated with a disease or disorder (e.g., increased or decreased expression in a bacterial strain indicative of antibiotic susceptibility).

As used herein, the term "next-generation sequencing (NGS)" refers to a variety of high-throughput sequencing technologies that parallelize the sequencing process, producing thousands or millions of sequence reads at once. NGS parallelization of sequencing reactions can generate hundreds of megabases to gigabases of nucleotide sequence reads in a single instrument run. Unlike conventional sequencing techniques, such as Sanger sequencing, which typically report the average genotype of an aggregate collection of molecules, NGS technologies typically digitally tabulate the sequence of numerous individual DNA fragments (sequence reads discussed in detail below), such that low frequency variants (e.g., variants present at less than about 10%, 5% or 1% frequency in a heterogeneous population of nucleic acid molecules) can be detected. The term "massively parallel" can also be used to refer to the simultaneous generation of sequence information from many different template molecules by NGS. NGS sequencing platforms include, but are not limited to, the following: Massively Parallel Signature Sequencing (Lynx Therapeutics); 454 pyro-sequencing (454 Life Sciences/Roche Diagnostics); solid-phase, reversible dye-terminator sequencing (Solexa/Illumina); SOLiD technology (Applied Biosystems); Ion semiconductor sequencing (ion Torrent); and DNA nanoball sequencing (Complete Genomics). Descriptions of certain NGS platforms can be found in the following: Shendure, et al., "Next-generation DNA sequencing," Nature, 2008, vol. 26, No. 10, 135-1 145; Mardis, "The impact of next-generation sequencing

technology on genetics," Trends in Genetics, 2007, vol. 24, No. 3, pp. 133-141 ; Su, et al., "Next-generation sequencing and its applications in molecular diagnostics" Expert Rev Mol Diagn, 2011, 11 (3):333-43; and Zhang et al., "The impact of next-generation sequencing on genomics," J Genet Genomics, 201, 38(3): 95-109.

Nucleic acid molecules useful in the methods of the disclosure include any nucleic acid molecule that encodes a polypeptide of the disclosure or a fragment thereof. Such nucleic acid molecules need not be 100% identical with an endogenous nucleic acid sequence, but will typically exhibit substantial identity. Polynucleotides having "substantial identity" to an endogenous sequence are typically capable of hybridizing with at least one strand of a double-stranded nucleic acid molecule. Nucleic acid molecules useful in the methods of the disclosure include any nucleic acid molecule that encodes a polypeptide of the disclosure or a fragment thereof. Such nucleic acid molecules need not be 100% identical with an endogenous nucleic acid sequence, but will typically exhibit substantial identity. Polynucleotides having "substantial identity" to an endogenous sequence are typically capable of hybridizing with at least one strand of a double-stranded nucleic acid molecule. By "hybridize" is meant pair to form a double-stranded molecule between complementary polynucleotide sequences (e.g., a gene described herein), or portions thereof, under various conditions of stringency. (See, e.g., Wahl, G. M. and S. L. Berger (1987) Methods Enzymol. 152:399; Kimmel, A. R. (1987) Methods Enzymol. 152:507).

For example, stringent salt concentration will ordinarily be less than about 750 mM NaCl and 75 mM trisodium citrate, preferably less than about 500 mM NaCl and 50 mM trisodium citrate, and more preferably less than about 250 mM NaCl and 25 mM trisodium citrate. Low stringency hybridization can be obtained in the absence of organic solvent, e.g., formamide, while high stringency hybridization can be obtained in the presence of at least about 35% formamide, and more preferably at least about 50% formamide. Stringent temperature conditions will ordinarily include temperatures of at least about 30°C, more preferably of at least about 37°C, and most preferably of at least about 42°C. Varying additional parameters, such as hybridization time, the concentration of detergent, e.g., sodium dodecyl sulfate (SDS), and the inclusion or exclusion of carrier DNA, are well known to those skilled in the art. Various levels of stringency are accomplished by combining these various conditions as needed. In a preferred: embodiment, hybridization will occur at 30° C in 750 mM NaCl, 75 mM trisodium citrate, and 1% SDS. In a more preferred embodiment, hybridization will occur at 37° C in 500 mM NaCl, 50 mM trisodium citrate, 1% SDS, 35%

formamide, and 100 μg /ml denatured salmon sperm DNA (ssDNA). In a most preferred embodiment, hybridization will occur at 42° C in 250 mM NaCl, 25 mM trisodium citrate, 1% SDS, 50% formamide, and 200 μg/ml ssDNA. Useful variations on these conditions will be readily apparent to those skilled in the art.

For most applications, washing steps that follow hybridization will also vary in stringency. Wash stringency conditions can be defined by salt concentration and by temperature. As above, wash stringency can be increased by decreasing salt concentration or by increasing temperature. For example, stringent salt concentration for the wash steps will preferably be less than about 30 mM NaCl and 3 mM trisodium citrate, and most preferably less than about 15 mM NaCl and 1.5 mM trisodium citrate. Stringent temperature conditions for the wash steps will ordinarily include a temperature of at least about 25°C, more preferably of at least about 42°C, and even more preferably of at least about 68°C. In a preferred embodiment, wash steps will occur at 25°C in 30 mM NaCl, 3 mM trisodium citrate, and 0.1% SDS. In a more preferred embodiment, wash steps will occur at 42 C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. In a more preferred embodiment, wash steps will occur at 68°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. Additional variations on these conditions will be readily apparent to those skilled in the art. Hybridization techniques are well known to those skilled in the art and are described, for example, in Benton and Davis (Science 196:180, 1977); Grunstein and Hogness (Proc. Natl. Acad. Sci., USA 72:3961, 1975); Ausubel et al. (Current Protocols in Molecular Biology, Wiley Interscience, New York, 2001); Berger and Kimmel (Guide to Molecular Cloning Techniques, 1987, Academic Press, New York); and Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York.

By "substantially identical" is meant a polypeptide or nucleic acid molecule exhibiting at least 50% identity to a reference amino acid sequence (for example, any one of the amino acid sequences described herein) or nucleic acid sequence (for example, any one of the nucleic acid sequences described herein). Preferably, such a sequence is at least 60%, more preferably 80% or 85%, and more preferably 90%, 95% or even 99% identical at the amino acid level or nucleic acid to the sequence used for comparison.

Sequence identity is typically measured using sequence analysis software (for example, Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, Wis. 53705, BLAST, BESTFIT, GAP,

or PILEUP/PRETTYBOX programs). Such software matches identical or similar sequences by assigning degrees of homology to various substitutions, deletions, and/or other modifications. Conservative substitutions typically include substitutions within the following groups: glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid, asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. In an exemplary approach to determining the degree of identity, a BLAST program may be used, with a probability score between e-3 and e-100 indicating a closely related sequence.

Unless specifically stated or obvious from context, as used herein, the term "or" is understood to be inclusive. Unless specifically stated or obvious from context, as used herein, the terms "a", "an", and "the" are understood to be singular or plural.

The term "probe" as used herein refers to an oligonucleotide that binds specifically to a target mRNA. A probe can be single stranded at the time of hybridization to a target.

By "reference" is meant a standard or control condition.

A "reference sequence" is a defined sequence used as a basis for sequence comparison. A reference sequence may be a subset of or the entirety of a specified sequence; for example, a segment of a full-length mRNA or cDNA or gene sequence, or the complete mRNA or cDNA or gene sequence. For nucleic acids, the length of the reference nucleic acid sequence will generally be at least about 25 nucleotides, about 50 nucleotides, about 60 nucleotides, about 75 nucleotides, about 100 nucleotides, or about 300 nucleotides, or any integer thereabout or therebetween.

As used herein, the term "subject" includes humans and mammals (e.g., mice, rats, pigs, cats, dogs, and horses). In many embodiments, subjects are mammals, particularly primates, especially humans. In some embodiments, subjects are livestock such as cattle, sheep, goats, cows, swine, and the like; poultry such as chickens, ducks, geese, turkeys, and the like; and domesticated animals particularly pets such as dogs and cats. In some embodiments (e.g., particularly in research contexts) subject mammals will be, for example, rodents (e.g., mice, rats, hamsters), rabbits, primates, or swine such as inbred pigs and the like.

As used herein, the terms "treatment," "treating," "treat" and the like, refer to obtaining a desired pharmacologic and/or physiologic effect (e.g., reduction or elimination of a bacterial infection). The effect can be prophylactic in terms of completely or partially preventing a disease or infection or symptom thereof and/or can be therapeutic in terms of a partial or complete cure for a disease or infection and/or adverse effect attributable to the disease or infection. "Treatment," as

used herein, covers any treatment of a disease or condition or infection in a mammal, particularly in a human, and includes: (a) preventing the disease or infection from occurring in a subject which can be predisposed to the disease or infection but has not yet been diagnosed as having it; (b) inhibiting the disease or infection, e.g., arresting its development; and (c) relieving the disease or infection, e.g., reducing or eliminating a bacterial infection.

The phrase "pharmaceutically acceptable carrier" is art recognized and includes a pharmaceutically acceptable material, composition or vehicle, suitable for administering compounds of the present disclosure to mammals. The carriers include liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting the subject agent from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; phosphate buffer solutions; and other non-toxic compatible substances employed in pharmaceutical formulations.

The term "pharmaceutically acceptable salts, esters, amides, and prodrugs" as used herein refers to those carboxylate salts, amino acid addition salts, esters, amides, and prodrugs of the compounds of the present disclosure which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of patients without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the disclosure.

The term "salts" refers to the relatively non-toxic, inorganic and organic acid addition salts of compounds of the present disclosure. These salts can be prepared in situ during the final isolation and purification of the compounds or by separately reacting the purified compound in its free base form with a suitable organic or inorganic acid and isolating the salt thus formed. Representative

salts include the hydrobromide, hydrochloride, sulfate, bisulfate, nitrate, acetate, oxalate, valerate, oleate, palmitate, stearate, laurate, borate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate mesylate, glucoheptonate, lactobionate and laurylsulphonate salts, and the like. These may include cations based on the alkali and alkaline earth metals, such as sodium, lithium, potassium, calcium, magnesium, and the like, as well as non-toxic ammonium, tetramethylammonium, tetramethylammonium, methlyamine, dimethlyamine, trimethlyamine, triethlyamine, ethylamine, and the like. (See, for example, S. M. Barge et al., "Pharmaceutical Salts," J. Pharm. Sci., 1977, 66:1-19 which is incorporated herein by reference.).

Ranges can be expressed herein as from "about" one particular value and/or to "about" another particular value. When such a range is expressed, another aspect includes from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent "about," it is understood that the particular value forms another aspect. It is further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint. It is also understood that there are a number of values disclosed herein, and that each value is also herein disclosed as "about" that particular value in addition to the value itself. It is also understood that throughout the application, data are provided in a number of different formats and that this data represent endpoints and starting points and ranges for any combination of the data points. For example, if a particular data point "10" and a particular data point "15" are disclosed, it is understood that greater than, greater than or equal to, less than, less than or equal to, and equal to 10 and 15 are considered disclosed as well as between 10 and 15. It is also understood that each unit between two particular units are also disclosed. For example, if 10 and 15 are disclosed, then 11, 12, 13, and 14 are also disclosed.

Ranges provided herein are understood to be shorthand for all of the values within the range. For example, a range of 1 to 50 is understood to include any number, combination of numbers, or sub-range from the group consisting 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 as well as all intervening decimal values between the aforementioned integers such as, for example, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, and 1.9. With respect to sub-ranges, "nested sub-ranges" that extend from either end point of the range are specifically contemplated. For example, a

nested sub-range of an exemplary range of 1 to 50 may comprise 1 to 10, 1 to 20, 1 to 30, and 1 to 40 in one direction, or 50 to 40, 50 to 30, 50 to 20, and 50 to 10 in the other direction.

A “therapeutically effective amount” of an agent described herein is an amount sufficient to provide a therapeutic benefit in the treatment of a condition or to delay or minimize one or more symptoms associated with the condition (e.g., an amount sufficient to reduce or eliminate a bacterial infection). A therapeutically effective amount of an agent means an amount of therapeutic agent, alone or in combination with other therapies, which provides a therapeutic benefit in the treatment of the condition. The term “therapeutically effective amount” can encompass an amount that improves overall therapy, reduces or avoids symptoms, signs, or causes of the condition, and/or enhances the therapeutic efficacy of another therapeutic agent.

By “KpMero4_C_KPN_00050 nucleic acid molecule” is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding “N” residues, that is part of the KpMero4 probeset.

```
>KpMero4_C_KPN_00050(SEQ ID NO: 1)
ATGAAGAACTGGAAAACGCTGCTTCTCGGTATCGCCATGATCGCGAATACCAGTTTCGCT
GCCCCCCAGGTGGTCGATAAAGTAGCGGCCGTCGTCAATAATGGCGTCGTGCTGGAAAGC
GACGTCGATGGTTTGATGCAATCGGTTAAGCTCAATGCNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCAGAAAGATCGTGCTTACCGCATGCTGA
TGAACCGCAAATTCTCTGAAGAAGCGGCAACCTGGATGCAGGAACAGCGCGCCAGTGCGT
ATGTTAAAATTCTGAGCAACTAAN
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By “KpMero4_C_KPN_00098 nucleic acid molecule” is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH

78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

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>KpMero4_C_KPN_00098 (SEQ ID NO: 2)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGTGAAATGC
GTACAGCGCGCCATCGACCAGGCCGAACTGATGGCGGATTGCCAGATTTCATCAGTTTAT
TTGGCACTTTCGGGTAAACATATAAGCTGTCAGAATGAAATCGGGATGGTACCGATTTCG
GAAGAAGAAGTGACGCAGGANNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNGTCCTGCACGTGATTCCGCAGGAATATGCTATCGACTACCAGG
AAGGGATTAAAAACCCGGTAGGGCTGTCCGGCGTGCGTATGCAGGCGAAGGTGCATCTGA
TCACCTGCCATAACGATATGGCNNNNNNNNNNNNNNNNNNGTGGAACGTTGTGGTCTGAA
AGTTGACCAACTTATTTTCGCCGGGTTAGCGGCCAGTTATTCGGTATTAACAGAAGACGA
ACGTGAGCTGGGCGTCTGCGTTGTGGANNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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By "KpMero4_C_KPN_00100 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

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>KpMero4_C_KPN_00100 (SEQ ID NO: 3)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNGCGATTGATGCCAGCACCCAGCGCTATACGCTGAACTTCTCGGCCGAT
GCGTTCATGCGTCAGATTAGCCGTGCGCGTACCTTCGGTTTTATGCGCGATATCGAATAT
CTGCAGTCCCGCGGCCTGTGCCTGGGCGGCAGCTTCGATTGTGCCATCGTTGTTGACGAT
TATCGCGTACTGAACGAAGACGGTCTGCGCTTTGAAGACGAATTTGTTCGCCACAAAATG
CTGGATGCGATCGGTGACCTGTTTATGTGTGGTCACAACATTATCGGCGCATTCACGGCG
TACAAATCGGGTCACGCGTTGAACAACAAACTGCTGCAGGCGGTNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNN
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By "KpMero4_C_KPN_01276 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH

78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_C_KPN_01276 (SEQ ID NO: 4)
ATGCTGGAGTTGTTGTTTCTGCTTTTACCCGTTGCCGCCGCTTACGGCTGGTACATGGGG
CGCAGAAGTGCACAACAGTCCAAACAGGACGATGCGAGCCGCCTGTCGCGAGATTACGTG
GCGGGGGTTAACTTCCTGCTCAGCAACCAGCAGGATAAAGCCGTCGACCTGTTCCTTGAT
ATGCTGAAAGAGGATACCGGTACCGTTGAGGCNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNC
CGGCGGCGTCGGCGCAGGATCTGGTGATGAACTTTTCCGCCGACTGCTGGCTGGAAGTGA
GCGATGCCACCGGTAAAAAACTGTTCAGCGGCCTGCAGCGTAAAGGCGGTAANNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_C_KPN_02846 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_C_KPN_02846 (SEQ ID NO: 5)
ATGAATACTGAAGCCACTCAAGATCATCAAGAAGCAAACACCACGGGCGCGCGTCTGCGT
CACGCCCGCGAACAACTCGGACTTAGCCAGCAAGCGGTGGCCGAACGCTTATGCCTGAAG
GTGTCCACGGTTCGTGATATTGAAGACGATAAGGCCCCCGCCGACCTCGCCTCCACCTTC
CTGCGCGGNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
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NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNC
CGGCGGCGTCGGCGCAGGATCTGGTGATGAACTTTTCCGCCGACTGCTGGCTGGAAGTGA
GCGATGCCACCGGTAAAAAACTGTTCAGCGGCCTGCAGCGTAAAGGCGGTAANNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_C_KPN_03317 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_C_KPN_03317 (SEQ ID NO: 6)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN--ATGGCCGGGGAACACGTCATTTTGCTG
GATGAGCAGGATCAGCCTGCCGGTATGCTGGAGAAGTATGCCGCCCATACGTTTGATACC

CCTTTACATCTCGCGTTTTCCTGCTGGCTGTTTAANNNNNNNNNNNNNNNNNNNNNNN
NNCGTTCGTTGGGCAAAAAAGCCTGGCCCGGGGTATGGACCAACTCGGTCTGCGGACACC
CCCAGCAGGGCGAGACCTTCGAGCAGGCCGTCACGCGCCGCTGTCGCTTCGAACTCGGTG
TGGAGATCTCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCGCGTGGTAAGCGAAGTGC
AGCCTAACGACGATGAAGTCATGGACTATCAGTGGGTTGACCTGGCAACCATGTTAAGCG
CGCTGGCCGCCACGCCGTGGGCGTTCAGCCCGTGGATGGTGCTGGAAGCGGAAAATCGGG
ACGCCCGCCAGGCGCTGACCGAN

By "KpMero4_C_KPN_03634 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_C_KPN_03634 (SEQ ID NO: 7)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAACGATACGGCA
GACGACTCCCCGGCGAGCTATAACGCCGCGGTGCGCCGCGCGGCGCCCGCCGTGGTGAAC
GTCTATAACCGCGCCCTTAACAGCACCAGCCATAATCAGCTGACGCTTGGCTCAGGGGTG
ATTATGGATCAGCGCGGCTATATCCTGACCAACAAGCATGTTATCAACGATGCCGATCAG
ATTATCGTCGCCCTGCAGGACGGCCGCGTCTTCGAAGCGCTGCTGGTAGGATCCGATTCC
CTCACNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNCAGGGGATTATCAGCGCCACAGGGCGCATTGGCCTCAATCCGAC
CGGCCGCCAGAACTTCCTGCAGACTGACGCCTCGATCAACCACGGTAACTCCGGCGGGGC
NCTGGTGAACTCCCTCGGCGAGCTGATGGGGATTAACACCCTCTCCTTTGACAAGAGCAA
TGACGGCGAAACGCCGGAAGGCATTGGCTTTGCGATCCCGTTCCAGTTAGCGACCAAAAT
TATGGATAAACTGATCCGCGATGGCCGGGTGATCCGCGGCTATATCGGCATTAGCGGCCG
GGAGATCGCCCCGCTGCACGCGCAGGGCGGAGGGATCGATCAGATTCAGGGGATCGTNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNGCGCTGGAGACGATGGATCAGGTGGCCGAG
ATCCGCCCGGGATCGGAAATTCCGGTGGTCATCATGCGTGATGATAAGAAAATCACGCTC
CATATCGCCGTCCAGGAATACCCGGCCACCAACTAAN

By "KpMero4_C_KPN_04666 nucleic acid molecule" is meant a control polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721; reference genome NC_009648) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_C_KPN_04666 (SEQ ID NO: 8)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGTTGGCGATCCTATTC
ATCCTGTTACTGATTTTCTTTTGTCAGAAATTAGTCAGGATCCTCGGCGCCGCGGTGGAT
GGCGATATCCCAACCAATCTGGTGCTCTCGCTGTTGGGGCTCGGCATCCCGGAGATGGCG
CAGCTTATCCTGCCGTTAAGTCTGTTCCTTGGCCTGCTNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNAACCCCGGTA
TGGCGGCGCTGGCCCAGGGCCAGTTCCAGCAGGCCAGCGATGGTAACGCGGTGATGTTTA
TCGAAAGCGTCAACGGCAACCGCTTCCATGACGTCTTCCTTGCCCAGCTGCGTCCGAAAG
GCAATGCGCGCCCCTCGGTGGTGGTGGCGGATTCCGGCGAGCTGTCGCAGCAGAAAGACG

GCTCGCAGGTGGTGACCCTCAACAAGGGCACCCGCTTTGAAGGCACCGCGATGCTGCGCG
ANNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNACCGACCG
CGCGCGCGCCGAACTGCACTGGCGCTTCACGCTGGTGGCGACCGTCTTCATTATGGCGCT
GATGGTGGTGCCGCTCAGCGTGGTGAACCCGCGTCAGGGCCGNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNGGCTATCTGGATGTGGGCGATTAACCTGCTCTATTTTGCGCTG
GCGGTGCTGTTAAACCTGTGGGACACGGTGCCGATGCGCCGCTTCCGCGCCCGTTTTAAT
AAAGGAGCGGCCTGAN

By "KpMero4_R01up_KPN_01226 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R01up_KPN_01226 (SEQ ID NO: 9)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNGAAGAACGCCGCGCGATGCACGATCTGATCGCCAGCGACACCTTCGATAAGGCGAAGG
CGGAAGCGCAGATCGATAAGATGGAAGCGCAGCATAAAGCGATGGCGCTGTCCCGCCTGG
AAACGCAGAACAAGATCTACAACATTCTGACNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNN

By "KpMero4_R02up_KPN_01107 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R02up_KPN_01107 (SEQ ID NO: 10)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNGTGGCTGCCGCGCTGGGCGTTGCAGCTGTCGCTGGTCTCAACGTG
TTGGATCGCGGCCCGCAGTATGCGCAAGTGGTCTCCAGTACACCGATTAAAGAAACCGTG
AAAACGCCGCGTCAGGAATGCCGCAATGTCACGGTGACTCATCGTCGTCCGGTNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_R03up_KPN_02345 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R03up_KPN_02345 (SEQ ID NO: 11)

ATGATGCGAATCGCGCTTTTCCTGCTGACGAACCTGGCAGTGATGGTCGTGTTCGGGCTG
GTGTTAAGCCTCACGGGGATCCAATCCAGCAGCATGACCGGTCTTCTGATTATGGCCCTG
CTGTTCGGCTTCGGTGGTTCTATCGTTTCGCTGATGATGTCGAAGTGGATGGCGCTGAAG
TCNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_R04up_KPN_02742 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R04up_KPN_02742 (SEQ ID NO: 12)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNATCACCCTGCTGCCATCGGTAAAATTACAAATAGGCGATCGTGACAATTAC
GGTAACTACTGGGACGGTGGCAGCTGGCGCGACCGTGATTACTGGCGTCGTCACTATGAA
TGGCGTGATAACCGTTGGCATCGTCATGACAACGGCTGGCACN

By "KpMero4_R05dn_KPN_02241 nucleic acid molecule" is meant a downregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R05dn_KPN_02241 (SEQ ID NO: 13)
ATGAAACGCAAAAACGCTTCGTTACTCGGTAACGTACTCATGGGGTTAGGGTTGGTGGTG
ATGGTTGTGGGGGTAGGTTACTCCATTCTGAACCAGCTTCCGCAGCTTAACCTGCCACAA
TTCTTTGCGCATGGCGCAATCCTAAGCATCTTCGTTGGCGCAGTGCTCTGGCTGGCCGGT
GCCCGTATTGGCGGCCACGAGCAGGTCAGCGACCGCTACTGGTGGGTGCGCCACTACGAT
AAACGCTGCCGTCGTAACCAGCATCGTCACAGCTAAN

By "KpMero4_R06up_KPN_03358 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R06up_KPN_03358 (SEQ ID NO: 14)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNAACATGGACTCCAACGGTCTGCTCAGCTCAGGCGCCGAAGCCTTC
CAGGCATACTCTCTCAGCGACGCGCAGGTGAAAACCTTAAGCGACCAGGCCTGTAAAGAG
ATGGACGCCAAAGCGAAAATCGCCCCGGCCAACAGTGAATACAGCCAGCGGCTGAACAAA

ATCGCGNCTGCGCTGGGCGATAACATCAATGGTCAGCCCGTGAACTACAAGGTCTATGAG
ACCAAGGATGTCAACGCCTTCGCCATGGCCAACGGCTGCATCCGCGTCTACAGCGGGCTG
ATGGATCTGATGAACGATAATGAAGTCGAGGCGGNGATCGGCCACGAAATGGGCCACGTC
GCGCTGGGCCACGTGAAGAAAGGCATGCAGGTCGCCCTGGGTACCAACGCCGTGCGTGCG
GCGGCGGCCTCCGCGGGCGGNNNNNNNNNNAGCCTGTCGCAGTCTCAGTTGGGCGATCTGG
GCGAAAAACTGGTGAACTCGCAGTTCTCCCAGCGTCAGGAATCGGAAGCGGATGACTACT
CTTACGACCTGCTGCGTAAGCGCGGTATCAATCCGTCGGGACTGGCCACCAGCTTCGAGA
AACTGGCCAAGCTGGAAGCCGGCCGTCAGAGCTCCATGTTTGACGATCACCCGGCATCNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_R07up_KPN_03934 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R07up_KPN_03934 (SEQ ID NO: 15)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNN----ATGCCTTATATTACCAAGCAGAATCAGGCGATTACTGCGGATCGT
AACTGGCTTATTTCCAAGCAGTACGATGCTCGCTGGTCGCCGACTGAGAAGGCGCGCCTG
AAGGATATCGCTNCCCGTTATAAGGTGAAGTGGTCAGGCAATACGCGTCATGTGCCCTGG
AACGCGCTGCTTGAGCGTGTCGACATTATTCCGAACAGCATGGTGGCGACCATGGCGGCG
GCGGAAAGTGGCTGGGGTACCTCCAGGCTGGCGCGCGAGAATAACAACCTGTTCGGCATG
AAGTGCGGCGCCGGTCGCTGCCGCGGCGCGATGAAAGGTTACTCGCAGTTTGAGTCNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN

By "KpMero4_R08dn_KPN_00868 nucleic acid molecule" is meant a downregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R08dn_KPN_00868 (SEQ ID NO: 16)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNGCCAATATCGATATTGACGCCTATCTGCAACTGCGA
AAGGCCAAAGGCTACATGTCAGTCAGCGAAAATGACCATCTGCGTGATAACTTGTTTGAG
CTTTGCCGTGAAATGCGTGCGCAGGCGCCGCGCCTGCAGAATGCCATTTCACCGNNNNNN
NNNNNNNNNNNNNNNNNNNNGGCGAATCGGTCGCCGCCGCTGCACTATGCCTGATGAGCG
GGCATCATGATTGTCCGCTATACATCGCTGTTAACGTAGAGAAGCTAGAACGCTGTCTGA
CAGGATTGACCTCAAATATTCATAAATTGAATAAATTGGCGCCAATCACTCATGCCTGAN

By "KpMero4_R09up_KPN_02342 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R09up_KPN_02342 (SEQ ID NO: 17)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGTGGCTATCTTATGGATTGGCGTATTATTG
AGCGGTTATGGGGTGTTATTCCACAGTGAGGAAAACGTCGGCGGTCTGGGTCTTAAGTGC
CAATACCTCACCGCCCGCGGAGTCAGCACCGCACTTTATGTTCATTCCGACAGCGGAGTG
ATCGGCGTCAGCAGTTGCCCTCTGCTGCGTAAAAGCACAACCGTGGTTGATAACGGCTAA
N

By "KpMero4_R10up_KPN_00833 nucleic acid molecule" is meant an upregulated responsive polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following Klebsiella pneumoniae (strain MGH 78578, also known as ATCC 700721) sequence, excluding "N" residues, that is part of the KpMero4 probeset.

>KpMero4_R10up_KPN_00833 (SEQ ID NO: 18)
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNATCGGCGTGGTGT
CTGCGCAAGGCGCAACCACTTTAGATGGTCTGGAAGCAAAACTGGCTGCTAAAGCCGAAG
CCGCTGGCGCGACCGGCTACAGCATTACTTCCGCTAACACCAACAACAAACTGAGCGGTA
CTGCGGTTATCTATAAATAAN

By "CRE2_KPC nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_KPC (SEQ ID NO: 19)
TATCGCCGTCTAGTTCTGCTGTCTTGTCTCTCATGGCCGCTGGCTGGCTTTTCTGCCACC
GCGCTGACCAACCTCGTCGCGGAACCATTCGCTAAACTCGAACAGGACTTTGGCGGCTCC
ATCGGTGTGTACGCGATGGATACCGGCTCAGGCGCAACTGTAAGTTACCGCGCTGAGGAG
CGCTTCCCACTGTGCAGCTCATTCAAGGGCTTTCTTGCTGCCGCTGTGCTGGCTCGCAGC
CAGCAGCAGGCCGGCTTGCTGGACACACCCATCCGTTACGGCAAAAATGCGCTGGTTCCG
TGGTCACCCATCTCGGAAAAATATCTGACAACAGGCATGACGGTGGCGGAGCTGTCCGCG
GCCGCCGTGCAATACAGTGATAACGCCGCCGCCAATTTGTTGCTGAAGGAGTTGGGCGGC
CCGGCCGGGCTGACGGCCTTCATGCGCTCTATCGGCGATACCACGTTCCGTCTGGACCGC
TGGGAGCTGGAGCTGAACTCCGCCATCCCAGGCGATGCGCGCGATACCTCATCGCCGCGC
GCCGTGACGGAAAGCTTACAAAAACTGACACTGGGCTCTGCACTGGCTGCGCCGCAGCGG
CAGCAGTTTGTTGATTGGCTAAAGGGAAACACGACCGGCAACCACCGCATCCGCGCGGCG
GTGCCGGCAGACTGGGCAGTCGGAGACAAAACCGGAACCTGCGGAGTGTATGGCACGGCA
AATGACTATGCCGTCGTCTGGCCCACTGGGCGCGCACCTATTGTGTTGGCCGTCTACACC
CGGGCGCCTAACAAGGATGACAAGCACAGCGAGGCCGTCATCGCCGCTGCGGCTAGACTC
GCGCTCGAGGGA

By "CRE2_NDM nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_NDM (SEQ ID NO: 20)
ATGGAATTGCCCAATATTATGCACCCGGTCGCGAAGCTGAGCACCGCATTAGCCGCTGCA
TTGATGCTGAGCGGGTGCATGCCCGGTGAAATCCGCCCGACGATTGGCCAGCAAATGGAA
ACTGGCGACCAACGGTTTGGCGATCTGGTTTTCCGCCAGCTCGCACCGAATGTCTGGCAG
CACACTTCCTATCTCGACATGCCGGGTTTCGGGGCAGTCGCTTCCAACGGTTTGATCGTC
AGGGATGGCGGCCGCGTGCTGGTGGTCGATACCGCCTGGACCGATGACCAGACCGCCCAG
ATCCTCAACTGGATCAAGCAGGAGATCAACCTGCCGGTCGCGCTGGCGGTGGTGACTCAC
GCGCATCAGGACAAGATGGGCGGTATGGACGCGCTGCATGCGGCGGGGATTGCGACTTAT
GCCAATGCGTTGTCGAACCAGCTTGCCCCGCAAGAGGGGATGGTTGCGGCGCAACACAGC
CTGACTTTCGCCGCCAATGGCTGGGTCGAACCAGCAACCGCGCCCAACTTTGGCCCGCTC

AAGGTATTTTACCCCGGCCCCGGCCACACCAGTGACAATATCACCGTTGGGATCGACGGC
ACCGACATCGCTTTTGGTGGCTGCCTGATCAAGGACAGCAAGGCCAAGTCGCTCGGCAAT
CTCGGTGATGCCGACACTGAGCACTACGCCGCGTCAGCGCGCGCGTTTGGTGCGGCGTTC
CCCAAGGCCAGCATGATCGTGATGAGCCATTCCGCCCCCGATAGCCGCGCCGCAATCACT
CATACGGCCCGCATGGCCGACAAGCTGCGCT

By "CRE2_OXA48 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_OXA48 (SEQ ID NO: 21)
ATGCGTGTATTAGCCTTATCGGCTGTGTTTTTGGTGGCATCGATTATCGGAATGCCTGCG
GTAGCAAAGGAATGGCAAGAAAACAAAAGTTGGAATGCTCACTTTACTGAACATAAATCA
CAGGGCGTAGTTGTGCTCTGGAATGAGAATAAGCAGCAAGGATTTACCAATAATCTTAAA
CGGGCGAACCAAGCATTTTTACCCGCATCTACCTTTAAAATTCCCAATAGCTTGATCGCC
CTCGATTTGGGCGTGGTTAAGGATGAACACCAAGTCTTTAAGTGGGATGGACAGACGCGC
GATATCGCCACTTGGAATCGCGATCATAATCTAATCACCGCGATGAAATATTCAGTTGTG
CCTGTTTATCAAGAATTTGCCCGCCAAATTGGCGAGGCACGTATGAGCAAGATGCTACAT
GCTTTCGATTATGGTAATGAGGACATTTCGGGCAATGTAGACAGTTTCTGGCTCGACGGT
GGTATTCGAATTTCGGCCACGGAGCAAATCAGCTTTTTAAGAAAGCTGTATCACAATAAG
TTACACGTATCGGAGCGCAGCCAGCGTATTGTCAAACAAGCCATGCTGACCGAAGCCAAT
GGTGACTATATTATTCGGGCTAAAACTGGATACTCGACTAGAATCGAACCTAAGATTGGC
TGGTGGGTCGGTTGGGTTGAACTTGATGATAATGTGTGGTTTTTTGCGATGAATATGGAT
ATGCCCACATCGGATGGTTTAGGGCTGCGCCAAGCCATCACAAAAGAAGTGCTCAAACAG
GAAAAAATTATTCCCT

By "CRE2_CTXM15 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_CTXM15 (SEQ ID NO: 22)
ATGGTTAAAAAATCACTGCGCCAGTTCACGCTGATGGCGACGGCAACCGTCACGCTGTTG
TTAGGAAGTGTGCCGCTGTATGCGCAAACGGCGGACGTACAGCAAAAACTTGCCGAATTA
GAGCGGCAGTCGGGAGGCAGACTGGGTGTGGCATTGATTAACACAGCAGATAATTCGCAA
ATACTTTATCGTGCTGATGAGCGCTTTGCGATGTGCAGCACCAGTAAAGTGATGGCCGCG
GCCGCGGTGCTGAAGAAAAGTGAAAGCGAACCGAATCTGTTAAATCAGCGAGTTGAGATC
AAAAAATCTGACCTTGTTAACTATAATCCGATTGCGGAAAAGCACGTCAATGGGACGATG
TCACTGGCTGAGCTTAGCGCGGCCGCGCTACAGTACAGCGATAACGTGGCGATGAATAAG
CTGATTGCTCACGTTGGCGGCCCGGCTAGCGTCACCGCGTTCGCCCGACAGCTGGGAGAC
GAAACGTTCCGTCTCGACCGTACCGAGCCGACGTTAAACACCGCCATTCCGGGCGATCCG
CGTGATACCACTTCACCTCGGGCAATGGCGCAAACTCTGCGGAATCTGACGCTGGGTAAA
GCATTGGGCGACAGCCAACGGGCGCAGCTGGTGACATGGATGAAAGGCAATACCACCGGT
GCAGCGAGCATTCAGGCTGGACTGCCTGCTTCCTGGGTTGTGGGGGATAAAACCGGCAGC
GGTGGCTATGGCACCACCAACGATATCGCGGTGATCTGGCCAAAAGATCGTGCGCCGCTG
ATTCTGGTCACTTACTTCACCCAGCCTCAACCTAAGGCAGAAAGCCGTCGCGATGTATTA
GCGTCGGCGGCTAAAATCGTCACCGACGGTTTGT

By "CRE2_OXA10 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_OXA10 (SEQ ID NO: 23)
ATGAAAACATTTGCCGCATATGTAATTATCGCGTGTCTTTCGAGTACGGCATTAGCTGGT
TCAATTACAGAAAATACGTCTTGGAACAAAGAGTTCTCTGCCGAAGCCGTCAATGGTGTC
TTCGTGCTTTGTAAAAGTAGCAGTAAATCCTGCGCTACCAATGACTTAGCTCGTGCATCA
AAGGAATATCTTCCAGCATCAACATTTAAGATCCCCAACGCAATTATCGGCCTAGAAACT

GGTGTCATAAAGAATGAGCATCAGGTTTTCAAATGGGACGGAAAGCCAAGAGCCATGAAG
CAATGGGAAAGAGACTTGACCTTAAGAGGGGCAATACAAGTTTCAGCTGTTCCCGTATTT
CAACAAATCGCCAGAGAAGTTGGCGAAGTAAGAATGCAGAAATACCTTAAAAAATTTTCC
TATGGCAACCAGAATATCAGTGGTGGCATTGACAAATTCTGGTTGGAAGGCCAGCTTAGA
ATTTCCGCAGTTAATCAAGTGGAGTTTCTAGAGTCTCTATATTTAAATAAATTGTCAGCA
TCTAAAGAAAACCAGCTAATAGTAAAAGAGGCTTTGGTAACGGAGGCGGCACCTGAATAT
CTAGTGCATTCAAAAACTGGTTTTTCTGGTGTGGGAACTGAGTCAAATCCTGGTGTCGCA
TGGTGGGTTGGGTGGGTTGAGAAGGAGACAGAGGTTTACTTTTTCGCCTTTAACATGGAT
ATAGACAACGAAAGTAAGTTGCCGCTAAGAAAATCCATTCCCACCAAAATCATGGAAAGT
GAGGGCATCATTGGTGGCT

By "CRE2_VIM_1 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_VIM_1 (SEQ ID NO: 24)
ATGTTTCAA---ATTCGCAGCTTTCTGGTTGGTATCAGTGCATTCGTCATGGCCGTACTT
GGATCAGCAGCATATTCCGCACAGCCTGGCGGTGAATATCCGACAGTAGATGACATACCG
GTAGGGGAAGTTCGGCTGTACAAGATTGGCGATGGCGTTTGGTCGCATATCGCAACTCAG
AAACTCGGTGACACGGTGTACTCGTCTAATGGACTTATCGTCCGCGATGCTGATGAGTTG
CTTCTTATTGATACAGCGTGGGGGGCGAAGAACACGGTAGCCCTTCTCGCGGAGATTGAA
AAGCAAATTGGACTTCCAGTAACGCGCTCAATTTCTACGCACTTCCATGACGATCGAGTC
GGTGGAGTTGATGTCCTCCGGGCGGCTGGAGTGGCAACGTACACCTCACCCTTGACACGC
CAGCTGGCCGAAGCGGCGGGAAACGAGGTGCCTGCGCACTCTCTAAAAGCGCTCTCCTCT
AGTGGAGATGTGGTGCGCTTCGGTCCCGTAGAGGTTTTCTATCCTGGTGCTGCGCATTCG
GGCGACAATCTTGTGGTATACGTGCCGGCCGTGCGCGTACTGTTTGGTGGCTGTGCAGTT
CATGAGGCGTCACGCGAATCCGCGGGTAATGTTGCCGATGCCAATTTGGCAGAATGGCCT
GCTACCATTAAACGAATTCAACAGCGGTATCCGGAAGCAGAGGTCGTCATCCCCGGCCAC
GGTCTACCGGGCGGTCTGGAATTGCTCCAACACACAACTAACGTTGTCAAAACGCACAAA
GTACGCCCGGTGGCCGAGT

By "CRE2_VIM_2 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_VIM_2 (SEQ ID NO: 25)
CGAGTGGTGAGTATCCGACAGTCAACGAAATTCCGGTCGGAGAGGTCCGGCTTTACCAGA
TTGCCGATGGTGTTTGGTCGCATATCGCAACGCAGTCGTTTGATGGCGCGGTCTACCCGT
CCAATGGTCTCATTGTCCGTGATGGTGATGAGTTGCTTTTGATTGATACAGCGTGGGGTG
CGAAAAACACAGCGGCACTTCTCGCGGAGATTGAGAAGCAAATTGGACTTCCCGTAACGC
GTGCAGTCTCCACGCACTTTCATGACGACCGCGTCGGCGGCGTTGATGTCCTTCGGGCGG
CTGGGGTGGCAACGTACGCATCACCGTCGACACGCCGGCTAGCCGAGG

By "CRE2_VIM_3 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_VIM_3 (SEQ ID NO: 26)
TACCCGTCCAATGGTCTCATTGTCCGTGATGGTGATGAGTTGCTTTTGATTGATACAGCG
TGGGGTGCGAAAAACACAGCGGCACTTCTCGCGGAGATTGAGAAGCAAATTGGACTTCCC
GTAACGCGTGCAGTCTCCACGCACTTTCATGACGACCGCGTCGGCG

By "CRE2_IMP_1 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_1 (SEQ ID NO: 27)
GGAGCGGCTTTGCCTGATTTAAAAATCGAGAAGCTTGAAGAAGGTGTTTATGTTCATACA

TCGTTCGAAGAAGTTAACGGTTGGGGTGTTGTTTCTAAACACGGTTTGGTGGTTCTTGTA
AACACTGACGCCTATCTGATTGACACTCCATTT

By "CRE2_IMP_2 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_2 (SEQ ID NO: 28)
ACTGAAAAGTTAGTCAATTGGTTTGTGGAGCGCGGCTATAAAATCAAAGGCACTATTTCC
TCACATTTCCATAGCGACAGCACAGGNGGAATAGAGTGGCTTAATTCTCAATCTATTCCC
ACGTATGCATCTGAATTAACAAATGAACTT

By "CRE2_IMP_3 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_3 (SEQ ID NO: 29)
TCATTTAGCGGAGTTAGTTATTGGCTAGTTAAAAATAAAATTGAAGTTTTTTATCCCGGC
CCGGGGCACACTCAAGATAACGTAGTGGTTTGGTTACCTGAAAAGAAAATTTTATTCGGT
GGTTGTTTTGTTAAACCGGACGGTCTTGGTAATTTGG

By "CRE2_IMP_4 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_4 (SEQ ID NO: 30)
CTGACGCCTATCTGATTGACACTCCATTTACTGCTACAGATACTGAAAAGTTAGTCAATT
GGTTTGTGGAGCGCGGCTATAAAATCAAAGGCACTATTTCCTCACATTTCCATAGCGACA
GCACAGGGGGAATAGAGTGGCTTAATTCTC

By "CRE2_IMP_5 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_5 (SEQ ID NO: 31)
ATGAAAAAAATATTTGTGTTATTTGTATTTTTGTTTTGCAGTATTACTGCCGCCGGAGAG
TCTTTGCCTGATATAAAAATTGAGAAACTTGACGAAGATGTTTATGTTCATACTTCTTTT
GAAAAAAAAAACGGCTGGGGTGTTATTACTAAACACGGCTTGGTGGTTCTTGTAAATACT
GATGCCTATATAATTGACACTCCATTTACAGCTAAAGATACTGAAAAATTAGTCCGCTGG
TTTGTGGGGCGTGGTTATAAAATCAAAGGCAGTATTTCCTCACATTTTCATAGCGATAGC
GCAGGTGGAATTGAGTGGCTTAATTCTCAATCTATCCCCACATATGCATCTAAATTAACA
AATGAGCTTCTTAAAAAGAACGGTAATGCGCAAGCCGAAAACTCATTTAGTGGCGTTAGC
TATTGGCTAGTTAAACATAAAATTGAAGTTTTCTATCCAGGACCAGGGCACACTCAGGAT
AATGTAGTGGTTTGGTTGCCTGAAAAGAAAATTTTATTTGGCGGTTGTTTTATTAAGCCG
GACGGTCTTGGTTATTTGGGAGACGCAAATCTAGAAGCATGGCCTAAGTCCGCAGAAACA
TTAATGTCTAAGTATGGTAATGCAAAACTGGTTGTTTCGAGTCATAGTGAAATTGGGGGC
GCATCACTATTGAAGCGCACTTGGGAGCAGGCTGTTAAGGGGCTAAAAGAAAGTAAAAAA
CCATCACAGCCAAACAAA

By "CRE2_IMP_6 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_6 (SEQ ID NO: 32)
CTGAGGCTTATCTAATTGACACTCCATTTACGGCTAAAGATACTGAAAAGTTAGTCACTT
GGTTTGTGGAACGTGGCTATAAAATAAAAGGCAGTATTTCCTCTCATTTTCATAGCGACA
GCACGGGCGGAATAGAGTGGCTTAATTCTCAATCTATCCCCACGTATGCATCTGAATTAA
CAAATG

By "CRE2_IMP_7 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_7 (SEQ ID NO: 33)
TATGCATCTGAATTAACAAATGAACTTCTTAAAAAAGACGGTAAGGTACAAGCTAAAAAT
TCATTTAGCGGAGTTAGCTATTGGCTAGTTAAGAAAAAGATTGAAGTTTTTTATCCTGGT
CCAGGGCACACTCCAGATAACGTAGTGGTTTGGC

By "CRE2_IMP_8 nucleic acid molecule" is meant a polynucleotide that is 95%, 96%, 97%, 98%, or 100% identical to the following sequence, and is part of the Cre2 probeset.

>CRE2_IMP_8 (SEQ ID NO: 34)
GGGCACACTCAAGATAACGTAGTGGTTTGGTTACCTGAAAAGAAAATTTTATTCGGTGGT
TGTTTTGTTAAACCGGACGGTCTTGGTAATTTGGGTGACGCAAATTTAGAAGCTTGGCCA
AAGTCCGCCAAAATATTAATGTCTAAATATG

Other features and advantages of the disclosure will be apparent from the following description of the preferred embodiments thereof, and from the claims. Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All published foreign patents and patent applications cited herein are incorporated herein by reference. All other published references, documents, manuscripts and scientific literature cited herein are incorporated herein by reference. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

The following detailed description, given by way of example, but not intended to limit the disclosure solely to the specific embodiments described, may best be understood in conjunction with the accompanying drawings, in which:

FIGS. 1A-1C are diagrams depicting a binding and detection of a bipartite probe structure including Probe A and Probe B according to an exemplary embodiment of the disclosure. FIG. 1A shows the bipartite probe bound to an exemplary target nucleic acid. FIG. 1B shows an exemplary embodiment in which Probe A and Probe B may be detected by tags that are directly coupled to one or both Probes. FIG. 1C shows an exemplary embodiment in which Probe A and Probe B may be detected by tags that are in directly coupled to one or both Probes.

FIGS. 2A-2D depict MA plots showing RNA-Seq data. FIG. 2A demonstrates that RNA-Seq data upon antibiotic exposure revealed differential gene expression between susceptible and resistant strains. Susceptible (left panels) or resistant (right panels) clinical isolates of *K. pneumoniae* (top), *E. coli* (middle), or *A. baumannii* (bottom) were treated with meropenem (left, 60 min), ciprofloxacin (center, 30 min), or gentamicin (right, 60 min) at CLSI breakpoint concentrations. Data are presented as MA plots, with mean transcript abundance plotted on the x-axis and fold-induction compared with untreated strains on the y-axis; each axis is $\log_2$ transformed. Transcripts whose expression was observed as statistically significantly changed upon antibiotic exposure are shown in red. FIGS. 2B-2D show that a timecourse of RNA-Seq data upon antibiotic exposure revealed differential gene expression between susceptible and resistant clinical isolates. Susceptible (left panels) or resistant (right panels) clinical isolates of *K. pneumoniae* (FIG. 2B), *E. coli* (FIG. 2C), or *A. baumannii* (FIG. 2D) were treated with meropenem (left), ciprofloxacin (center), or gentamicin (right) at CLSI breakpoint concentrations for the indicated times. Data are presented as MA plots, with mean transcript abundance plotted on the x-axis and fold-induction compared with untreated strains on the y-axis; each axis is $\log_2$ transformed. Transcripts whose expression is statistically significantly changed upon antibiotic exposure are shown in red.

FIG. 3 shows that NanoString® data from dozens of antibiotic-responsive genes distinguished susceptible from resistant isolates. Heatmaps of normalized, log-transformed fold-induction of antibiotic-responsive transcripts from 18-24 clinical isolates of *K. pneumoniae* (top), *E. coli* (middle), or *A. baumannii* (bottom) treated at CLSI breakpoint concentrations with meropenem (left), ciprofloxacin (center), or gentamicin (right), with strains arranged in order of MIC for each antibiotic. CLSI classifications are shown below. All antibiotic-responsive transcripts chosen as described from RNA-Seq data are shown here; the subset of these chosen by reliefF as the 10 most discriminating transcripts are shown in FIG. 6 below. * = strains with large inoculum effects in meropenem MIC; + = one-dilution errors; x = strains discordant by more than one dilution.

FIGS. 4A and 4B show that a one-dimensional projection of NanoString® data distinguished susceptible from resistant isolates and reflected MIC. FIG. 4A shows phase 1 NanoString® data from FIGS. 2A-2D above (i.e., normalized, log-transformed fold-induction for each responsive transcript), analyzed as described to generate squared projected distance (SPD) metrics (y-axes) for each strain (see Supplemental Methods below), and binned by CLSI classifications (x-axes), for the same 18-24 isolates shown in FIGS. 3 above and 6 and 7A below. By definition, an SPD of 0

indicates a transcriptional response to antibiotic equivalent to that of an average susceptible strain, while an SPD of 1 indicates a response equivalent to that of an average resistant strain. See Supplemental Methods sections below for details. Data are summarized as box-and-whisker plots, where boxes extend from 25th to 75th percentile for each category, with middle line at median, and whiskers extending from minimum to maximum; all data points are displayed as well. Note that for *A. baumannii* and meropenem, the clustering of the majority of susceptible strains by this simple metric (aside from one outlier which was misclassified as resistant by GoPhAST-R) underscores the true differences in transcription between susceptible and resistant isolates, despite the more subtle-appearing differences in heatmaps for this combination (FIGS. 3 and 6), which is largely caused by one strain exhibiting an exaggerated transcriptional response (seen here as the strain with a markedly negative SPD) that affects scaling of the heatmap. FIG. 4B shows the same SPD data (y-axes) plotted against broth microdilution MICs (x-axes), which revealed that the magnitude of the transcriptional response to antibiotic exposure correlated with MIC. In both FIGS. 4A and 4B, strains with large inoculum effect upon meropenem treatment have been displayed in red and enlarged. Vertical dashed line indicates the CLSI breakpoint between susceptible and not susceptible (i.e., intermediate or resistant).

FIG. 5 depicts a schematic of the data analysis scheme of the instant disclosure, including the "two-phase" machine learning approach to feature selection and strain classification employed herein. The schematic representation shows major data analysis steps employed for identifying antibiotic-responsive transcriptional signatures from RNA-Seq data, validating and optimizing these signatures using NanoString® in two phases, and using these signatures to classify strains of unknown MIC, also in two phases. First, candidate antibiotic-responsive and control transcripts were chosen from RNA-Seq data using custom scripts built around the DESeq2 package, and conserved regions of these transcripts were identified for targeting in a hybridization assay. In phase 1 (implemented for all pathogen-antibiotic pairs), these candidate transcripts were quantitated on the NanoString® assay platform, and the resulting data were partitioned by strain into training and testing cohorts. Ten transcripts that best distinguished susceptible from resistant strains within the training cohort were then selected (step 1A) using the reliefF feature selection algorithm (implemented via the CORElearn package), then used to train an ensemble classifier (step 1B) on the same training cohort using a random forest algorithm (implemented via the caret package). This trained classifier was then used to predict susceptibilities of strains in the testing cohort (step 1C), and accuracy was

assessed by comparing with broth microdilution results (Table 10). In phase 2 (implemented for *K. pneumoniae* + meropenem and ciprofloxacin), the same process was repeated, but the phase 1 training and testing cohorts were combined into a single, larger training cohort for feature selection (step 2A) and classifier training (step 2B), and a new set of strains was obtained as a testing cohort. The 10 genes selected from the phase 2 training cohort were measured from this phase 2 testing cohort, and the trained classifier was used for AST on these new strains (step 2C), with accuracy again assessed by comparison with broth microdilution (Table 10). See Supplemental Methods for detailed descriptions of each of these analysis steps.

FIG. 6 shows that NanoString® data for top 10 antibiotic-responsive transcripts distinguished susceptible from resistant strains. Heatmaps of normalized, log-transformed fold-induction of top 10 antibiotic-responsive transcripts from 18-24 clinical isolates of *K. pneumoniae* (top), *E. coli* (middle), or *A. baumannii* (bottom) treated at CLSI breakpoint concentrations with meropenem (left), ciprofloxacin (center), or gentamicin (right) are shown, with strains arranged in order of MIC for each antibiotic. Gene identifiers are listed at right, along with gene names if available. CLSI classifications of each strain based on broth microdilution are shown below. * = strains with large inoculum effects in meropenem MIC; + = one-dilution errors; **x** = strains discordant by more than one dilution.

FIGS. 7A and 7B show that GoPhAST-R accurately classified clinical isolates. FIG. 7A shows the probability of resistance obtained from a random forest model trained on NanoString® data and tested on validation cohort (y-axis), as compared with standard CLSI classification based on broth microdilution MIC (x-axis), for the nine indicated pathogen-antibiotic combinations tested in phase 1. FIG. 7B shows the probability of resistance obtained from a random forest model trained on NanoString® data and tested on validation cohort (y-axis), as compared with standard CLSI classification based on broth microdilution MIC (x-axis), for the new *K. pneumoniae* isolates tested in phase 2 for meropenem and ciprofloxacin susceptibility. Horizontal dashed lines indicate 50% chance of resistance based on random forest model. Vertical dashed lines indicate CLSI breakpoint between susceptible and not susceptible (i.e. intermediate/resistant); isolates also colored by CLSI classification as indicated. Numbers in each quadrant indicate concordant (green) and discordant (black) classifications between GoPhAST-R and broth microdilution. Carbapenemase (square outline) and select ESBL (diamond outline) gene content as detected by GoPhAST-R are also

displayed on meropenem plots (none were found in the *A. baumannii* validation cohort). * = strains with large inoculum effects in meropenem MIC.

FIG. 8 shows NanoString® data for top 10 antibiotic-responsive transcripts for strains tested in phase 2. Heatmaps of normalized, log-transformed fold-induction of top 10 antibiotic-responsive transcripts observed from 25-31 clinical isolates of *K. pneumoniae* treated at CLSI breakpoint concentrations with meropenem (left) or ciprofloxacin (right) are shown, with strains arranged in order of MIC for each antibiotic. CLSI classifications are shown below. * = strain with large inoculum effects in meropenem MIC; + = one-dilution error; x = strain discordant by more than one dilution. Note that the 10 responsive transcripts shown were the only 10 tested for this second phase of GoPhAST-R implementation.

FIGS. 9A-9C show that GoPhAST-R detected carbapenemase and ESBL gene content from tested strains. Known carbapenemase and select ESBL transcript content based on WGS data (left panels) were compared with heatmaps of GoPhAST-R results (right panels) for all *K. pneumoniae* (FIG. 9A), *E. coli* (FIG. 9B), and *A. baumannii* (FIG. 9C) isolates tested for meropenem susceptibility for which WGS data were available. Heatmap intensity reflects normalized, background-subtracted, log-transformed NanoString® data from probes for the indicated gene families. Vertical dashed line separates carbapenemases (left) from ESBL genes (right). Phenotypic AST classification by broth microdilution and GoPhAST-R is shown at right ("S" = susceptible, "I" = intermediate, "R" = resistant; "*tr.*" = strain used in training cohort, thus not classified by GoPhAST-R). * = strains with large inoculum effects in meropenem MIC; **x** = strain discordant by more than one dilution.

FIG. 10 shows that GoPhAST-R detected antibiotic-responsive transcripts directly from positive blood culture bottles. Heatmaps are shown of normalized, log-transformed fold-induction of the top 10 ciprofloxacin-responsive transcripts from 8 positive blood culture bottles that grew either *E. coli* (6 strains, A-F) or *K. pneumoniae* (2 bottles, G-H). CLSI classifications of isolates, which were blinded until analysis was complete, are displayed below each heatmap.

FIGS. 11A and 11B show that GoPhAST-R accurately classified AST and detected key resistance elements directly from simulated positive blood culture bottles in <4 hours. FIG. 11A shows heatmaps of normalized, log-transformed fold-induction NanoString® data from the top 10 antibiotic-responsive transcripts directly from 12 simulated positive blood culture bottles for each indicated pathogen-antibiotic combination, which revealed antibiotic-responsive transcription in

susceptible but not resistant isolates. For meropenem, results of carbapenemase / ESBL gene detection are also displayed as a normalized, background-subtracted, log-transformed heatmap above. CLSI classifications of isolates, which were blinded until analysis was complete, are displayed below each heatmap. FIG. 11B shows the probability of resistance from random forest model trained by leave-one-out cross-validation on NanoString® data from FIG. 11A (y-axis) compared with standard CLSI classification based on broth microdilution MIC (x-axis) for each isolate. Horizontal dashed lines indicate 50% chance of resistance based on random forest model. Vertical dashed lines indicate CLSI breakpoint between susceptible and resistant; isolates have also been colored by CLSI classification as indicated. Carbapenemase (square outline) and select ESBL (diamond outline) gene content as detected by GoPhAST-R are also displayed on meropenem plots. See Supplemental Methods for details of spike-in protocol.

FIGS. 12A and 12B show for an exemplary GoPhAST-R workflow that the NanoString® Hyb & Seq™ platform distinguished phenotypically susceptible from resistant strains and detected genetic resistance determinants in <4 hours. FIG. 12A shows a schematic of GoPhAST-R workflow on the Hyb & Seq detection platform. It is contemplated that pathogen identification can either be performed prior to this process, or in parallel by multiplexing mRNA targets from multiple organisms. FIG. 12B, at left, shows the Hyb & Seq hybridization scheme, in which probe pairs targeting each RNA transcript are hybridized in crude lysate. Each probe A contains a unique barcode sequence (green) for detection and a shared 3' capture sequence; each probe B contains a biotin group (gray circle) for surface immobilization and a shared 5' capture sequence. At middle, the Hyb & Seq detection strategy is shown: immobilized, purified ternary probe-target complexes undergo sequential cycles of multi-step imaging for spatially resolved single-molecule detection. Each cycle consists of reporter probe binding and detection, UV cleavage, a second round of reporter probe binding and detection, and a low-salt wash to regenerate the unbound probe-target complex. 5 Hyb & Seq cycles were used to generate the data shown. See Supplemental Methods sections below for details. At right, pilot study results for accelerated meropenem susceptibility testing of 6 clinical *K. pneumoniae* isolates are shown. At right top, heatmaps of normalized, log-transformed fold-induction of top 10 meropenem-responsive transcripts measured using the instant Hyb & Seq workflow are shown, with strains arranged in order of MIC for each antibiotic. CLSI classifications are shown immediately below. At right bottom, heatmaps of normalized, background-subtracted,

log-transformed NanoString® data from carbapenemase ("CPase") and select ESBL transcripts measured in the same Hyb & Seq assay are shown.

FIGS. 13A-13D show phylogenetic trees that highlight the diversity of strains used in that instant disclosure. FIG. 13A shows phylogenetic trees of all sequenced isolates deposited in NCBI for *Klebsiella pneumoniae* isolates, with all sequenced isolates used in the instant disclosure indicated by colored arrowheads around the periphery. FIG. 13B shows phylogenetic trees of all sequenced isolates deposited in NCBI for *Escherichia coli* isolates, with all sequenced isolates used in the instant disclosure indicated by colored arrowheads around the periphery. FIG. 13C shows phylogenetic trees of all sequenced isolates deposited in NCBI for *Acinetobacter baumanii* isolates isolates, with all sequenced isolates used in the instant disclosure indicated by colored arrowheads around the periphery. FIG. 13D shows phylogenetic trees of all sequenced isolates deposited in NCBI for *Pseudomonas aeruginosa* isolates, with all sequenced isolates used in the instant disclosure indicated by colored arrowheads around the periphery (ciprofloxacin sensitive strains are indicated by blue arrowheads and ciprofloxacin resistant strains are indicated by red arrowheads). See Supplemental Methods sections below for details.

FIGS. 14A-14F show that RNA-Seq and NanoString® data revealed differential gene expression that distinguished susceptible from resistant clinical isolates for *S. aureus* + levofloxacin and *P. aeruginosa* + ciprofloxacin. FIG. 14A shows RNA-Seq data from susceptible or resistant clinical isolates of *S. aureus* treated with the indicated fluoroquinolone levofloxacin at 1 mg/L for 60 minutes. Data are presented as MA plots, with mean transcript abundance plotted on the x-axis and fold-induction compared with untreated strains on the y-axis; each axis is $\log_2$ transformed. Transcripts whose expression is statistically significantly changed upon antibiotic exposure are shown in red. FIG. 14B shows heatmaps of normalized, log-transformed fold-induction of antibiotic-responsive transcripts from 24 clinical isolates of *S. aureus* treated with the indicated fluoroquinolone levofloxacin at 1 mg/L for 60 minutes. NanoString® data from all candidate transcripts are shown at left, and top 10 transcripts selected from Phase 1 testing are shown at right. (FIG. 14C = S. aureus + levofloxacin; FIG. 14F = P. aeruginosa + ciprofloxacin) FIG. 14C depicts the probability of *S. aureus* resistance to the indicated fluoroquinolone levofloxacin from random forest model trained on Phase 1 NanoString® data from derivation cohort and tested on validation cohort (y-axis) compared with standard CLSI classification based on broth microdilution MIC (x-axis). Horizontal dashed lines indicate 50% chance of resistance based on random forest model.

Vertical dashed lines indicate CLSI breakpoint between susceptible and not susceptible (i.e. intermediate/resistant); isolates also colored by CLSI classification as indicated. Numbers in each quadrant indicate concordant (green) and discordant (black) classifications between GoPhAST-R and broth microdilution. FIG. 14D shows RNA-Seq data from susceptible or resistant clinical isolates of *P. aeruginosa* treated with the indicated fluoroquinolone ciprofloxacin at 1 mg/L for 60 minutes. Data are presented as MA plots, with mean transcript abundance plotted on the x-axis and fold-induction compared with untreated strains on the y-axis; each axis is $\log_2$ transformed. Transcripts whose expression is statistically significantly changed upon antibiotic exposure are shown in red. FIG. 14E shows heatmaps of normalized, log-transformed fold-induction of antibiotic-responsive transcripts from 24 clinical isolates of *P. aeruginosa* treated with the indicated fluoroquinolone ciprofloxacin at 1 mg/L for 60 minutes. NanoString® data from all candidate transcripts are shown at left, and top 10 transcripts selected from Phase 1 testing are shown at right. FIG. 14F depicts the probability of *P. aeruginosa* resistance to the indicated fluoroquinolone ciprofloxacin from random forest model trained on Phase 1 NanoString® data from derivation cohort and tested on validation cohort (y-axis) compared with standard CLSI classification based on broth microdilution MIC (x-axis). Horizontal dashed lines indicate 50% chance of resistance based on random forest model. Vertical dashed lines indicate CLSI breakpoint between susceptible and not susceptible (i.e. intermediate/resistant); isolates also colored by CLSI classification as indicated. Numbers in each quadrant indicate concordant (green) and discordant (black) classifications between GoPhAST-R and broth microdilution.

DETAILED DESCRIPTION OF THE DISCLOSURE

The present disclosure is based, at least in part, on the discovery of specific mRNA signature patterns that provide rapid phenotypic detection of single and multiple types of antibiotic resistance/susceptibility in specific microbial organisms (e.g., bacteria). In particular, the techniques herein relate, at least in part, to compositions, methods, and kits for rapid antibiotic susceptibility testing (AST) in microbial organisms (e.g., bacteria). The techniques herein provide compositions and methods that provide rapid phenotypic detection of antibiotic resistance/susceptibility in microbial pathogens, and are faster than the prior art growth-based phenotypic assays that currently comprise the gold standard. The techniques herein also provide compositions and methods that enable simultaneous detection of multiple resistance genes in the same assay. In this manner, the

techniques herein enable more accurate determination of antibiotic resistance, as well as providing: 1) mechanistic explanations for key antibiotic resistant strains, 2) epidemiologic tracking of known resistance mechanisms, and 3) immediate identification of unknown or potentially novel resistance mechanisms (such as, e.g., discordant cases when a resistant organism does not display a known resistance phenotype). Currently, detection of antibiotic resistance genes typically requires separate PCR or sequencing assays, which require different assay infrastructure and often necessitate sending samples out to reference laboratories.

The techniques herein may be used for clinical diagnostics, e.g., to rapidly determine antibiotic susceptibility profiles on patient samples and easily allow antibiotic susceptibility testing (AST) to be performed on bacteria from any source, including environmental isolates. The techniques herein are based on the following steps: sample acquisition, processing to enrich for bacteria and remove host material (in order to increase signal-to-noise), antibiotic exposure, bacterial lysis, RNA measurement (hybridization followed by detection), and data interpretation. Advantageously, the techniques herein may be implemented within a single reaction that does not require sample purification.

As mentioned above, current growth-based antibiotic susceptibility testing (AST) is too slow to inform key clinical decisions. While genotypic assays hold promise, they remain incompletely predictive of susceptibility. The techniques herein provide rapid assays for combined *geno*typic and *ph*enotypic *AST* through *R*NA detection (i.e., GoPhAST-R) that classifies strains with >94-99% accuracy by coupling machine learning analysis of quantitative early transcriptional responses to antibiotic exposure with simultaneous detection of key genetic resistance determinants. This two-pronged approach provides phenotypic AST as fast as <4 hours, increases accuracy of resistance detection, works directly from positive blood cultures, facilitates molecular epidemiology, and enables early detection of emerging resistance mechanisms.

Antibiotic resistance is one of the most pressing medical problems of modern times (Fauci & Morens; Nathan & Cars). The rise of multidrug resistant organisms (MDROs) has been recognized as one of the most serious threats to human health (Holdren *et al.*; WHO). Delays in identifying MDROs can lead to increased mortality (Kumar *et al.*; Kadri *et al.*) and increased use of broad-spectrum antibiotics to further select for resistant organisms. Rapid antibiotic susceptibility testing (AST) with pathogen identification would transform the care of infected patients while ensuring that the available antibiotic arsenal is deployed as efficiently as possible.

The current gold standard AST assays of measuring growth in the presence of an antibiotic, such as broth microdilution (Wiegand *et al.*), directly answer the key question of whether the antibiotic inhibits pathogen growth; however, their dependence on serial growth requires 2-3 days from sample collection to results. As an alternative approach, a new generation of assays has emerged to rapidly detect genotypic resistance determinants, yet these are simply proxies for antibiotic resistance in select cases with monogenic determinants (e.g., MRSA Xpert, VRE Xpert, GeneXpert; see Boehme *et al.*, Ioannidis *et al.*, Marlowe *et al.*, Marner *et al.*, and Wolk *et al.*), or limited to a subset of resistance determinants for a specific drug class (McMullen *et al.*, Smith *et al.*, Traczewski *et al.*, Sullivan *et al.*, Walker *et al. J Clin Microbiol*, Walker *et al. Clin Chem*, and Salimnia *et al.*). Such approaches fall short of universal AST because of the incomplete knowledge of the innumerable resistance-causing genes and mutations across a wide range of pathogens and antibiotics, and the interactions of these genetic factors with the wide diversity of genomic backgrounds within any given bacterial species (Arzanlou *et al.*; Cerqueira *et al.*). Genotypic resistance detection does, however, have the benefit of facilitating molecular epidemiology by allowing specific resistance mechanisms to be identified and tracked (Cerqueira *et al.*; Woodworth *et al.*). Whole genome sequencing (WGS) coupled with machine learning has promised the possibility of a more universal genomic approach to AST (Allcock *et al.*; Bradley *et al.*; Didelot *et al.*; Li, Y. *et al.*; and Nguyen *et al.*). But while the genomics revolution has undeniably transformed the microbiology field's understanding of antibiotic resistance (Burnham *et al.*; Gupta, S.K. *et al.*; Jia *et al.*; McArthur *et al.*; and Zankari *et al.*), as a clinical diagnostic, WGS remains technically demanding, costly, and slow. Moreover, the complexity and variability of bacterial genomes present serious challenges to the ability to predict antibiotic susceptibility with sufficient accuracy to direct patient care (Bhattacharyya *et al.*; Milheirico *et al.*; and Ellington *et al.*). Additionally, the inability to predict the emergence of new resistance mechanisms means that genotypic resistance detection, whether targeted or comprehensive, is fundamentally reactive as new resistance determinants are reported (see e.g., Caniaux *et al.* 2017; Ford 2018; Garcia-Alvarez *et al.* 2011; Liakopoulos *et al.* 2016; Liu *et al.* 2016; Ma *et al.* 2018; Paterson *et al.* 2014; Sun *et al.* 2018). While certain bacterial species or antibiotic classes are more amenable to genetic resistance prediction (see e.g., Bradley *et al.* 2015; Consortium *et al.* 2018), this approach is not readily generalizable (Bhattacharyya *et al.*; Ellington *et al.*; Rossen *et al.*; and Tagini & Greub). These gaps in genetic susceptibility prediction have motivated a number of novel approaches that focus on phenotypic AST but with a more rapid

result, including rapid automated microscopy (see e.g., Charnot-Katsikas *et al.* 2018; Choi *et al.* 2017; Humphries and Di Martino 2019; Marschal *et al.* 2017), ultrafine mass measurements (see e.g., Cermak *et al.* 2016; Longo *et al.* 2013), and others (see e.g., Barczak *et al*; Quach *et al.* 2016; and van Belkum *et al.* 2017).

Of the current MDROs, carbapenem resistant organisms are the most alarming, as their resistance to this class of broad-spectrum antibiotics often leaves few to no treatment options available (Gupta, N. *et al.*; Iovleva & Doi *et al.*; and Nordmann *et al.* 2012). Yet phenotypic carbapenem resistance detection can be challenging (Lutgring and Limbago 2016; Miller and Humphries 2016), as some carbapenemase-producing strains, even those carrying canonical resistance determinants such as *bla*$_{KPC}$, may be mistakenly identified as susceptible by current phenotypic assays (Anderson *et al.* 2007; Arnold *et al.* 2011; Centers for Disease and Prevention 2009; Chea *et al.* 2015; Gupta, V. *et al.* 2018; Nordmann *et al.* 2009; and Chea *et al.*) while failing clinical carbapenem therapy (Weisenberg *et al.* 2009). Rapid genotypic approaches are now available that use multiplexed PCR assays to detect several common carbapenemases in carbapenem-resistant *Enterobactericeae* (CRE) (see e.g., Evans *et al.* 2016; Smith *et al.* 2016; Sullivan *et al.* 2014). While one advantage of these assays is that they identify the specific mechanism of resistance when present, they fail to identify a significant fraction (13-68%) of CRE isolates with unknown or non-carbapenemase resistance mechanisms (see e.g., Cerqueira *et al.* 2017; Woodworth *et al.* 2018; Ye *et al.* 2018). For non-*Enterobacteriaceae,* this problem is even more challenging, as unexplained genetic resistance mechanisms account for the vast majority of resistance. For example; just 1.9% of over 1000 carbapenem-resistant *Pseudomonas* in the 2017 CDC survey were found to encode known carbapenemases (see e.g., Woodworth *et al.* 2018). These challenges have left clinical microbiology laboratories still seeking consensus on how to best apply the multiple possible workflows that currently exist for detecting carbapenem resistance (McMullen *et al.*; Humphries, R.M.), including phenotypic (CLSI), genetic (McMullen *et al.*, Smith *et al.*, Traczewski *et al.*, Sullivan *et al.*, Walker *et al. J Clin Microbiol*, Walker *et al. Clin Chem*), and biochemical (Humphries, R.M.) assays.

The present disclosure provides a diagnostic approach that has been termed *G*enotypic and *Ph*enotypic *AST* through *R*NA detection (GoPhAST-R), which addresses the above-mentioned prior art problems by detecting both genotype and phenotype in a single assay. Advantageously, this allows for integration of all information while simultaneously providing information about both

resistance prediction and molecular epidemiology. mRNA is uniquely informative in this regard, as it encodes genotypic information in its sequence and phenotypic information in its abundance in response to antibiotic exposure. For example, susceptible cells that are stressed upon antibiotic exposure look transcriptionally distinct from resistant cells that are not (Barczak *et al.* 2012). Leveraging this principle for rapid phenotypic AST built upon multiplexed hybridization-based detection of early transcriptional responses that occur within minutes of antibiotic exposure, the present disclosure defines a phenotypic measure that distinguishes susceptible (by measuring a response in susceptible strains) from resistant organisms, agnostic to the mechanism of resistance. As described in detail below, these techniques are demonstrated for three major antibiotic classes – fluoroquinolones, aminoglycosides, and importantly, carbapenems – in *Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Staphylococcus aureus*, four gram-negative and one gram-positive pathogens that are classified as "critical" or "high priority" threats by the World Health Organization (Tacconelli *et al.*) and have a propensity for multi-drug resistance through diverse mechanisms that are difficult to determine based solely on genotypic determinants.

The working examples herein describe a generalizable process to extend this approach to any pathogen-antibiotic pair of interest, in certain aspects and without wishing to be bound by theory, the process requires only that an antibiotic elicit a differential transcriptional response in susceptible versus resistant isolates, a biological phenomenon that to date appears to be universal. An analytical framework is described to classify organisms as susceptible or resistant on the basis of 10-transcript signatures detected in a simple multiplexed fluorescent hybridization-based assay on an RNA detection platform (NanoString® nCounter™; Geiss *et al.*), demonstrating >94-99% categorical agreement with broth microdilution. For carbapenems, a simultaneous genotypic detection of key resistance determinants is incorporated into the same assay to improve accuracy of resistance detection, facilitate molecular epidemiology, and guide antibiotic selection for CRE treatment from among the newer available agents (Lomovskaya *et al.* 2017; Marshall *et al.* 2017; van Duin and Bonomo 2016), which has clearly demonstrated the superiority of GoPhAST-R techniques described herein over prior art approaches that measure either genotype or phenotype alone. This important feature shows that several of the discrepant results between GoPhAST-R and broth microdilution occur in carbapenemase-producing strains likely misclassified as susceptible by the gold standard, and correctly classified as resistant by GoPhAST-R. In this regard, the GoPhAST-R techniques

described herein can be deployed directly on a positive blood culture bottle with a simple workflow, reporting phenotypic AST within hours of a positive culture, thus 24-36 hours faster than gold standard prior art methods in a head-to-head comparison, yielding AST results with 99% categorical agreement. Finally, GoPhAST-R can determine antibiotic susceptibilities in under 4 hours, using a pilot next-generation RNA detection platform (NanoString® Hyb & Seq™). Together, the techniques herein establish GoPhAST-R as a novel, accurate, rapid approach that can simultaneously report phenotypic and genotypic data and thus leverages the advantages of both approaches.

Treatment Selection

The methods described herein can be used for selecting, and then optionally administering, an optimal treatment (e.g., an antibiotic course) for a subject. Thus the methods described herein include methods for the treatment of bacterial infections. Generally, the methods include administering a therapeutically effective amount of a treatment as described herein, to a subject who is in need of, or who has been determined to be in need of, such treatment.

As used in this context, to "treat" means to ameliorate at least one symptom of the bacterial infection.

An "effective amount" is an amount sufficient to effect beneficial or desired results. For example, a therapeutic amount is one that achieves the desired therapeutic effect (e.g reduction or elimination of a bacterial infection). This amount can be the same or different from a prophylactically effective amount, which is an amount necessary to prevent onset of disease or disease symptoms. An effective amount can be administered in one or more administrations, applications or dosages. A therapeutically effective amount of a therapeutic compound (i.e., an effective dosage) depends on the therapeutic compounds selected. The compositions can be administered from one or more times per day to one or more times per week; including once every other day. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the bacterial infection, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of the therapeutic compounds described herein can include a single treatment or a series of treatments.

Dosage, toxicity and therapeutic efficacy of the therapeutic compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining

the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds which exhibit high therapeutic indices are preferred. While compounds that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

The data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the disclosure, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 (i.e., the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

Combination Treatments

The compositions and methods of the present disclosure may be used two direct the administration of combination antibiotic therapies to treat particular bacterial infections. In order to increase the effectiveness of a treatment with the compositions of the present disclosure, e.g., an antibiotic selected and/or administered as a single agent, or to augment the protection of another therapy (second therapy), it may be desirable to combine these compositions and methods with one another, or with other agents and methods effective in the treatment, amelioration, or prevention of diseases and pathologic conditions, for example, an antibiotic infection.

Administration of a composition of the present disclosure to a subject will follow general protocols for the administration described herein, and the general protocols for the administration of a particular secondary therapy will also be followed, taking into account the toxicity, if any, of the treatment. It is expected that the treatment cycles would be repeated as necessary. It also is contemplated that various standard therapies may be applied in combination with the described therapies.

Pharmaceutical Compositions

Agents of the present disclosure can be incorporated into a variety of formulations for therapeutic use (e.g., by administration) or in the manufacture of a medicament (e.g., for treating or preventing a bacterial infection) by combining the agents with appropriate pharmaceutically acceptable carriers or diluents, and may be formulated into preparations in solid, semi-solid, liquid or gaseous forms. Examples of such formulations include, without limitation, tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants, gels, microspheres, and aerosols.

Pharmaceutical compositions can include, depending on the formulation desired, pharmaceutically-acceptable, non-toxic carriers of diluents, which are vehicles commonly used to formulate pharmaceutical compositions for animal or human administration. The diluent is selected so as not to affect the biological activity of the combination. Examples of such diluents include, without limitation, distilled water, buffered water, physiological saline, PBS, Ringer's solution, dextrose solution, and Hank's solution. A pharmaceutical composition or formulation of the present disclosure can further include other carriers, adjuvants, or non-toxic, nontherapeutic, nonimmunogenic stabilizers, excipients and the like. The compositions can also include additional substances to approximate physiological conditions, such as pH adjusting and buffering agents, toxicity adjusting agents, wetting agents and detergents.

Further examples of formulations that are suitable for various types of administration can be found in Remington's Pharmaceutical Sciences, Mace Publishing Company, Philadelphia, PA, 17th ed. (1985). For a brief review of methods for drug delivery, see, Langer, Science 249: 1527-1533 (1990).

For oral administration, the active ingredient can be administered in solid dosage forms, such as capsules, tablets, and powders, or in liquid dosage forms, such as elixirs, syrups, and suspensions. The active component(s) can be encapsulated in gelatin capsules together with inactive ingredients and powdered carriers, such as glucose, lactose, sucrose, mannitol, starch, cellulose or cellulose derivatives, magnesium stearate, stearic acid, sodium saccharin, talcum, magnesium carbonate. Examples of additional inactive ingredients that may be added to provide desirable color, taste, stability, buffering capacity, dispersion or other known desirable features are red iron oxide, silica gel, sodium lauryl sulfate, titanium dioxide, and edible white ink.

Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric-coated for selective disintegration in the gastrointestinal tract. Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

Formulations suitable for parenteral administration include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives.

As used herein, the term "pharmaceutically acceptable salt" refers to those salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts of amines, carboxylic acids, and other types of compounds, are well known in the art. For example, S. M. Berge, et al. describe pharmaceutically acceptable salts in detail in J Pharmaceutical Sciences 66 (1977):1-19, incorporated herein by reference. The salts can be prepared in situ during the final isolation and purification of the compounds (e.g., FDA-approved compounds) of the application, or separately by reacting a free base or free acid function with a suitable reagent, as described generally below. For example, a free base function can be reacted with a suitable acid. Furthermore, where the compounds to be administered of the application carry an acidic moiety, suitable pharmaceutically acceptable salts thereof may, include metal salts such as alkali metal salts, e.g. sodium or potassium salts; and alkaline earth metal salts, e.g. calcium or magnesium salts. Examples of pharmaceutically acceptable, nontoxic acid addition salts are salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid or by using other methods used in the art such as ion exchange. Other pharmaceutically acceptable salts include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate,

hemisulfate, heptanoate, hexanoate, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, loweralkyl sulfonate and aryl sulfonate.

Additionally, as used herein, the term "pharmaceutically acceptable ester" refers to esters that hydrolyze in vivo and include those that break down readily in the human body to leave the parent compound (e.g., an FDA-approved compound where administered to a human subject) or a salt thereof. Suitable ester groups include, for example, those derived from pharmaceutically acceptable aliphatic carboxylic acids, particularly alkanoic, alkenoic, cycloalkanoic and alkanedioic acids, in which each alkyl or alkenyl moeity advantageously has not more than 6 carbon atoms. Examples of particular esters include formates, acetates, propionates, butyrates, acrylates and ethylsuccinates.

Furthermore, the term "pharmaceutically acceptable prodrugs" as used herein refers to those prodrugs of the certain compounds of the present application which are, within the scope of sound medical judgment, suitable for use in contact with the issues of humans and lower animals with undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the application. The term "prodrug" refers to compounds that are rapidly transformed in vivo to yield the parent compound of an agent of the instant disclosure, for example by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol.14 of the A.C.S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, (1987), both of which are incorporated herein by reference.

The components used to formulate the pharmaceutical compositions are preferably of high purity and are substantially free of potentially harmful contaminants (e.g., at least National Food (NF) grade, generally at least analytical grade, and more typically at least pharmaceutical grade).

Moreover, compositions intended for in vivo use are usually sterile. To the extent that a given compound must be synthesized prior to use, the resulting product is typically substantially free of any potentially toxic agents, particularly any endotoxins, which may be present during the synthesis or purification process. Compositions for parental administration are also sterile, substantially isotonic and made under GMP conditions.

Formulations may be optimized for retention and stabilization in a subject and/or tissue of a subject, e.g., to prevent rapid clearance of a formulation by the subject. Stabilization techniques include cross-linking, multimerizing, or linking to groups such as polyethylene glycol, polyacrylamide, neutral protein carriers, etc. in order to achieve an increase in molecular weight.

Other strategies for increasing retention include the entrapment of the agent in a biodegradable or bioerodible implant. The rate of release of the therapeutically active agent is controlled by the rate of transport through the polymeric matrix, and the biodegradation of the implant. The transport of drug through the polymer barrier will also be affected by compound solubility, polymer hydrophilicity, extent of polymer cross-linking, expansion of the polymer upon water absorption so as to make the polymer barrier more permeable to the drug, geometry of the implant, and the like. The implants are of dimensions commensurate with the size and shape of the region selected as the site of implantation. Implants may be particles, sheets, patches, plaques, fibers, microcapsules and the like and may be of any size or shape compatible with the selected site of insertion.

The implants may be monolithic, i.e. having the active agent homogenously distributed through the polymeric matrix, or encapsulated, where a reservoir of active agent is encapsulated by the polymeric matrix. The selection of the polymeric composition to be employed will vary with the site of administration, the desired period of treatment, patient tolerance, the nature of the disease to be treated and the like. Characteristics of the polymers will include biodegradability at the site of implantation, compatibility with the agent of interest, ease of encapsulation, a half-life in the physiological environment.

Biodegradable polymeric compositions which may be employed may be organic esters or ethers, which when degraded result in physiologically acceptable degradation products, including the monomers. Anhydrides, amides, orthoesters or the like, by themselves or in combination with other monomers, may find use. The polymers will be condensation polymers. The polymers may be cross-linked or non-cross-linked. Of particular interest are polymers of hydroxyaliphatic carboxylic

acids, either homo- or copolymers, and polysaccharides. Included among the polyesters of interest are polymers of D-lactic acid, L-lactic acid, racemic lactic acid, glycolic acid, polycaprolactone, and combinations thereof. By employing the L-lactate or D- lactate, a slowly biodegrading polymer is achieved, while degradation is substantially enhanced with the racemate. Copolymers of glycolic and lactic acid are of particular interest, where the rate of biodegradation is controlled by the ratio of glycolic to lactic acid. The most rapidly degraded copolymer has roughly equal amounts of glycolic and lactic acid, where either homopolymer is more resistant to degradation. The ratio of glycolic acid to lactic acid will also affect the brittleness of in the implant, where a more flexible implant is desirable for larger geometries. Among the polysaccharides of interest are calcium alginate, and functionalized celluloses, particularly carboxymethylcellulose esters characterized by being water insoluble, a molecular weight of about 5 kD to 500 kD, etc. Biodegradable hydrogels may also be employed in the implants of the individual instant disclosure. Hydrogels are typically a copolymer material, characterized by the ability to imbibe a liquid. Exemplary biodegradable hydrogels which may be employed are described in Heller in: Hydrogels in Medicine and Pharmacy, N. A. Peppes ed., Vol. III, CRC Press, Boca Raton, Fla., 1987, pp 137-149.

Pharmaceutical Dosages

Pharmaceutical compositions of the present disclosure containing an agent described herein may be used (e.g., administered to an individual, such as a human individual, in need of treatment with an antibiotic) in accord with known methods, such as oral administration, intravenous administration as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerobrospinal, intracranial, intraspinal, subcutaneous, intraarticular, intrasynovial, intrathecal, topical, or inhalation routes.

Dosages and desired drug concentration of pharmaceutical compositions of the present disclosure may vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary artisan. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles described in Mordenti, J. and Chappell, W. "The Use of Interspecies Scaling in Toxicokinetics," In Toxicokinetics and New Drug Development, Yacobi et al., Eds, Pergamon Press, New York 1989, pp.42-46.

For *in vivo* administration of any of the agents of the present disclosure, normal dosage amounts may vary from about 10 ng/kg up to about 100 mg/kg of an individual's and/or subject's body weight or more per day, depending upon the route of administration. In some embodiments, the dose amount is about 1 mg/kg/day to 10 mg/kg/day. For repeated administrations over several days or longer, depending on the severity of the disease, disorder, or condition to be treated, the treatment is sustained until a desired suppression of symptoms is achieved.

An effective amount of an agent of the instant disclosure may vary, e.g., from about 0.001 mg/kg to about 1000 mg/kg or more in one or more dose administrations for one or several days (depending on the mode of administration). In certain embodiments, the effective amount per dose varies from about 0.001 mg/kg to about 1000 mg/kg, from about 0.01 mg/kg to about 750 mg/kg, from about 0.1 mg/kg to about 500 mg/kg, from about 1.0 mg/kg to about 250 mg/kg, and from about 10.0 mg/kg to about 150 mg/kg.

An exemplary dosing regimen may include administering an initial dose of an agent of the disclosure of about 200 μg/kg, followed by a weekly maintenance dose of about 100 μg/kg every other week. Other dosage regimens may be useful, depending on the pattern of pharmacokinetic decay that the physician wishes to achieve. For example, dosing an individual from one to twenty-one times a week is contemplated herein. In certain embodiments, dosing ranging from about 3 μg/kg to about 2 mg/kg (such as about 3 μg/kg, about 10 μg/kg, about 30 μg/kg, about 100 μg/kg, about 300 μg/kg, about 1 mg/kg, or about 2 mg/kg) may be used. In certain embodiments, dosing frequency is three times per day, twice per day, once per day, once every other day, once weekly, once every two weeks, once every four weeks, once every five weeks, once every six weeks, once every seven weeks, once every eight weeks, once every nine weeks, once every ten weeks, or once monthly, once every two months, once every three months, or longer. Progress of the therapy is easily monitored by conventional techniques and assays. The dosing regimen, including the agent(s) administered, can vary over time independently of the dose used.

Pharmaceutical compositions described herein can be prepared by any method known in the art of pharmacology. In general, such preparatory methods include the steps of bringing the agent or compound described herein (i.e., the "active ingredient") into association with a carrier or excipient, and/or one or more other accessory ingredients, and then, if necessary and/or desirable, shaping, and/or packaging the product into a desired single- or multi-dose unit.

Pharmaceutical compositions can be prepared, packaged, and/or sold in bulk, as a single unit dose, and/or as a plurality of single unit doses. A "unit dose" is a discrete amount of the pharmaceutical composition comprising a predetermined amount of the active ingredient. The amount of the active ingredient is generally equal to the dosage of the active ingredient which would be administered to a subject and/or a convenient fraction of such a dosage such as, for example, one-half or one-third of such a dosage.

Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a pharmaceutical composition described herein will vary, depending upon the identity, size, and/or condition of the subject treated and further depending upon the route by which the composition is to be administered. The composition may comprise between 0.1% and 100% (w/w) active ingredient.

Pharmaceutically acceptable excipients used in the manufacture of provided pharmaceutical compositions include inert diluents, dispersing and/or granulating agents, surface active agents and/or emulsifiers, disintegrating agents, binding agents, preservatives, buffering agents, lubricating agents, and/or oils. Excipients such as cocoa butter and suppository waxes, coloring agents, coating agents, sweetening, flavoring, and perfuming agents may also be present in the composition.

Exemplary diluents include calcium carbonate, sodium carbonate, calcium phosphate, dicalcium phosphate, calcium sulfate, calcium hydrogen phosphate, sodium phosphate lactose, sucrose, cellulose, microcrystalline cellulose, kaolin, mannitol, sorbitol, inositol, sodium chloride, dry starch, cornstarch, powdered sugar, and mixtures thereof.

Exemplary granulating and/or dispersing agents include potato starch, corn starch, tapioca starch, sodium starch glycolate, clays, alginic acid, guar gum, citrus pulp, agar, bentonite, cellulose, and wood products, natural sponge, cation-exchange resins, calcium carbonate, silicates, sodium carbonate, cross-linked poly(vinyl-pyrrolidone) (crospovidone), sodium carboxymethyl starch (sodium starch glycolate), carboxymethyl cellulose, cross-linked sodium carboxymethyl cellulose (croscarmellose), methylcellulose, pregelatinized starch (starch 1500), microcrystalline starch, water insoluble starch, calcium carboxymethyl cellulose, magnesium aluminum silicate (Veegum), sodium lauryl sulfate, quaternary ammonium compounds, and mixtures thereof.

Exemplary surface active agents and/or emulsifiers include natural emulsifiers (e.g., acacia, agar, alginic acid, sodium alginate, tragacanth, chondrux, cholesterol, xanthan, pectin, gelatin, egg yolk, casein, wool fat, cholesterol, wax, and lecithin), colloidal clays (e.g., bentonite (aluminum

silicate) and Veegum (magnesium aluminum silicate)), long chain amino acid derivatives, high molecular weight alcohols (e.g., stearyl alcohol, cetyl alcohol, oleyl alcohol, triacetin monostearate, ethylene glycol distearate, glyceryl monostearate, and propylene glycol monostearate, polyvinyl alcohol), carbomers (e.g., carboxy polymethylene, polyacrylic acid, acrylic acid polymer, and carboxyvinyl polymer), carrageenan, cellulosic derivatives (e.g., carboxymethylcellulose sodium, powdered cellulose, hydroxymethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose), sorbitan fatty acid esters (e.g., polyoxyethylene sorbitan monolaurate (Tween® 20), polyoxyethylene sorbitan (Tween® 60), polyoxyethylene sorbitan monooleate (Tween® 80), sorbitan monopalmitate (Span® 40), sorbitan monostearate (Span® 60), sorbitan tristearate (Span® 65), glyceryl monooleate, sorbitan monooleate (Span® 80), polyoxyethylene esters (e.g., polyoxyethylene monostearate (Myrj® 45), polyoxyethylene hydrogenated castor oil, polyethoxylated castor oil, polyoxymethylene stearate, and Solutol®), sucrose fatty acid esters, polyethylene glycol fatty acid esters (e.g., Cremophor®), polyoxyethylene ethers, (e.g., polyoxyethylene lauryl ether (Brij® 30)), poly(vinyl-pyrrolidone), diethylene glycol monolaurate, triethanolamine oleate, sodium oleate, potassium oleate, ethyl oleate, oleic acid, ethyl laurate, sodium lauryl sulfate, Pluronic® F-68, Poloxamer P-188, cetrimonium bromide, cetylpyridinium chloride, benzalkonium chloride, docusate sodium, and/or mixtures thereof.

Exemplary binding agents include starch (e.g., cornstarch and starch paste), gelatin, sugars (e.g., sucrose, glucose, dextrose, dextrin, molasses, lactose, lactitol, mannitol, etc.), natural and synthetic gums (e.g., acacia, sodium alginate, extract of Irish moss, panwar gum, ghatti gum, mucilage of isapol husks, carboxymethylcellulose, methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, microcrystalline cellulose, cellulose acetate, poly(vinyl-pyrrolidone), magnesium aluminum silicate (Veegum®), and larch arabogalactan), alginates, polyethylene oxide, polyethylene glycol, inorganic calcium salts, silicic acid, polymethacrylates, waxes, water, alcohol, and/or mixtures thereof.

Exemplary preservatives include antioxidants, chelating agents, antimicrobial preservatives, antifungal preservatives, antiprotozoan preservatives, alcohol preservatives, acidic preservatives, and other preservatives. In certain embodiments, the preservative is an antioxidant. In other embodiments, the preservative is a chelating agent.

Exemplary antioxidants include alpha tocopherol, ascorbic acid, acorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, monothioglycerol, potassium metabisulfite, propionic acid, propyl gallate, sodium ascorbate, sodium bisulfite, sodium metabisulfite, and sodium sulfite.

Exemplary chelating agents include ethylenediaminetetraacetic acid (EDTA) and salts and hydrates thereof (e.g., sodium edetate, disodium edetate, trisodium edetate, calcium disodium edetate, dipotassium edetate, and the like), citric acid and salts and hydrates thereof (e.g., citric acid monohydrate), fumaric acid and salts and hydrates thereof, malic acid and salts and hydrates thereof, phosphoric acid and salts and hydrates thereof, and tartaric acid and salts and hydrates thereof. Exemplary antimicrobial preservatives include benzalkonium chloride, benzethonium chloride, benzyl alcohol, bronopol, cetrimide, cetylpyridinium chloride, chlorhexidine, chlorobutanol, chlorocresol, chloroxylenol, cresol, ethyl alcohol, glycerin, hexetidine, imidurea, phenol, phenoxyethanol, phenylethyl alcohol, phenylmercuric nitrate, propylene glycol, and thimerosal.

Exemplary antifungal preservatives include butyl paraben, methyl paraben, ethyl paraben, propyl paraben, benzoic acid, hydroxybenzoic acid, potassium benzoate, potassium sorbate, sodium benzoate, sodium propionate, and sorbic acid.

Exemplary alcohol preservatives include ethanol, polyethylene glycol, phenol, phenolic compounds, bisphenol, chlorobutanol, hydroxybenzoate, and phenylethyl alcohol.

Exemplary acidic preservatives include vitamin A, vitamin C, vitamin E, beta-carotene, citric acid, acetic acid, dehydroacetic acid, ascorbic acid, sorbic acid, and phytic acid.

Other preservatives include tocopherol, tocopherol acetate, deteroxime mesylate, cetrimide, butylated hydroxyanisol (BHA), butylated hydroxytoluened (BHT), ethylenediamine, sodium lauryl sulfate (SLS), sodium lauryl ether sulfate (SLES), sodium bisulfite, sodium metabisulfite, potassium sulfite, potassium metabisulfite, Glydant® Plus, Phenonip®, methylparaben, Germall® 115, Germaben® II, Neolone®, Kathon®, and Euxyl®.

Exemplary buffering agents include citrate buffer solutions, acetate buffer solutions, phosphate buffer solutions, ammonium chloride, calcium carbonate, calcium chloride, calcium citrate, calcium glubionate, calcium gluceptate, calcium gluconate, D-gluconic acid, calcium glycerophosphate, calcium lactate, propanoic acid, calcium levulinate, pentanoic acid, dibasic calcium phosphate, phosphoric acid, tribasic calcium phosphate, calcium hydroxide phosphate, potassium acetate, potassium chloride, potassium gluconate, potassium mixtures, dibasic potassium phosphate, monobasic potassium phosphate, potassium phosphate mixtures, sodium acetate, sodium

bicarbonate, sodium chloride, sodium citrate, sodium lactate, dibasic sodium phosphate, monobasic sodium phosphate, sodium phosphate mixtures, tromethamine, magnesium hydroxide, aluminum hydroxide, alginic acid, pyrogen-free water, isotonic saline, Ringer's solution, ethyl alcohol, and mixtures thereof.

Exemplary lubricating agents include magnesium stearate, calcium stearate, stearic acid, silica, talc, malt, glyceryl behanate, hydrogenated vegetable oils, polyethylene glycol, sodium benzoate, sodium acetate, sodium chloride, leucine, magnesium lauryl sulfate, sodium lauryl sulfate, and mixtures thereof.

Exemplary natural oils include almond, apricot kernel, avocado, babassu, bergamot, black current seed, borage, cade, camomile, canola, caraway, carnauba, castor, cinnamon, cocoa butter, coconut, cod liver, coffee, corn, cotton seed, emu, eucalyptus, evening primrose, fish, flaxseed, geraniol, gourd, grape seed, hazel nut, hyssop, isopropyl myristate, jojoba, kukui nut, lavandin, lavender, lemon, litsea cubeba, macademia nut, mallow, mango seed, meadowfoam seed, mink, nutmeg, olive, orange, orange roughy, palm, palm kernel, peach kernel, peanut, poppy seed, pumpkin seed, rapeseed, rice bran, rosemary, safflower, sandalwood, sasquana, savoury, sea buckthorn, sesame, shea butter, silicone, soybean, sunflower, tea tree, thistle, tsubaki, vetiver, walnut, and wheat germ oils. Exemplary synthetic oils include, but are not limited to, butyl stearate, caprylic triglyceride, capric triglyceride, cyclomethicone, diethyl sebacate, dimethicone 360, isopropyl myristate, mineral oil, octyldodecanol, oleyl alcohol, silicone oil, and mixtures thereof.

Liquid dosage forms for oral and parenteral administration include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredients, the liquid dosage forms may comprise inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils (e.g., cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof. Besides inert diluents, the oral compositions can include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, and perfuming agents. In certain embodiments for parenteral administration, the conjugates described herein are mixed with solubilizing agents such as Cremophor®, alcohols, oils, modified oils, glycols, polysorbates, cyclodextrins, polymers, and mixtures thereof.

Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions can be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation can be a sterile injectable solution, suspension, or emulsion in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that can be employed are water, Ringer's solution, U.S.P., and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed including synthetic mono- or di-glycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium prior to use.

In order to prolong the effect of a drug, it is often desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This can be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution, which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered drug form may be accomplished by dissolving or suspending the drug in an oil vehicle.

Compositions for rectal or vaginal administration are typically suppositories which can be prepared by mixing the conjugates described herein with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol, or a suppository wax which are solid at ambient temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active ingredient.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active ingredient is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or (a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, (b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidinone, sucrose, and acacia, (c) humectants such as glycerol, (d) disintegrating agents such as agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate, (e) solution retarding agents such as paraffin, (f) absorption accelerators such as quaternary ammonium

compounds, (g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, (h) absorbents such as kaolin and bentonite clay, and (i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets, and pills, the dosage form may include a buffering agent.

Solid compositions of a similar type can be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the art of pharmacology. They may optionally comprise opacifying agents and can be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of encapsulating compositions which can be used include polymeric substances and waxes. Solid compositions of a similar type can be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polethylene glycols and the like.

The active ingredient can be in a micro-encapsulated form with one or more excipients as noted above. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings, release controlling coatings, and other coatings well known in the pharmaceutical formulating art. In such solid dosage forms the active ingredient can be admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may comprise, as is normal practice, additional substances other than inert diluents, e.g., tableting lubricants and other tableting aids such a magnesium stearate and microcrystalline cellulose. In the case of capsules, tablets and pills, the dosage forms may comprise buffering agents. They may optionally comprise opacifying agents and can be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of encapsulating agents which can be used include polymeric substances and waxes.

Dosage forms for topical and/or transdermal administration of an agent (e.g., an antibiotic) described herein may include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants, and/or patches. Generally, the active ingredient is admixed under sterile conditions with a pharmaceutically acceptable carrier or excipient and/or any needed preservatives and/or buffers as can be required. Additionally, the present disclosure contemplates the use of transdermal patches,

which often have the added advantage of providing controlled delivery of an active ingredient to the body. Such dosage forms can be prepared, for example, by dissolving and/or dispensing the active ingredient in the proper medium. Alternatively or additionally, the rate can be controlled by either providing a rate controlling membrane and/or by dispersing the active ingredient in a polymer matrix and/or gel.

Suitable devices for use in delivering intradermal pharmaceutical compositions described herein include short needle devices. Intradermal compositions can be administered by devices which limit the effective penetration length of a needle into the skin. Alternatively or additionally, conventional syringes can be used in the classical mantoux method of intradermal administration. Jet injection devices which deliver liquid formulations to the dermis via a liquid jet injector and/or via a needle which pierces the stratum corneum and produces a jet which reaches the dermis are suitable. Ballistic powder/particle delivery devices which use compressed gas to accelerate the compound in powder form through the outer layers of the skin to the dermis are suitable.

Formulations suitable for topical administration include, but are not limited to, liquid and/or semi-liquid preparations such as liniments, lotions, oil-in-water and/or water-in-oil emulsions such as creams, ointments, and/or pastes, and/or solutions and/or suspensions. Topically administrable formulations may, for example, comprise from about 1% to about 10% (w/w) active ingredient, although the concentration of the active ingredient can be as high as the solubility limit of the active ingredient in the solvent. Formulations for topical administration may further comprise one or more of the additional ingredients described herein.

A pharmaceutical composition described herein can be prepared, packaged, and/or sold in a formulation suitable for pulmonary administration via the buccal cavity. Such a formulation may comprise dry particles which comprise the active ingredient and which have a diameter in the range from about 0.5 to about 7 nanometers, or from about 1 to about 6 nanometers. Such compositions are conveniently in the form of dry powders for administration using a device comprising a dry powder reservoir to which a stream of propellant can be directed to disperse the powder and/or using a self-propelling solvent/powder dispensing container such as a device comprising the active ingredient dissolved and/or suspended in a low-boiling propellant in a sealed container. Such powders comprise particles wherein at least 98% of the particles by weight have a diameter greater than 0.5 nanometers and at least 95% of the particles by number have a diameter less than 7 nanometers. Alternatively, at least 95% of the particles by weight have a diameter greater than 1

nanometer and at least 90% of the particles by number have a diameter less than 6 nanometers. Dry powder compositions may include a solid fine powder diluent such as sugar and are conveniently provided in a unit dose form.

Low boiling propellants generally include liquid propellants having a boiling point of below 65° F. at atmospheric pressure. Generally the propellant may constitute 50 to 99.9% (w/w) of the composition, and the active ingredient may constitute 0.1 to 20% (w/w) of the composition. The propellant may further comprise additional ingredients such as a liquid non-ionic and/or solid anionic surfactant and/or a solid diluent (which may have a particle size of the same order as particles comprising the active ingredient).

Pharmaceutical compositions described herein formulated for pulmonary delivery may provide the active ingredient in the form of droplets of a solution and/or suspension. Such formulations can be prepared, packaged, and/or sold as aqueous and/or dilute alcoholic solutions and/or suspensions, optionally sterile, comprising the active ingredient, and may conveniently be administered using any nebulization and/or atomization device. Such formulations may further comprise one or more additional ingredients including, but not limited to, a flavoring agent such as saccharin sodium, a volatile oil, a buffering agent, a surface active agent, and/or a preservative such as methylhydroxybenzoate. The droplets provided by this route of administration may have an average diameter in the range from about 0.1 to about 200 nanometers.

Formulations described herein as being useful for pulmonary delivery are useful for intranasal delivery of a pharmaceutical composition described herein. Another formulation suitable for intranasal administration is a coarse powder comprising the active ingredient and having an average particle from about 0.2 to 500 micrometers. Such a formulation is administered by rapid inhalation through the nasal passage from a container of the powder held close to the nares.

Formulations for nasal administration may, for example, comprise from about as little as 0.1% (w/w) to as much as 100% (w/w) of the active ingredient, and may comprise one or more of the additional ingredients described herein. A pharmaceutical composition described herein can be prepared, packaged, and/or sold in a formulation for buccal administration. Such formulations may, for example, be in the form of tablets and/or lozenges made using conventional methods, and may contain, for example, 0.1 to 20% (w/w) active ingredient, the balance comprising an orally dissolvable and/or degradable composition and, optionally, one or more of the additional ingredients described herein. Alternately, formulations for buccal administration may comprise a powder and/or

an aerosolized and/or atomized solution and/or suspension comprising the active ingredient. Such powdered, aerosolized, and/or aerosolized formulations, when dispersed, may have an average particle and/or droplet size in the range from about 0.1 to about 200 nanometers, and may further comprise one or more of the additional ingredients described herein.

A pharmaceutical composition described herein can be prepared, packaged, and/or sold in a formulation for ophthalmic administration. Such formulations may, for example, be in the form of eye drops including, for example, a 0.1-1.0% (w/w) solution and/or suspension of the active ingredient in an aqueous or oily liquid carrier or excipient. Such drops may further comprise buffering agents, salts, and/or one or more other of the additional ingredients described herein. Other opthalmically-administrable formulations which are useful include those which comprise the active ingredient in microcrystalline form and/or in a liposomal preparation. Ear drops and/or eye drops are also contemplated as being within the scope of this disclosure.

Although the descriptions of pharmaceutical compositions provided herein are principally directed to pharmaceutical compositions which are suitable for administration to humans, it will be understood by the skilled artisan that such compositions are generally suitable for administration to animals of all sorts. Modification of pharmaceutical compositions suitable for administration to humans in order to render the compositions suitable for administration to various animals is well understood, and the ordinarily skilled veterinary pharmacologist can design and/or perform such modification with ordinary experimentation.

FDA-approved drugs provided herein are typically formulated in dosage unit form for ease of administration and uniformity of dosage. It will be understood, however, that the total daily usage of the agents described herein will be decided by a physician within the scope of sound medical judgment. The specific therapeutically effective dose level for any particular subject or organism will depend upon a variety of factors including the disease being treated and the severity of the disorder; the activity of the specific active ingredient employed; the specific composition employed; the age, body weight, general health, sex, and diet of the subject; the time of administration, route of administration, and rate of excretion of the specific active ingredient employed; the duration of the treatment; drugs used in combination or coincidental with the specific active ingredient employed; and like factors well known in the medical arts.

The agents and compositions provided herein can be administered by any route, including enteral (e.g., oral), parenteral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal,

subcutaneous, intraventricular, transdermal, interdermal, rectal, intravaginal, intraperitoneal, topical (as by powders, ointments, creams, and/or drops), mucosal, nasal, bucal, sublingual; by intratracheal instillation, bronchial instillation, and/or inhalation; and/or as an oral spray, nasal spray, and/or aerosol. Specifically contemplated routes are oral administration, intravenous administration (e.g., systemic intravenous injection), regional administration via blood and/or lymph supply, and/or direct administration to an affected site. In general, the most appropriate route of administration will depend upon a variety of factors including the nature of the agent (e.g., its stability in the environment of the gastrointestinal tract), and/or the condition of the subject (e.g., whether the subject is able to tolerate oral administration). In certain embodiments, the agent or pharmaceutical composition described herein is suitable for topical administration to the eye of a subject.

The exact amount of an agent required to achieve an effective amount will vary from subject to subject, depending, for example, on species, age, and general condition of a subject, severity of the side effects or disorder, identity of the particular agent, mode of administration, and the like. An effective amount may be included in a single dose (e.g., single oral dose) or multiple doses (e.g., multiple oral doses). In certain embodiments, when multiple doses are administered to a subject or applied to a tissue or cell, any two doses of the multiple doses include different or substantially the same amounts of an agent (e.g., an antibiotic) described herein.

As noted elsewhere herein, a drug of the instant disclosure may be administered *via* a number of routes of administration, including but not limited to: subcutaneous, intravenous, intrathecal, intramuscular, intranasal, oral, transepidermal, parenteral, by inhalation, or intracerebroventricular.

The term "injection" or "injectable" as used herein refers to a bolus injection (administration of a discrete amount of an agent for raising its concentration in a bodily fluid), slow bolus injection over several minutes, or prolonged infusion, or several consecutive injections/infusions that are given at spaced apart intervals.

In some embodiments of the present disclosure, a formulation as herein defined is administered to the subject by bolus administration.

The FDA-approved drug or other therapy is administered to the subject in an amount sufficient to achieve a desired effect at a desired site (e.g., reduction of cancer size, cancer cell abundance, symptoms, etc.) determined by a skilled clinician to be effective. In some embodiments of the disclosure, the agent is administered at least once a year. In other embodiments of the disclosure, the agent is administered at least once a day. In other embodiments of the disclosure,

the agent is administered at least once a week. In some embodiments of the disclosure, the agent is administered at least once a month.

Additional exemplary doses for administration of an agent of the disclosure to a subject include, but are not limited to, the following: 1-20 mg/kg/day, 2-15 mg/kg/day, 5-12 mg/kg/day, 10 mg/kg/day, 1-500 mg/kg/day, 2-250 mg/kg/day, 5-150 mg/kg/day, 20-125 mg/kg/day, 50-120 mg/kg/day, 100 mg/kg/day, at least 10 μg/kg/day, at least 100 μg/kg/day, at least 250 μg/kg/day, at least 500 μg/kg/day, at least 1 mg/kg/day, at least 2 mg/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, at least 20 mg/kg/day, at least 50 mg/kg/day, at least 75 mg/kg/day, at least 100 mg/kg/day, at least 200 mg/kg/day, at least 500 mg/kg/day, at least 1 g/kg/day, and a therapeutically effective dose that is less than 500 mg/kg/day, less than 200 mg/kg/day, less than 100 mg/kg/day, less than 50 mg/kg/day, less than 20 mg/kg/day, less than 10 mg/kg/day, less than 5 mg/kg/day, less than 2 mg/kg/day, less than 1 mg/kg/day, less than 500 μg/kg/day, and less than 500 μg/kg/day.

In certain embodiments, when multiple doses are administered to a subject or applied to a tissue or cell, the frequency of administering the multiple doses to the subject or applying the multiple doses to the tissue or cell is three doses a day, two doses a day, one dose a day, one dose every other day, one dose every third day, one dose every week, one dose every two weeks, one dose every three weeks, or one dose every four weeks. In certain embodiments, the frequency of administering the multiple doses to the subject or applying the multiple doses to the tissue or cell is one dose per day. In certain embodiments, the frequency of administering the multiple doses to the subject or applying the multiple doses to the tissue or cell is two doses per day. In certain embodiments, the frequency of administering the multiple doses to the subject or applying the multiple doses to the tissue or cell is three doses per day. In certain embodiments, when multiple doses are administered to a subject or applied to a tissue or cell, the duration between the first dose and last dose of the multiple doses is one day, two days, four days, one week, two weeks, three weeks, one month, two months, three months, four months, six months, nine months, one year, two years, three years, four years, five years, seven years, ten years, fifteen years, twenty years, or the lifetime of the subject, tissue, or cell. In certain embodiments, the duration between the first dose and last dose of the multiple doses is three months, six months, or one year. In certain embodiments, the duration between the first dose and last dose of the multiple doses is the lifetime of the subject, tissue, or cell. In certain embodiments, a dose (e.g., a single dose, or any dose of multiple doses) described herein includes independently between 0.1 μg and 1 μg, between 0.001 mg and 0.01 mg,

between 0.01 mg and 0.1 mg, between 0.1 mg and 1 mg, between 1 mg and 3 mg, between 3 mg and 10 mg, between 10 mg and 30 mg, between 30 mg and 100 mg, between 100 mg and 300 mg, between 300 mg and 1,000 mg, or between 1 g and 10 g, inclusive, of an agent (e.g., an antibiotic) described herein. In certain embodiments, a dose described herein includes independently between 1 mg and 3 mg, inclusive, of an agent (e.g., an antibiotic) described herein. In certain embodiments, a dose described herein includes independently between 3 mg and 10 mg, inclusive, of an agent (e.g., an antibiotic) described herein. In certain embodiments, a dose described herein includes independently between 10 mg and 30 mg, inclusive, of an agent (e.g., an antibiotic) described herein. In certain embodiments, a dose described herein includes independently between 30 mg and 100 mg, inclusive, of an agent (e.g., an antibiotic) described herein.

It will be appreciated that dose ranges as described herein provide guidance for the administration of provided pharmaceutical compositions to an adult. The amount to be administered to, for example, a child or an adolescent can be determined by a medical practitioner or person skilled in the art and can be lower or the same as that administered to an adult. In certain embodiments, a dose described herein is a dose to an adult human whose body weight is 70 kg.

It will be also appreciated that an agent (e.g., an antibiotic) or composition, as described herein, can be administered in combination with one or more additional pharmaceutical agents (e.g., therapeutically and/or prophylactically active agents), which are different from the agent or composition and may be useful as, e.g., combination therapies. The agents or compositions can be administered in combination with additional pharmaceutical agents that improve their activity (e.g., activity (e.g., potency and/or efficacy) in treating a disease in a subject in need thereof, in preventing a disease in a subject in need thereof, in reducing the risk of developing a disease in a subject in need thereof, in inhibiting the replication of a virus, in killing a virus, etc. in a subject or cell. In certain embodiments, a pharmaceutical composition described herein including an agent (e.g., an antibiotic) described herein and an additional pharmaceutical agent shows a synergistic effect that is absent in a pharmaceutical composition including one of the agent and the additional pharmaceutical agent, but not both.

In some embodiments of the disclosure, a therapeutic agent distinct from a first therapeutic agent of the disclosure is administered prior to, in combination with, at the same time, or after administration of the agent of the disclosure. In some embodiments, the second therapeutic agent is

selected from the group consisting of a chemotherapeutic, an antioxidant, an anti-inflammatory agent, an antimicrobial, a steroid, etc.

The agent or composition can be administered concurrently with, prior to, or subsequent to one or more additional pharmaceutical agents, which may be useful as, e.g., combination therapies. Pharmaceutical agents include therapeutically active agents. Pharmaceutical agents also include prophylactically active agents. Pharmaceutical agents include small organic molecules such as drug compounds (e.g., compounds approved for human or veterinary use by the U.S. Food and Drug Administration as provided in the Code of Federal Regulations (CFR)), peptides, proteins, carbohydrates, monosaccharides, oligosaccharides, polysaccharides, nucleoproteins, mucoproteins, lipoproteins, synthetic polypeptides or proteins, small molecules linked to proteins, glycoproteins, steroids, nucleic acids, DNAs, RNAs, nucleotides, nucleosides, oligonucleotides, antisense oligonucleotides, lipids, hormones, vitamins, and cells. In certain embodiments, the additional pharmaceutical agent is a pharmaceutical agent useful for treating and/or preventing a disease described herein. Each additional pharmaceutical agent may be administered at a dose and/or on a time schedule determined for that pharmaceutical agent. The additional pharmaceutical agents may also be administered together with each other and/or with the agent or composition described herein in a single dose or administered separately in different doses. The particular combination to employ in a regimen will take into account compatibility of the agent described herein with the additional pharmaceutical agent(s) and/or the desired therapeutic and/or prophylactic effect to be achieved. In general, it is expected that the additional pharmaceutical agent(s) in combination be utilized at levels that do not exceed the levels at which they are utilized individually. In some embodiments, the levels utilized in combination will be lower than those utilized individually.

Dosages for a particular agent of the instant disclosure may be determined empirically in individuals who have been given one or more administrations of the agent.

Administration of an agent of the present disclosure can be continuous or intermittent, depending, for example, on the recipient's physiological condition, whether the purpose of the administration is therapeutic or prophylactic, and other factors known to skilled practitioners. The administration of an agent may be essentially continuous over a preselected period of time or may be in a series of spaced doses.

Guidance regarding particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Patent Nos. 4,657,760; 5,206,344; or 5,225,212. It is within the scope of the

instant disclosure that different formulations will be effective for different treatments and different disorders, and that administration intended to treat a specific organ or tissue may necessitate delivery in a manner different from that to another organ or tissue. Moreover, dosages may be administered by one or more separate administrations, or by continuous infusion. For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms occurs. However, other dosage regimens may be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

Kits

The instant disclosure also provides kits containing agents of this disclosure for use in the methods of the present disclosure. Kits of the instant disclosure may include one or more containers comprising an agent (e.g., a sample preparation reagent) of this disclosure and/or may contain agents (e.g., oligonucleotide primers, probes, and one or more detectable probes or probe sets etc.) for identifying a cancer or subject as possessing one or more variant sequences. In some embodiments, the kits further include instructions for use in accordance with the methods of this disclosure. In some embodiments, these instructions comprise a description of sample preparation and target binding/signal detection protocol. In some embodiments, the instructions comprise a description of how to detect antibiotic susceptibility and direct therapeutic intervention accordingly.

The instructions generally include information as to dosage, dosing schedule, and route of administration for the intended treatment. The containers may be unit doses, bulk packages (e.g., multi-dose packages) or sub-unit doses. Instructions supplied in the kits of the instant disclosure are typically written instructions on a label or package insert (e.g., a paper sheet included in the kit), but machine-readable instructions (e.g., instructions carried on a magnetic or optical storage disk) are also acceptable.

The label or package insert indicates that the composition is used for treating, e.g., a class bacterial infections, in a subject. Instructions may be provided for practicing any of the methods described herein.

The kits of this disclosure are in suitable packaging. Suitable packaging includes, but is not limited to, vials, bottles, jars, flexible packaging (e.g., sealed Mylar or plastic bags), and the like. In certain embodiments, at least one active agent in the composition is one or more by apartheid probe sets designed for detecting specific mRNAs or mRNA signature profiles. The container may further comprise a second pharmaceutically active agent.

Kits may optionally provide additional components such as buffers and interpretive information. Normally, the kit comprises a container and a label or package insert(s) on or associated with the container.

The practice of the present disclosure employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art. See, e.g., Maniatis et al., 1982, Molecular Cloning (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Sambrook et al., 1989, Molecular Cloning, 2nd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Sambrook and Russell, 2001, Molecular Cloning, 3rd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Ausubel et al., 1992), Current Protocols in Molecular Biology (John Wiley & Sons, including periodic updates); Glover, 1985, DNA Cloning (IRL Press, Oxford); Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988, Antibodies, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Jakoby and Pastan, 1979; Nucleic Acid Hybridization (B. D. Hames & S. J. Higgins eds. 1984); Transcription And Translation (B. D. Hames & S. J. Higgins eds. 1984); Culture Of Animal Cells (R. I. Freshney, Alan R. Liss, Inc., 1987); Immobilized Cells And Enzymes (IRL Press, 1986); B. Perbal, A Practical Guide To Molecular Cloning (1984); the treatise, Methods In Enzymology (Academic Press, Inc., N.Y.); Gene Transfer Vectors For Mammalian Cells (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); Methods In Enzymology, Vols. 154 and 155 (Wu et al. eds.), Immunochemical Methods In Cell And Molecular Biology (Mayer and Walker, eds., Academic Press, London, 1987); Handbook Of Experimental Immunology, Volumes I- IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, Essential Immunology, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan et al., Manipulating the Mouse Embryo, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986); Westerfield, M., The zebrafish book. A guide for the laboratory use of zebrafish (Danio rerio), (4th Ed., Univ. of Oregon Press, Eugene, 2000).

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by

reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Reference will now be made in detail to exemplary embodiments of the disclosure. While the disclosure will be described in conjunction with the exemplary embodiments, it will be understood that it is not intended to limit the disclosure to those embodiments. To the contrary, it is intended to cover alternatives, modifications, and equivalents as may be included within the spirit and scope of the disclosure as defined by the appended claims. Standard techniques well known in the art or the techniques specifically described below were utilized.

EXAMPLES

Example 1: Rapid Phenotypic Detection of Antibiotic Resistance

The techniques herein allow for rapid phenotypic detection of antibiotic resistance, faster than growth-based phenotypic assays that currently comprise the gold standard. Advantageously, the techniques herein provide compositions and methods that allow simultaneous detection of multiple resistance genes in the same assay. Additionally, the techniques herein provide more accurate determination of resistance, as well as mechanistic explanations for key antibiotic resistant strains, epidemiologic tracking of known resistance mechanisms, and immediate identification of unknown or potentially novel resistance mechanisms (e.g., discordant cases when a resistant organism does not display a known resistance phenotype). Currently, detection of antibiotic resistance genes typically requires separate PCR or sequencing assays, which require different assay infrastructure and often necessitate sending samples out to reference laboratories.

The phenotypic antibiotic susceptibility testing (AST) portion of the techniques herein relies on quantitative measurement of the most antibiotic-responsive transcripts in a microbial pathogen upon antibiotic exposure. According to the techniques herein, RNA-Seq may be used to identify antibiotic responsive genes that change the most in susceptible, but not resistant, bacterial strains in response to exposure to an antibiotic. In this way, the nucleic acid targets for use in AST may be identified.

Once antibiotic responsive nucleic acid targets are identified, they can be assayed with target specific probes or sets of probes. According to the techniques herein, target specific probes may

include bipartite probes (e.g., Probe A and Probe B) as shown in FIG. 1A. In embodiments, each such probe may range in length from about 15-100, 25-75, 30-70, 40-60, or 45-55 nucleotides in length. In embodiments, each such probe may be about 50 nucleotides in length. As shown in FIG. 1A, Probe A and Probe B are oriented in a tail to head configuration (e.g., the 3' end of Probe B is positioned proximate to the 5' end of Probe A). In embodiments, the 3' end of Probe B abuts the 5'and of Probe A; however, it is contemplated within the scope of the disclosure that a gap of about 1-50 nucleotides may occur between the 3' end of Probe B and the 5'end of Probe A. As shown in FIGS. 1B-1C, bipartite probes according to the techniques herein may be detected via directly coupled tags or indirectly coupled tags, respectively.

Current assay conditions: hybridization of the bipartite probe sets at 65-67˚C for 1 hour, then detection on a NanoString® Sprint instrument. Briefly, 3 µl of crude lysate is incubated with unlabeled probe pairs (e.g. probe sets) for each target along with labeled NanoString® Elements TagSet reagents. Standard hybridization conditions according to the manufacturer's protocol are followed, except hybridizations are incubated for one hour at 67˚C instead of the recommended 16-24 hours. Hybridizations are then loaded and processed on a Sprint instrument (NanoString®) for purification and quantitative detection. These methods have been validated on: bacteria in pure culture; clinical urine samples; clinical blood culture samples.

Example 2: Genetic Basis for Carbapenem Resistance

To test and validate the techniques described herein, the genetic basis for carbapenem resistance, carbapenemases, was assessed by identifying and measuring the most important, transmissible cause of resistance to this last-line antibiotic. The techniques herein allowed antibiotic-responsive transcripts to be detected quantitatively, and in a multiplexed fashion in a single assay from crude lysate, which enhanced the speed of detection while minimizing sample processing/manipulation. The techniques herein were conducted on the NanoString® assay platform; however, one of skill in the art will readily comprehend that these techniques are not dependent on a single detection platform and may be conducted on any of a variety of detection platforms for quantitative RNA measurement (e.g., NanoString®, SHERLOCK, qRT-PCR, microarrays, etc.) capable of providing the above features.

The analysis herein identified seventeen relevant target sequences to be targeted by the Cre2 probe targets (e.g., probeset), which are shown in **Table 1**.

Table 1: Cre2 Target Sequences

CRE2 Probe Targets:

Target:	target sequence in gene
ST258_wzi_1(SEQ ID NO: 35)	ACCAGTCAATAAATAAAGCGTTCCCTCATGCCGATACTCTGAAAGGTGTTCAGCTGGGATGGAGTGGGAATGTTTATCAGTCGGTTCGAATTAACACTTC
ST258_wzy_1(SEQ ID NO: 36)	AAAAAACTAATCTATATATTGCTAATACCAATTGCAGGCTTAGCAGTTTTTGCAATTTTTCAGGAGAGGCTGTCGCATGATGGTTATACATCATATGAAC
ST58_wzi_2(SEQ ID NO: 37)	AAACCTTCCTATTCCTCTGAGCAGGTAGTTCTGGCTCGTATCAATCAGCGACTGTCAGCGTTAAAAGCCGATTTCCGGGTCACCGGCTATACCTCGACCG
ST258_wzy_2(SEQ ID NO: 38)	GCCAACATTTATCAGCTATAAAGCGCAACTTTACTTTGACCTGAATACGGAAGGAGACCTTAAAAGAGTTACAGCAGTTGCAATGGGATTTGGAAGTCTT
CRE2_KPC_0.95(SEQ ID NO: 39)	ACCCATCTCGGAAAAATATCTGACAACAGGCATGACGGTGGCGGAGCTGTCCGCGGCCGCCGTGCAATACAGTGATAACGCCGCCGCCAATTTGTTGCTG
CRE2_NDM_0.95(SEQ ID NO: 40)	CAAATGGAAACTGGCGACCAACGGTTTGGCGATCTGGTTTTCCGCCAGCTCGCACCGAATGTCTGGCAGCACACTTCCTATCTCGACATGCCGGGTTTCG
CRE2_OXA48_0.95(SEQ ID NO: 41)	TGCTACATGCTTTCGATTATGGTAATGAGGACATTTCGGGCAATGTAGACAGTTTCTGGCTCGACGGTGGTATTCGAATTTCGGCCACGGAGCAAATCAG
CRE2_CTXM15_0.95(SEQ ID NO: 42)	AGTGAAAGCGAACCGAATCTGTTAAATCAGCGAGTTGAGATCAAAAAATCTGACCTTGTTAACTATAATCCGATTGCGGAAAAGCACGTCAATGGGACGA
CRE2_IMP_1_0.95(SEQ ID NO: 43)	GAAGAAGGTGTTTATGTTCATACATCGTTCGAAGAAGTTAACGGTTGGGGTGTTGTTTCTAAACACGGTTTGGTGGTTCTTGTAAACACTGACGCCTATC
CRE2_IMP_3_8_0.95(SEQ ID NO: 44)	GTTTTTTATCCCGGCCCGGGGCACACTCAAGATAACGTAGTGGTTTGGTTACCTGAAAAGAAAATTTTATTCGGTGGTTGTTTTGTTAAACCGGACGGTC
CRE2_IMP_2_4_0.95(SEQ ID NO: 45)	GAAAAGTTAGTCAATTGGTTTGTGGAGCGCGGCTATAAAATCAAAGGCACTATTTCCTCACATTTCCATAGCGACAGCACAGGGGGAATAGAGTGGCTTA
CRE2_IMP_5_0.95(SEQ ID NO: 46)	AAGTATGGTAATGCAAAACTGGTTGTTTCGAGTCATAGTGAAATTGGGGGCGCATCACTATTGAAGCGCACTTGGGAGCAGGCTGTTAAGGGGCTAAAAG
CRE2_IMP_6_0.95(SEQ ID NO: 47)	GAAAAGTTAGTCACTTGGTTTGTGGAACGTGGCTATAAAATAAAAGGCAGTATTTCCTCTCATTTTCATAGCGACAGCACGGGCGGAATAGAGTGGCTTA
CRE2_IMP_7_0.95(SEQ ID NO: 48)	TATGCATCTGAATTAACAAATGAACTTCTTAAAAAAGACGGTAAGGTACAAGCTAAAAATTCATTTAGCGGAGTTAGCTATTGGCTAGTTAAGAAAAAGA
CRE2_VIM_1_0.95(SEQ ID NO: 49)	CTCTAGTGGAGATGTGGTGCGCTTCGGTCCCGTAGAGGTTTTCTATCCTGGTGCTGCGCATTCGGGCGACAATCTTGTGGTATACGTGCCGGCCGTGCGC
CRE2_VIM_2_3_0.95(SEQ ID NO: 50)	TGATGGTGATGAGTTGCTTTTGATTGATACAGCGTGGGGTGCGAAAAACACAGCGGCACTTCTCGCGGAGATTGAGAAGCAAATTGGACTTCCCGTAACG
OXA10_0.95(SEQ ID NO: 51)	CATAAAGAATGAGCATCAGGTTTTCAAATGGGACGGAAAGCCAAGAGCCATGAAGCAATGGGAAAGAGACTTGACCTTAAGAGGGGCAATACAAGTTTCA

The analysis herein also identified eighteen relevant target sequences to be targeted by KpMero4 probe targets (e.g., probeset), which are shown in **Table 2**.

Table 2: KpMero4 Target Sequences

KpMero4 Probes Targets:

Target:	target sequence in gene
KpMero4_C_KPN_00050_0.97(SEQ ID NO: 52)	AGATCGTGCTTACCGCATGCTGATGAACCGCAAATTCTCTGAAGAAGCGGCAACCTGGATGCAGGAACAGCGCGCCAGTGCGTATGTTAAAATTCTGAGC
KpMero4_C_KPN_00098_0.97(SEQ ID NO: 53)	GGAACGTTGTGGTCTGAAAGTTGACCAACTTATTTTCGCCGGGTTAGCGGCCAGTTATTCGGTATTAACAGAAGACGAACGTGAGCTGGGCGTCTGCGTT
KpMero4_C_KPN_00100_0.97(SEQ ID NO: 54)	TCGATTGTGCCATCGTTGTTGACGATTATCGCGTACTGAACGAAGACGGTCTGCGCTTTGAAGACGAATTTGTTCGCCACAAAATGCTGGATGCGATCGG
KpMero4_C_KPN_01276_0.92(SEQ ID NO: 55)	ATGCTGGAGTTGTTGTTTCTGCTTTTACCCGTTGCCGCCGCTTACGGCTGGTACATGGGGCGCAGAAGTGCACAACAGTCCAAACAGGACGATGCGAGCC
KpMero4_C_KPN_02846_0.95(SEQ ID NO: 56)	GCGCAGGATCTGGTGATGAACTTTTCCGCCGACTGCTGGCTGGAAGTGAGCGATGCCACCGGTAAAAAACTGTTCAGCGGCCTGCAGCGTAAAGGCGGTA
KpMero4_C_KPN_03317_0.92(SEQ ID NO: 57)	ATGGCCGGGGAACACGTCATTTTGCTGGATGAGCAGGATCAGCCTGCCGGTATGCTGGAGAAGTATGCCGCCCATACGTTTGATACCCCTTTACATCTCG
KpMero4_C_KPN_03634_0.92(SEQ ID NO: 58)	AGCAATGACGGCGAAACGCCGGAAGGCATTGGCTTTGCGATCCCGTTCCAGTTAGCGACCAAAATTATGGATAAACTGATCCGCGATGGCCGGGTGATCC
KpMero4_C_KPN_04666_0.97(SEQ ID NO: 59)	CAGGCCAGCGATGGTAACGCGGTGATGTTTATCGAAAGCGTCAACGGCAACCGCTTCCATGACGTCTTCCTTGCCCAGCTGCGTCCGAAAGGCAATGCGC
KpMero4_R01up_KPN_01226_0.97(SEQ ID NO: 60)	GCGCGATGCACGATCTGATCGCCAGCGACACCTTCGATAAGGCGAAGGCGGAAGCGCAGATCGATAAGATGGAAGCGCAGCATAAAGCGATGGCGCTGTC
KpMero4_R02up_KPN_01107_0.97(SEQ ID NO: 61)	GCTGTCGCTGGTCTCAACGTGTTGGATCGCGGCCCGCAGTATGCGCAAGTGGTCTCCAGTACACCGATTAAAGAAACCGTGAAAACGCCGCGTCAGGAAT
KpMero4_R03up_KPN_02345_0.95(SEQ ID NO: 62)	ATGCGAATCGCGCTTTTCCTGCTGACGAACCTGGCAGTGATGGTCGTGTTCGGGCTGGTGTTAAGCCTCACGGGGATCCAATCCAGCAGCATGACCGGTC
KpMero4_R04up_KPN_02742_0.97(SEQ ID NO: 63)	CAAATAGGCGATCGTGACAATTACGGTAACTACTGGGACGGTGGCAGCTGGCGCGACCGTGATTACTGGCGTCGTCACTATGAATGGCGTGATAACCGTT
KpMero4_R05dn_KPN_02241_0.92(SEQ ID NO: 64)	GGGTAGGTTACTCCATTCTGAACCAGCTTCCGCAGCTTAACCTGCCACAATTCTTTGCGCATGGCGCAATCCTAAGCATCTTCGTTGGCGCAGTGCTCTG
KpMero4_R06up_KPN_03358_0.92(SEQ ID NO: 65)	GGGCGAAAAACTGGTGAACTCGCAGTTCTCCCAGCGTCAGGAATCGGAAGCGGATGACTACTCTTACGACCTGCTGCGTAAGCGCGGTATCAATCCGTCG
KpMero4_R07up_KPN_03934_0.92(SEQ ID NO: 66)	TGCCTTATATTACCAAGCAGAATCAGGCGATTACTGCGGATCGTAACTGGCTTATTTCCAAGCAGTACGATGCTCGCTGGTCGCCGACTGAGAAGGCGCG
KpMero4_R08dn_KPN_00868_0.92(SEQ ID NO: 67)	TGCAACTGCGAAAGGCCAAAGGCTACATGTCAGTCAGCGAAAATGACCATCTGCGTGATAACTTGTTTGAGCTTTGCCGTGAAATGCGTGCGCAGGCGCC
KpMero4_R09up_KPN_02342_0.97(SEQ ID NO: 68)	TATGGGGTGTTATTCCACAGTGAGGAAAACGTCGGCGGTCTGGGTCTTAAGTGCCAATACCTCACCGCCCGCGGAGTCAGCACCGCACTTTATGTTCATT
KpMero4_R10up_KPN_00833_0.97(SEQ ID NO: 69)	AACCACTTTAGATGGTCTGGAAGCAAAACTGGCTGCTAAAGCCGAAGCCGCTGGCGCGACCGGCTACAGCATTACTTCCGCTAACACCAACAACAAACTG

To facilitate identification of Cre2 probe targets, bipartite probes comprising a probe A and a probe B were constructed as shown in **Table 3** and **Table 4**, respectively.

Table 3: Cre2 Probe A Sequences

CRE2 probes:	
Target:	probe A sequence
ST258_wzi_1 (SEQ ID NO: 70)	AACACCTTTCAGAGTATCGGCATGAGGGAACGCTTTATTTATTGACTGGTCCTCAAGACCTAAGCGACAGCGTGACCTTGTTTCA
ST258_wzy_1 (SEQ ID NO: 71)	AAAACTGCTAAGCCTGCAATTGGTATTAGCAATATATAGATTAGTTTTTTCATCCTCTTCTTTTCTTGGTGTTGAGAAGATGCTC
ST58_wzi_2 (SEQ ID NO: 72)	CGCTGATTGATACGAGCCAGAACTACCTGCTCAGAGGAATAGGAAGGTTTCACAATTCTGCGGGTTAGCAGGAAGGTTAGGGAAC
ST258_wzy_2 (SEQ ID NO: 73)	CCGTATTCAGGTCAAAGTAAAGTTGCGCTTTATAGCTGATAAATGTTGGCCTGTTGAGATTATTGAGCTTCATCATGACCAGAAG
CRE2_KPC_0.95 (SEQ ID NO: 74)	ACAGCTCCGCCACCGTCATGCCTGTTGTCAGATATCAAAGACGCCTATCTTCCAGTTTGATCGGGAAACT
CRE2_NDM_0.95 (SEQ ID NO: 75)	AGCTGGCGGAAAACCAGATCGCCAAACCGTTGGTCGCCAGTTTCCATTTGCGAACCTAACTCCTCGCTACATTCCTATTGTTTTC
CRE2_OXA48_0.95 (SEQ ID NO: 76)	GTCTACATTGCCCGAAATGTCCTCATTACCATAATCGAAAGCATGTAGCACCAATTTGGTTTTACTCCCCTCGATTATGCGGAGT
CRE2_CTXM15_0.95 (SEQ ID NO: 77)	GATTTTTTGATCTCAACTCGCTGATTTAACAGATTCGGTTCGCTTTCACTCTTTCGGGTTATATCTATCATTTACTTGACACCCT
CRE2_IMP_1_0.95 (SEQ ID NO: 78)	CCCCAACCGTTAACTTCTTCGAACGATGTATGAACATAAACACCTTCTTCCAACAGCCACTTTTTTTCCAAATTTTGCAAGAGCC
CRE2_IMP_3_8_0.95 (SEQ ID NO: 79)	AACCAAACCACTACGTTATCTTGAGTGTGCCCCGGGCCGGGATAAAAAACCACCGTGTGGACGGCAACTCAGAGATAACGCATAT
CRE2_IMP_2_4_0.95 (SEQ ID NO: 80)	GTGCCTTTGATTTTATAGCCGCGCTCCACAAACCAATTGACTAACTTTTCCCTGGAGTTTATGTATTGCCAACGAGTTTGTCTTT
CRE2_IMP_5_0.95 (SEQ ID NO: 81)	CCCCCAATTTCACTATGACTCGAAACAACCAGTTTTGCATTACCATACTTCAGATAAGGTTGTTATTGTGGAGGATGTTACTACA
CRE2_IMP_6_0.95 (SEQ ID NO: 82)	CTGCCTTTTATTTTATAGCCACGTTCCACAAACCAAGTGACTAACTTTTCCTTCCTTCCTGTGTTCCAGCTACAAACTTAGAAAC
CRE2_IMP_7_0.95 (SEQ ID NO: 83)	TGTACCTTACCGTCTTTTTTAAGAAGTTCATTTGTTAATTCAGATGCATACATAAAATTGGTTTTGCCTTTCAGCAATTCAACTT

CRE2_VIM_1_0.95 (SEQ ID NO: 84)	GAAAACCTCTACGGGACCGAAGCGCACCACATCTCCACTAGAGCTGGTCAAGACTTGCATGAGGACCCGCAAATTCCT
CRE2_VIM_2_3_0.95(SEQ ID NO: 85)	CGCACCCCACGCTGTATCAATCAAAAGCAACTCATCACCATCACTTTCGTTGGGACGCTTGAAGCGCAAGTAGAAAAC
OXA10_0.95 (SEQ ID NO: 86)	TGGCTCTTGGCTTTCCGTCCCATTTGAAAACCTGATGCTCATTCTTTATGCCAGCAGACCTGCAATATCAAAGTTATAAGCGCGT

Table 4: Cre2 Probe B Sequences

CRE2 probes:

Target:	probe B sequence
ST258_wzi_1 (SEQ ID NO: 87)	CGAAAGCCATGACCTCCGATCACTCGAAGTGTTAATTCGAACCGACTGATAAACATTCCCACTCCATCCCAGCTG
ST258_wzy_1 (SEQ ID NO: 88)	CGAAAGCCATGACCTCCGATCACTCGTTCATATGATGTATAACCATCATGCGACAGCCTCTCCTGAAAAATTGCA
ST58_wzi_2 (SEQ ID NO: 89)	CGAAAGCCATGACCTCCGATCACTCCGGTCGAGGTATAGCCGGTGACCCGGAAATCGGCTTTTAACGCTGACAGT
ST258_wzy_2 (SEQ ID NO: 90)	CGAAAGCCATGACCTCCGATCACTCAAGACTTCCAAATCCCATTGCAACTGCTGTAACTCTTTTAAGGTCTCCTT
CRE2_KPC_0.95 (SEQ ID NO: 91)	CGAAAGCCATGACCTCCGATCACTCCAGCAACAAATTGGCGGCGGCGTTATCACTGTATTGCACGGCGGCCGCGG
CRE2_NDM_0.95 (SEQ ID NO: 92)	CGAAAGCCATGACCTCCGATCACTCCGAAACCCGGCATGTCGAGATAGGAAGTGTGCTGCCAGACATTCGGTGCG
CRE2_OXA48_0.95 (SEQ ID NO: 93)	CGAAAGCCATGACCTCCGATCACTCCTGATTTGCTCCGTGGCCGAAATTCGAATACCACCGTCGAGCCAGAAACT
CRE2_CTXM15_0.95 (SEQ ID NO: 94)	CGAAAGCCATGACCTCCGATCACTCTCGTCCCATTGACGTGCTTTTCCGCAATCGGATTATAGTTAACAAGGTCA
CRE2_IMP_1_0.95 (SEQ ID NO: 95)	CGAAAGCCATGACCTCCGATCACTCGATAGGCGTCAGTGTTTACAAGAACCACCAAACCGTGTTTAGAAACAACA
CRE2_IMP_3_8_0.95 (SEQ ID NO: 96)	CGAAAGCCATGACCTCCGATCACTCGACCGTCCGGTTTAACAAAACAACCACCGAATAAAATTTTCTTTTCAGGT
CRE2_IMP_2_4_0.95 (SEQ ID NO: 97)	CGAAAGCCATGACCTCCGATCACTCTAAGCCACTCTATTCCCCCTGTGCTGTCGCTATGGAAATGTGAGGAAATA
CRE2_IMP_5_0.95 (SEQ ID NO: 98)	CGAAAGCCATGACCTCCGATCACTCCCCTTAACAGCCTGCTCCCAAGTGCGCTTCAATAGTGATGCG
CRE2_IMP_6_0.95 (SEQ ID NO: 99)	CGAAAGCCATGACCTCCGATCACTCTAAGCCACTCTATTCCGCCCGTGCTGTCGCTATGAAAATGAGAGGAAATA

CRE2_IMP_7_0.95 (SEQ ID NO: 100)	CGAAAGCCATGACCTCCGATCACTCTCTTTTTCTTAACTAGCCAATAGCTAACT CCGCTAAATGAATTTTTAGCT
CRE2_VIM_1_0.95 (SEQ ID NO: 101)	CGAAAGCCATGACCTCCGATCACTCCGTATACCACAAGATTGTCGCCCGAATGC GCAGCACCAGGATA
CRE2_VIM_2_3_0.95(SEQ ID NO: 102)	CGAAAGCCATGACCTCCGATCACTCCAATTTGCTTCTCAATCTCCGCGAGAAGT GCCGCTGTGTTTTT
OXA10_0.95 (SEQ ID NO: 103)	CGAAAGCCATGACCTCCGATCACTCTGAAACTTGTATTGCCCCTCTTAAGGTCA AGTCTCTTTCCCATTGCTTCA

Similarly, to facilitate identification of KpMero4 probe targets, bipartite probes comprising a probe A and a probe B were constructed as shown in **Table 5** and **Table 6**, respectively.

Table 5: KpMero4 Probe A Sequences

KpMero4 probes:	
Target:	probe A sequence
KpMero4_C_KPN_00050_0.97(SEQ ID NO: 104)	CCGCTTCTTCAGAGAATTTGCGGTTCATCAGCATGCGGTAAGCACGATCCT GCCAATGCACTCGATCTTGTCATTTTTTTGCG
KpMero4_C_KPN_00098_0.97(SEQ ID NO: 105)	CCGCTAACCCGGCGAAAATAAGTTGGTCAACTTTCAGACCACAACGTTCCC AAACTGGAGAGAGAAGTGAAGACGATTTAACCCA
KpMero4_C_KPN_00100_0.97(SEQ ID NO: 106)	ACCGTCTTCGTTCAGTACGCGATAATCGTCAACAACGATGGCACAATCGAC GATTGCTGCATTCCGCTCAACGCTTGAGGAAGTA
KpMero4_C_KPN_01276_0.92(SEQ ID NO: 107)	CAGCCGTAAGCGGCGGCAACGGGTAAAAGCAGAAACAACAACTCCAGCATC TGAGGCTGTTAAAGCTGTAGCAACTCTTCCACGA
KpMero4_C_KPN_02846_0.95(SEQ ID NO: 108)	CTCACTTCCAGCCAGCAGTCGGCGGAAAAGTTCATCACCAGACTAGGACGC AAATCACTTGAAGAAGTGAAAGCGAG
KpMero4_C_KPN_03317_0.92(SEQ ID NO: 109)	CCGGCAGGCTGATCCTGCTCATCCAGCAAAATGACGTGTTCCCCACGCGAT GACGTTCGTCAAGAGTCGCATAATCT
KpMero4_C_KPN_03634_0.92(SEQ ID NO: 110)	TGGAACGGGATCGCAAAGCCAATGCCTTCCGGCGTTTCGCCGCATTTGGAA TGATGTGTACTGGGAATAAGACGACG
KpMero4_C_KPN_04666_0.97(SEQ ID NO: 111)	TTGCCGTTGACGCTTTCGATAAACATCACCGCGTTACCATCGCTGGCCTGC ACAAGAATCCCTGCTAGCTGAAGGAGGGTCAAAC
KpMero4_R01up_KPN_01226_0.97(SEQ ID NO: 112)	CGCCTTCGCCTTATCGAAGGTGTCGCTGGCGATCAGATCGTGCTTGACGTA GATTGCTATCAGGTTACGATGACTGC
KpMero4_R02up_KPN_01107_0.97(SEQ ID NO: 113)	ACTTGCGCATACTGCGGGCCGCGATCCAACACGTTGAGACCACTTACAGAT CGTGTGCTCATGACTTCCACAGACGT
KpMero4_R03up_KPN_02345_0.95(SEQ ID NO: 114)	AACACGACCATCACTGCCAGGTTCGTCAGCAGGAAAAGCGCGATTCGCATC TTGGAGGAGTTGATAGTGGTAAAACAACATTAGC

KpMero4_R04up_KPN_02742_0.97(SEQ ID NO: 115)	CAGCTGCCACCGTCCCAGTAGTTACCGTAATTGTCACGATCGCCTACGTATATATCCAAGTGGTTATGTCCGACGGC
KpMero4_R05dn_KPN_02241_0.92(SEQ ID NO: 116)	TTGTGGCAGGTTAAGCTGCGGAAGCTGGTTCAGAATGGAGTAACCTACCAGCAAGAAGGAGTATGGAACTTATAGCAAGAGAG
KpMero4_R06up_KPN_03358_0.92(SEQ ID NO: 117)	CTTCCGATTCCTGACGCTGGGAGAACTGCGAGTTCACCAGTTCACCCCTCCAAACGCATTCTTATTGGCAAATGGAA
KpMero4_R07up_KPN_03934_0.92(SEQ ID NO: 118)	CCAGTTACGATCCGCAGTAATCGCCTGATTCTGCTTGGTAATATAAGGCACCCGAAGCAATACTGTCGTCACTCTGTATGTCCGT
KpMero4_R08dn_KPN_00868_0.92(SEQ ID NO: 119)	ATGGTCATTTTCGCTGACTGACATGTAGCCTTTGGCCTTTCGCCGGGAATCGGCATTTCGCATTCTTAGGATCTAAA
KpMero4_R09up_KPN_02342_0.97(SEQ ID NO: 120)	TTAAGACCCAGACCGCCGACGTTTTCCTCACTGTGGAATAACACCCCATACCGATCTTCATAACGGACAAACTGAACGGGCCATT
KpMero4_R10up_KPN_00833_0.97(SEQ ID NO: 121)	CGGCTTCGGCTTTAGCAGCCAGTTTTGCTTCCAGACCATCTAAAGCGCTATGCAGACGAGCTGGCAGAGGAGAGAAATCA

Table 6: KpMero4 Probe B Sequences

KpMero4 probes:	
Target:	probe B sequence
KpMero4_C_KPN_00050_0.97(SEQ ID NO: 122)	CGAAAGCCATGACCTCCGATCACTCCAGAATTTTAACATACGCACTGGCGCGCTGTTCCTGCATCCAGGTTG
KpMero4_C_KPN_00098_0.97(SEQ ID NO: 123)	CGAAAGCCATGACCTCCGATCACTCAACGCAGACGCCCAGCTCACGTTCGTCTTCTGTTAATACCGAATAACTGG
KpMero4_C_KPN_00100_0.97(SEQ ID NO: 124)	CGAAAGCCATGACCTCCGATCACTCCCGATCGCATCCAGCATTTTGTGGCGAACAAATTCGTCTTCAAAGCGCAG
KpMero4_C_KPN_01276_0.92(SEQ ID NO: 125)	CGAAAGCCATGACCTCCGATCACTCGTTTGGACTGTTGTGCACTTCTGCGCCCCATGTAC
KpMero4_C_KPN_02846_0.95(SEQ ID NO: 126)	CGAAAGCCATGACCTCCGATCACTCTTACGCTGCAGGCCGCTGAACAGTTTTTTACCGGTGGCATCG
KpMero4_C_KPN_03317_0.92(SEQ ID NO: 127)	CGAAAGCCATGACCTCCGATCACTCCGAGATGTAAAGGGGTATCAAACGTATGGGCGGCATACTTCTCCAGCATA
KpMero4_C_KPN_03634_0.92(SEQ ID NO: 128)	CGAAAGCCATGACCTCCGATCACTCGGATCACCCGGCCATCGCGGATCAGTTTATCCATAATTTTGGTCGCTAAC
KpMero4_C_KPN_04666_0.97(SEQ ID NO: 129)	CGAAAGCCATGACCTCCGATCACTCATTGCCTTTCGGACGCAGCTGGGCAAGGAAGACGTCATGGAAGCGG

KpMero4_R01up_KPN_01226_0.97(SEQ ID NO: 130)	CGAAAGCCATGACCTCCGATCACTCCATCGCTTTATGCTGCGCTTCCATCTTATCGATCTGCGCTTC
KpMero4_R02up_KPN_01107_0.97(SEQ ID NO: 131)	CGAAAGCCATGACCTCCGATCACTCCTGACGCGGCGTTTTCACGGTTTCTTTAATCGGTGTACTGGAGACC
KpMero4_R03up_KPN_02345_0.95(SEQ ID NO: 132)	CGAAAGCCATGACCTCCGATCACTCCTGGATTGGATCCCCGTGAGGCTTAACACCAGCCCG
KpMero4_R04up_KPN_02742_0.97(SEQ ID NO: 133)	CGAAAGCCATGACCTCCGATCACTCAACGGTTATCACGCCATTCATAGTGACGACGCCAGTAATCACGGTCGCGC
KpMero4_R05dn_KPN_02241_0.92(SEQ ID NO: 134)	CGAAAGCCATGACCTCCGATCACTCCAGAGCACTGCGCCAACGAAGATGCTTAGGATTGCGCCATGCGCAAAGAA
KpMero4_R06up_KPN_03358_0.92(SEQ ID NO: 135)	CGAAAGCCATGACCTCCGATCACTCCGACGGATTGATACCGCGCTTACGCAGCAGGTCGTAAGAGTAGTCATCCG
KpMero4_R07up_KPN_03934_0.92(SEQ ID NO: 136)	CGAAAGCCATGACCTCCGATCACTCCCTTCTCAGTCGGCGACCAGCGAGCATCGTACTGCTTGGAAATAAG
KpMero4_R08dn_KPN_00868_0.92(SEQ ID NO: 137)	CGAAAGCCATGACCTCCGATCACTCGGCGCCTGCGCACGCATTTCACGGCAAAGCTCAAACAAGTTATCACGCAG
KpMero4_R09up_KPN_02342_0.97(SEQ ID NO: 138)	CGAAAGCCATGACCTCCGATCACTCAATGAACATAAAGTGCGGTGCTGACTCCGCGGGCGGTGAGGTATTGGCAC
KpMero4_R10up_KPN_00833_0.97(SEQ ID NO: 139)	CGAAAGCCATGACCTCCGATCACTCTTGGTGTTAGCGGAAGTAATGCTGTAGCCGGTCGCGCCAG

Antibiotic susceptibility testing is typically done by growth-based assays, including broth microdilution (may be automated e.g. on VITEK-2), disk diffusion, or E-test. Other approaches to rapid phenotypic AST include automated microscopy (Accelerate Diagnostics), ultrafine mass measurements (LifeScale). Genotypic approaches include resistance gene detection by PCR or other nucleic acid amplification methods, including Cepheid, BioFire, etc. but are limited to cases for which the genetic basis for resistance is well characterized.

Example 3: AST in ESKAPE pathogens

The techniques herein are currently being used to conduct AST for: *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter baumanii* for three different drug classes (meropenem ciprofloxacin; gentamicin) along with carbapenemase detection. Additionally, the techniques herei are you being used to conduct AST on all of the ESKAPE pathogens including: Enterococcu faecalis, Enterococcus faecium, Staphylococcus aureus, K. pneumoniae, A. baumanii, Pseudomona aeruginosa, E. coli, and Enterobacter cloacae with respect to all major clinically relevant drug classe (e.g., carbapenems, penicillins, cephalosporins, aminoglycosides, fluoroquinolones, rifamycins, an the like). The techniques herein are also being extended to conduct AST on Mycobacteriun tuberculosis for all first-line and second-line drugs as well as the newer agents, bedaquiline an delamanid.

For example, FIGS. 2A-2D, which are described in further detail below, are MA plot showing RNA-Seq data upon antibiotic exposure. FIG. 2A shows MA plots of susceptible (lef panels) or resistant (right panels) *Klebsiella pneumoniae*, *Escherichia coli* or *Acinetobacte baumanii* treated with meropenem for 60 min (left column), ciprofloxacin for 30 min (middl column), or gentamicin for 30-60 min (right column). Transcripts whose expression is statistically significantly changed upon antibiotic exposure are shown in red.

Additionally, FIGS. 4A and 4B, which are described in further detail below, depict graph showing that the squared projected distance (SPD) from transcriptional signatures reflecte antibiotic susceptibility. Clinical isolates of *Klebsiella pneumoniae*, *Escherichia coli* o *Acinetobacter baumanii* were treated with meropenem for 60 min (left column), ciprofloxacin fo 30 min (middle column), or gentamicin for 30-60 min (right column).

Example 4: Determining optimal transcriptional signatures to discriminate between susceptible and resistant bacteria

To identify the optimal transcripts that most robustly distinguish susceptible and resistant bacteria after brief antibiotic exposure, the transcriptomic responses of two susceptible and two resistant clinical isolates of *K. pneumoniae*, *E. coli*, and *A. baumannii* (see **Table** 7 below) treated with either meropenem (a carbapenem that inhibits cell wall biosynthesis), ciprofloxacin (a fluoroquinolone that targets DNA gyrase and topoisomerase), or gentamicin (an aminoglycoside that inhibits protein synthesis) were compared at clinical breakpoint concentrations (CLSI 2018) over time (e.g., 0, 10, 30, 60 minutes) using RNA-Seq. To enable these comparisons, a method optimized and modified from RNAtag-Seq (Shishkin et al. 2015), now termed RNAtag-Seqv2.0, wa developed to dramatically decrease the cost and increase the throughput of library construction. Fo each pathogen, each antibiotic elicited a transcriptional response within 30-60 minutes i susceptible, but not in resistant, organisms (**FIGS. 2A-2D**).

To identify transcripts that best distinguish susceptible from resistant strains for eac pathogen-antibiotic combination, a large number of candidate antibiotic-responsive transcripts fro these RNA-Seq datasets was initially selected for evaluation in more clinical isolates usin NanoString®. Complicating transcript selection is the fact that antibiotics arrest growth o susceptible strains, resulting in the rapid divergence of culture density and growth phase of treate and untreated cultures, factors that alone affect the transcription of hundreds of genes that ca mistakenly be interpreted as the direct result of antibiotic exposure but may not generalize acros growth conditions. To enrich for genes specifically perturbed by antibiotic exposure, DESeq2 (Love Huber, and Anders 2014) was used to identify transcripts whose abundance changed most robustl upon antibiotic exposure (**Table 9**), followed by Fisher's combined probability test to identif transcripts whose expression changed more upon antibiotic treatment than under any phase o growth during the timecourse. Gene ontology enrichment analysis on the resulting gene lists (**Tabl 8**) revealed that meropenem affected lipopolysaccharide biosynthesis in both *Enterobacteriacea* species, and induced a heat shock response in both *E. coli* and *Acinetobacter*. Ciprofloxacin induce the SOS response in all three species. Gentamicin induced the unfolded protein response and quinon binding in all three species. The top 60-100 responsive genes (see Methods) were selected a candidates for inclusion in the initial transcriptional signature (**FIG. 3; Table 9**). For normalizatio of these responsive genes across samples, DESeq2 was also used to select 10-20 transcripts for eac

pathogen-antibiotic pair that were most invariant to antibiotic treatment and growth phase ("control transcripts"; see Methods below).

Example 5: A rapid, multiplexed phenotypic assay to classify sensitive and resistant bacteria

For each of the selected genes for each pathogen-antibiotic pair, probes for multiplexed detection were designed using NanoString®, a simple, quantitative fluorescent hybridization platform that does not require nucleic acid purification (Barczak *et al.* 2012; Geiss *et al.* 2008). Because diversity among clinical strains in gene content or sequence may hinder probe hybridization, a homology masking algorithm was devised to identify conserved regions of each target gene (see Methods below), then designed pairs of 50mer probes to the specified conserved regions of the remaining responsive and control transcripts for each pathogen-antibiotic pair (**Table 9**). Using an assay protocol that was modified from the standard NanoString® nCounter assay to accelerate detection (see Methods below), these probes were used to quantify their cognate transcripts in 18-24 diverse clinical isolates of each species collected from various geographic locations (**Table 7**), spanning the breadth of the known phylogenetic landscape of each species (Letunic & Bork) (**FIGS. 13A-13D**). Because of the homology screening step in probe design, each probe recognizes the target transcript from its cognate species, thereby enabling simultaneous species identification through mRNA recognition (see, e.g., Barczak *et al.*). Normalized expression signatures of all responsive genes are shown as heatmaps (**FIG. 3**) and summarized as one dimensional projections (**FIGS. 4A-4B**). For each pathogen-antibiotic pair tested, the transcriptional profile of susceptible strains was distinct from that of resistant strains (**FIG. 4A**), with the magnitude of the transcriptional response reflecting the MIC of the exposed isolate (**FIG. 4B**).

To further test the generalizability of this approach, the above-described steps from RNA Seq through NanoString® detection of candidate responsive and control genes were repeated for two additional species including a Gram-positive pathogen, *S. aureus*, a common cause of serious infections, and *P. aeruginosa*, another high-priority and frequently multidrug-resistant Gram negative pathogen, each treated with a fluoroquinolone, levofloxacin (given its greater potency against Gram positives (Hooper *et al.*)) and ciprofloxacin, respectively (**FIGS. 14A-14F**). Each showed a robust transcriptional response in susceptible clinical isolates, but no response in resistant isolates, by both RNA-Seq (**FIGS. 14A and 14D**) and NanoString® (**FIGS. 14B and 14E**). The overall responses of both pathogens to fluoroquinolones involved up-regulation of the SOS response as expected (**Table 8**), including canonical DNA damage-responsive transcripts like *lexA*, *recA*,

recX, *uvrA*, and *uvrB*, which were generally consistent with the genes identified for the other three Gram negative pathogens. However, the specific genes selected from the RNA-Seq data to best distinguish susceptible from resistant isolates included features particular to each species, even for such a stereotypical response pathway. In fact, *recA* was the only feature selected as a candidate responsive gene in all five species; *lexA* and *uvrA* emerged in four of the five, but no other single transcript was selected in more than three, underscoring the importance of deriving each antibiotic response signature individually.

Importantly, the expression signatures alone merely show that reliable differences occur in the transcriptional response in susceptible versus resistant organisms, while AST requires binary classification of a strain as susceptible or resistant. To address this general classification problem machine-learning algorithms were deployed (**FIG. 5, phase 1**), first to identify the most informativ transcripts, and second to use these select transcripts to classify unknown isolates. To avoi overtraining, the tested strains were partitioned into a training (derivation) cohort for both featur selection and classifier training, and a testing (validation) cohort as a naïve strain set for assessin classifier performance. ReliefF (Robnik-Šikonja and Kononenko 2003) was used to identify the 1 transcripts whose normalized expression best distinguished susceptible from resistant organism among the training cohort (**FIGS. 6, 14B, 14E; Table 9**). Although fewer than 10 transcripts wer required to robustly distinguish between the strains thus far tested, more genes were kept in th optimized signature to lessen the potential impact of unanticipated diversity in gene content sequence, or regulation among clinical isolates.

Next, an ensemble classifier was trained using the random forest algorithm (Liaw & Wiener to perform binary classification of isolates in the derivation cohort based solely on these selecte features. Finally, this trained classifier was tested on the validation cohort. Across all 11 bacteria antibiotic combinations, 109 isolates were used as derivation strains for training, and 108 isolate were tested as validation. The ensemble classifier correctly classified 100 of these 108 (93% categorical agreement, 95% confidence interval [CI] 87-96% by Jeffrey's interval (Brown *et al.*)) including 51 of 52 resistant isolates (1.9% very major error rate, 95% CI 0.21-8.6%) and 35 of 3 susceptible isolates (7.9% major error rate, 95% CI 2.3-20%), compared with standard brot microdilution (**FIGS. 7A, 14C, 14F**; **Table 10**). Of note, both categorical agreement and rates o very major and major errors are typically reported on a natural distribution of isolates. In contrast as disclosed herein, a "challenge set" of isolates was deliberately assembled, one that wa

intentionally overrepresented for isolates near the clinical breakpoints, which will tend to artificially inflate all errors, since discrepant classifications are more common for strains with MICs near the breakpoint – both due to possible errors in the assay and to one-dilution errors inherent in the gold standard broth microdilution assay (CLSI). Consistent with this, all major and very major errors in Phase 1 testing involved strains less than or equal to two dilutions away from the breakpoint ("+" in **FIG. 3**). Two apparent major errors exhibited large inoculum effects ("*" in **FIG. 6** and **FIG. 3**, discussed below) in carbapenemase-producing strains reported as resistant by GoPhAST-R but susceptible by standard broth microdiluton. These two likely represent isolates that are misclassified as susceptible by the gold standard method (Anderson *et al.* 2007; Centers for Disease and Prevention 2009; Nordmann, Cuzon, and Naas 2009; Weisenberg *et al.* 2009) but correctly recognized as resistant by GoPhAST-R.

To assess this approach to classification as it would be deployed on unknown isolates, and to ensure against overtraining on the initial set of isolates, a second, iterative round of training was performed on all strains from the initial phase of classification and tested a new set of *Klebsiella pneumoniae* isolates treated with meropenem and ciprofloxacin (**FIG. 5, phase 2**). The initial derivation and validation cohorts were combined into a single, larger training cohort, on which feature selection was repeated and retrained for the ensemble classifier. The top 10 features chosen in phase 2 were very similar to those chosen in phase 1 (**Table 9**), with 78% mean overlap in gene content, mean Jaccard similarity coefficient 0.67, and mean Spearman correlation coefficient 0.5[illegible] across all pathogen-antibiotic combinations. This refined classifier was then applied to predict susceptibility in a new test set of 25-30 isolates for each antibiotic (**FIG. 8**), this time measuring only the top 10 selected responsive transcripts, rather than the 60-100 transcripts measured in phase 1. Here, GoPhAST-R correctly classified 52 of 55 strains (95% categorical agreement, 95% CI 86 98%) (**FIG. 7B**), including all 25 resistant isolates (0% very major error rate, 95% CI 0-9.5%) and 25 of 27 susceptible isolates (7.4% major error rate, 95% CI 1.6-22%), compared with broth microdilution. One of the three discrepant isolates is only one dilution from the breakpoint (**FIG. 8**) and another exhibits a large inoculum effect (**FIG. 8**) in a carbapenemase-producing strain that was reported as resistant by GoPhAST-R, likely the same phenomenon described above.

Three isolates classified as meropenem-resistant by GoPhAST-R but susceptible by broth microdilution exhibited a large inoculum effect. These three isolates, a *K. pneumoniae* (BAA2524

and two *E. coli* (BAA2523 and AR0104), all had MICs of 0.5-1 mg/L on standard broth microdilution with an inoculum of 10^5 cfu/mL, but MICs of ≥32 mg/L with an inoculum of 10^7 cfu/mL. Each of these strains carried a carbapenemase gene: BAA2523 and BAA2524 contained *bla*$_{OXA-48}$, and AR0104 contained *bla*$_{KPC-4}$, as has been reported for other such strains with large inoculum effects (Adams-Sapper *et al.* 2015; Adler *et al.* 2015). While the clinical consequences of such large inoculum effects are uncertain, they may portend clinical failure (Paterson *et al.* 2001), particularly in the setting of carbapenemase production (Weisenberg *et al.* 2009); detection of this phenomenon is a known gap in standard broth microdilution assays (Humphries, R. M.) because they are performed at the lower inoculum (Smith and Kirby 2018; Wiegand, Hilpert, and Hancock 2008). GoPhAST-R recognized these strains as resistant, perhaps because the assay was performed at higher cell density (>10^7 cfu/mL), whereas conventional methods missed these CREs.

Importantly, the ability of the classifier disclosed herein to accurately call a strain susceptible or resistant was independent of resistance mechanism, as exemplified for meropenem resistance. In total, 22 of 47 meropenem-resistant isolates, including 7 of 22 *K. pneumoniae*, 4 of 12 *E. coli*, and 11 of 13 *A. baumannii*, lacked carbapenemases (**Table** 7; Cerqueira *et al.* 2017 (www)cdc.gov/ARIsolateBank/), yet 46 of these 47 isolates were correctly recognized as resistant by GoPhAST-R. These results underscore the ability of GoPhAST-R to assess phenotypic resistance agnostic to its genotypic basis.

Example 6: Combining genotypic and phenotypic information in a single assay improves accuracy in carbapenem resistance detection and enables molecular epidemiology

Since GoPhAST-R involves multiplexed, hybridization-based RNA detection, the techniques herein can readily accommodate simultaneous profiling of additional transcripts including genetic resistance determinants such as carbapenemases. GoPhAST-R can thus provide valuable epidemiological data as well as resolve discrepancies between phenotype-based detection and standard broth dilution methods by providing genotypic information. For example, in the three cases with discrepant classifications and prominent inoculum effects, each isolate carried a carbapenemase gene. By incorporating probes to simultaneously detect resistance determinants such as carbapenemase genes, the genotypic component of GoPhAST-R can provide complementary evidence to reinforce its phenotypic call of resistance. This can be critical for the complex case of CRE detection (Anderson *et al.* 2007; Arnold *et al.* 2011; Centers for Disease and Prevention 2009; Gupta *et al.* 2018; Nordmann, Cuzon, and Naas 2009; Weisenberg *et al.* 2009): even the American

Type Culture Collection, the source of archived strains BAA2523 and BAA2524, recognized this discrepancy in AST, noting that these carbapenemase-producing isolates were reported as susceptible upon deposition but tested resistant by other methods (ref: ATCC pdf comments (see e.g., World Wide Web at (www)atcc.org/~/ps/BAA-2523.ashx).

Indeed, the most common known mechanism for carbapenem resistance among the *Enterobacteriaceae* involves the acquisition of one of several known carbapenemase genes (see e.g., Woodworth *et al.* 2018), most commonly the KPC, NDM, OXA-48, IMP, and VIM families (Martinez-Martinez and Gonzalez-Lopez 2014; Nordmann, Dortet, and Poirel 2012). Thus, probes were incorporated for these carbapenemases into the GoPhAST-R assay for meropenem AST, as well as two extended-spectrum beta-lactamase (ESBL) gene families that have been associated with carbapenem resistance when expressed in the context of porin loss-of-function, CTX-M-15 (Canton *et al.*; Cubero *et al.*) and OXA-10 (Ma *et al.* 2018) (**Table 9**). Of note, conventional PCR-based detection of the IMP and VIM gene families has been challenging because of their genetic diversity (Kaase *et al.*) and the relative intolerance of PCR to point mutations in primer binding sites especially towards the 3' end of the primer (Paterson *et al.*; Klungthong *et al.*). In contrast hybridization is more tolerant to point mutations and is amenable to a multiplexed format that allows the inclusion of multiple probes to recognize different regions of the same target, and thus identify targets with greater diversity. For instance, the currently disclosed GoPhAST-R includes 4 separate probe pairs to increase robustness of IMP detection (**Table 9**; see section below on Homology Masking).

GoPhAST-R detected all 39 carbapenemase genes across 38 strains known to be present by WGS, including at least one member of each of the five targeted classes, and all 29 ESBL genes across 26 strains; no signal was detected in the 25 meropenem-resistant strains nor the 38 susceptible isolates known to lack these gene families, across all three species (**FIGS. 9A-9C; Table 7**). This included detection of OXA-48 or KPC in the three cases of discrepant phenotypic AST classification and prominent inoculum effects. Thus, in a single assay, GoPhAST-R can provide both phenotypic AST and genotypic information about resistance mechanism.

Example 7: GoPhAST-R can measure antibiotic susceptibility directly from positive blood culture bottles

Previous work had demonstrated that a simulated positive blood culture bottle contains sufficient bacteria to permit mRNA detection (Hou *et al.* 2015). To demonstrate one clinical

application, GoPhAST-R was used to rapidly determine ciprofloxacin susceptibility in blood culture bottles that grew gram-negative rods from the MGH clinical microbiology laboratory. Ciprofloxacin was chosen because no rapid genotypic method exists for detection of fluoroquinolone resistance due to the diversity of genetic alterations that can cause fluoroquinolone resistance, and because of the relative prevalence of fluoroquinolone resistance, making it feasible to acquire both sensitive and resistant cases. Six clincal *E. coli* and two *K. pneumoniae* positive blood cultures were tested (**FIG. 10**) and the techniques herein made it possible to clearly distinguish three susceptible from three resistant *E. coli*; both *K. pneumoniae* species were susceptible. Given the relative scarcity of gentamicin and meropenem resistant isolates available for the instant studies, to test assay performance in this growth format, simulated positive blood cultures were generated by spiking in susceptible or resistant isolates of *K. pneumoniae* and *E. coli*. GoPhAST-R detected optimized transcriptional signatures for each pathogen/antibiotic pair directly from these positive blood culture bottles (**FIG. 11A**), and AST prediction using a random forest model and leave-one-out cross validation (Efron & Gong) (**FIG. 11B**) correctly classified 71 of 72 blood cultures (99% categorical agreement with broth microdilution, 95% CI 94-100%), including 0% very major error rate (31 of 31 resistant isolates classified correctly; 95% CI 0-7.7%) and 2.6% major error rate (37 of 38 susceptible isolates classified correctly; 95% CI 0.29-11%).

Example 8: A next-generation NanoString® detection platform, Hyb & Seq™, accelerates GoPhAST-R to <4 hours

GoPhAST-R was deployed on an exemplary next-generation nucleic detection platform NanoString® Hyb & Seq™ (J. Beechem, AGBT Precision Health 2017), that features accelerated detection technology, thus enabling AST in <4 hours (**FIG. 12A**). Relative to the nCounter detection platform, Hyb & Seq™ (**FIG. 12B, left panel**) enables accelerated hybridization by utilizing unlabeled reporter probes that are far smaller and thus equilibrate far faster than the standard nCounter probes, which are covalently attached to a bulky set of fluorophores during hybridization. Accelerated optical scanning enables fluorescent barcoding of these smaller reporter probes via sequential cycles of binding, detection, and removal of complementary barcoded fluorophores (**FIG. 12B, middle panel**; see Methods). On a prototype Hyb & Seq instrument, GoPhAST-R can measure expression signatures to determine antibiotic susceptibility in <4 hours, as demonstrated with *K. pneumoniae* for both phenotypic meropenem-responsive transcriptional signatures and detection of carbapenemase and select beta-lactamase genes (**FIG. 12B, right panel**). A head-to-head time trial

on simulated blood culture bottles demonstrated GoPhAST-R results in <4 hours from the time of culture positivity, compared with 28-40 hours in the MGH clinical microbiology laboratory by standard methods, which entailed subculture followed by AST determination on a VITEK-2.

As discussed herein, fast, accurate antibiotic susceptibility testing is a critical need in the battle against escalating antibiotic resistance. Advantageously, the ability of the presently disclosed AST assays to be conducted in hours instead of days can inform decisions on antibiotic administration closer to real-time, which may both improve individual patient outcomes (Kumar *et al.* 2006) and minimize needless use of broad-spectrum antibiotics for susceptible organisms (Maurer *et al.*). Growth-based assays are fundamentally limited in speed by the doubling time of the pathogen, and genotypic assays are limited by the inability to comprehensively define the ever growing diversity and complexity of bacterial antibiotic resistance mechanisms. At least in part by quantifying a refined set of transcripts whose antibiotic-induced expression reflects susceptibility GoPhAST-R provides a conceptually distinct approach to rapid phenotypic antibiotic resistance detection, agnostic to resistance mechanism and extendable to any antibiotic class, while simultaneously providing select, complementary genotypic information that can both improve the accuracy of phenotypic classification and provide valuable epidemiologic data for identifying the emergence and tracking the spread of resistance. Considering the widespread adoption of rapid pathogen identification by matrix-associated laser desorption and ionization / time-of-flight (MALDI-TOF) mass spectrometry in 2 hours from subcultured colonies streaked from blood culture bottles (Florio *et al.*; Tanner *et al.*; Perez *et al.*), this comparatively more informative AST assay directly from blood culture bottles in <4 hours promises to be transformative. Probes have been designed herein to target regions conserved across all sequenced members of their parent species thereby allowing each probeset to encode species identity in its reactivity profile. Since the NanoString® platform described herein can multiplex up to 800 probes in a single assay (Geiss *et al.*), the actual deployed test is expected to combine all 20 probes used for each pathogen-antibiotic pair (**Table 9**) into a single multi-species probeset for each antibiotic, thereby providing simultaneous pathogen identification along with AST. Alternatively, it is expected that species can be identified prior to AST on the same NanoString® platform using a more sensitive rRNA-based assay (Bhattacharyya *et al.*). The machine learning approach to strain classification developed for GoPhAST-R provides actionable information in excellent categorical agreement with the gold standard broth microdilution assay and should continue to improve in accuracy as it is trained on an

increasing number of strains. Taken all together, omitting carbapenemase-producing strains with ambiguous and likely errant susceptible classification by the gold standard assay, GoPhAST-R correctly classified 100 of 106 strains (94%) in phase 1 and 52 of 54 strains (96%) in phase 2, as well as 71 of 72 (99%) simulated blood cultures, with 8 of the 9 discrepancies occurring on strains within two dilutions of the clinical breakpoint.

By integrating genotypic and early phenotypic information in a single rapid, highly multiplexed RNA detection assay, GoPhAST-R offers several advantages over the current gold standard that are unique among other rapid AST assays under development. First, like other phenotypic assays, it determines susceptibility agnostic to mechanism of resistance, a clear advantage over genotypic AST assays. Second, combining genotypic and phenotypic information enhances AST accuracy over conventional growth-based methods. This combined approach notably improves sensitivity of resistance detection in certain cases such as carbapenemase-producing *Enterobacteriaceae* that test susceptible by standard methods but may rapidly evolve resistance upon treatment (see e.g., Anderson *et al.* 2007; Arnold *et al.* 2011; Centers for Disease and Prevention 2009; Gupta, V. *et al.* 2018; Nordmann, Cuzon, and Naas 2009; Weisenberg *et al.* 2009). Third, the identification of carbapenem resistance determinants can guide antibiotic choice for some resistant isolates, as certain novel beta-lactamase inhibitors like avibactam or vaborbactam will overcome some classes of carbapenemases (e.g., KPC) but not others (e.g., metallo-beta-lactamases such as the NDM class) (Lomovskaya *et al.*; Marshall *et al.*; van Duin & Bonomo). Solely phenotypic assay would currently require additional, serial testing to provide this level of guidance. Fourth, the ability to track resistance determinants in conjunction with a phenotypic assay enables molecular epidemiology without requiring additional testing for use in local, regional, national, or global tracking. The techniques herein demonstrate this advantage for one major class of high-value resistance determinants, the carbapenemases (Woodworth *et al.* 2018); this combined approach can be extended readily to other critical emerging resistance determinants, such as *mcr* genes, plasmid borne colistin resistance determinants recently found in the *Enterobacteriaceae* (Caniaux *et al.* 2017 Liakopoulos *et al.* 2016; Liu *et al.* 2016; Sun *et al.* 2018), or even to detect the presence of key bacterial toxins such as *Shiga* toxin (Rasko *et al.* 2011) in seamless conjunction with a phenotypic AST assay. Fifth, strains with unknown mechanism of resistance, such as CREs without carbapenemases, can be immediately identified from a single assay; such isolates could be flagged for further study such as WGS if desired. Sixth, the graded relationship between transcriptional

response and MIC (**FIGS. 14B and 14E**) underscores the biology that underpins the strategy: the more susceptible the strain, the greater its transcriptional response to antibiotic exposure. This relationship allows GoPhAST-R to be informed by clinical breakpoint concentrations, thus leveraging decades of careful study linking in vitro strain behavior to clinical outcomes (CLSI). This relationship also explains why the majority of discrepancies between GoPhAST-R and broth microdilution occurred on strains with MICs close to the breakpoint. By contrast, the inability to map to MIC is considered a liability of genotypic assays, including WGS (Ellington *et al.*). Finally, as a hybridization-based assay, GoPhAST-R will tolerate mutation in its detection targets more robustly than PCR-based assays (see e.g., Klungthong *et al.* 2010; Paterson, Harrison, and Holmes 2014). This enables GoPhAST-R to more readily detect resistance determinants with marked sequence variation such as the IMP family of carbapenemases, which is challenging to detect by PCR (Kaase *et al.* 2012). The phenotypic portion of the assay is particularly robust to sequence variation, both because it incorporates the behavior of multiple targets to provide redundancy, and because it measures fold-induction of the target gene by antibiotic, so a target gene that has mutated beyond recognition would not inform AST classification when registered as absent.

The instant disclosure has therefore provided an important proof of principle of a new approach to AST, for expected application to clinical practice. Genetic diversity within a species poses a fundamental challenge to the generalizability of bacterial molecular diagnostics, including transcription-based assays (Wadsworth *et al.*). The instant GoPhAST-R technique addresses this crucial challenge in a number of ways. First, for each pathogen-antibiotic pair, GoPhAST-R is trained and tested on a geographically and phylogenetically diverse set of strains: strains in the instant disclosure were obtained from multiple geographic regions that sample across the entire phylogeny of each species (**FIGS. 13A-13D**), notably including the CDC's Antibiotic Resistance Isolate Bank collection ((www)cdc.gov/ARIsolateBank/) that is intended as a test set for new diagnostic assays. Additionally, by targeting transcripts affected by antibiotics, which by definition affect core bacterial processes required for bacterial survival and whose transcriptional regulation is thus generally conserved (Wadsworth *et al.*), GoPhAST-R measures responses that are also likely to be conserved and therefore generalizable. Indeed, the fact that GoPhAST-R performed well on test strains that were selected randomly relative to training strains, that the sets of genes selected through iterative phase 1 and 2 training were relatively similar, and that the same classes of antibiotic elicit responses in similar pathways (**Table 8**) and even homologous genes (**Table 9**) across differen

species, all point to the ability of GoPhAST-R to account for the genetic diversity within a species. In addition to accommodating the potential variable transcriptional responses of strains within a species, by focusing on the most conserved regions of core transcripts by imposing a homology screen in the probe design process, GoPhAST-R also takes into account variability in genetic sequence of conserved genes in different strains. The initial sample set described herein attempted to capture significant diversity; yet larger numbers of strains will likely improve the current techniques further. By employing a classification process built on machine-learning algorithms that can be iteratively refined as more strains are tested, GoPhAST-R is able to incorporate new diversity to asymptotically improve performance. With wider testing, while the specific classifiers will improve, the general strategy and approach remains valid. Indeed, the capacity to learn through iterative retraining is one of the strengths of this approach as it is used more broadly. Likewise extending this assay to more pathogen and antibiotic pairs will be advantageous for widespread clinical utility.

To extend GoPhAST-R in this manner, the entire pathway described herein for signature derivation, from RNA-Seq to iterative phases of NanoString® refinement and validation, are employed and advanced towards implementation in a clinical setting. Some antibiotics elicit responses in predictable pathways, exemplified by fluoroquinolones up-regulating SOS-response transcripts; however, it is expected that applying the instant diagnostic assay to certain new pathogen-antibiotic pairs will be performed with additional rigor to meet clinical performance mandates. For instance, when the instant approach was applied herein to *S. aureus* and *P. aeruginosa* treated with fluoroquinolones, it was identified that experimental derivation resulted in refined transcriptional signatures and control genes that were not predictable from prior assays on related pathogen-antibiotic pairs, often involving hypothetical or uncharacterized ORFs. This observed difficulty in predicting the best-performing responsive and control genes by inference from other species highlights the significance, at least ideally, of individualizing the expression signature for each pathogen-antibiotic pair, a process that is equivalent to the individualization currently employed by CLSI to extend traditional AST assays to new pathogen-antibiotic pairs. Fortunately the experimental and computational approaches described herein allow for very rapid and conceptually straightforward extension to all pathogen-antibiotic combinations, and it is further noted that advances in RNA-Seq library construction and sequencing, described herein and elsewhere (Shishkin *et al.*), make a full derivation cycle for GoPhAST-R routine. Underscoring the

ready generalizability of this approach, preliminary RNA-Seq data have been generated for 50 additional pathogen-antibiotic pairs, spanning Gram positive, Gram negative, and mycobacteria, that demonstrate early differential transcriptional responses to antibiotics in all cases tested (data not shown). While GoPhAST-R cannot completely overcome the challenge of identifying delayed inducible resistance (though this would be true for any rapid phenotypic test), it is noted that GoPhAST-R is expected to accurately identify at least some of these cases through simultaneous genotypic detection of induced resistance determinants, where known.

Following the approach described herein as a blueprint, it is contemplated that GoPhAST-R can be extended to all other pathogens and antibiotic classes, including those with novel mechanisms of action and as-yet-unknown or newly emerging mechanisms of resistance. Because GoPhAST-R is specifically informed by MIC, it leverages decades of prior studies linking *in vitro* behavior to clinical outcomes (CLSI), thereby facilitating its extension to new pathogens or antibiotics. It is further contemplated that the instant approach can be expanded to other clinical specimen types beyond the instant demonstration performed upon cultured blood. Notably, while the application of a next-generation nucleic acid detection platform that can yield an answer in <4 hours has been described herein, a reliable transcriptional signature of susceptibility has actually been described as present in ≤1 hour for each of these key antibiotic classes. Thus, as RNA detection methods become faster and more sensitive, the GoPhAST-R approach is contemplated to offer even more rapid phenotypic AST on timescales that can inform early antibiotic decisions and thus transform infectious disease practice.

Example 9: Materials and Methods

Strain acquisition and characterization

All strains in this study (**Table 7**) were obtained from clinical or reference microbiological laboratories, including both local hospitals and MDRO strain collections from the Centers for Disease Control's Antibiotic Resistance Isolate Bank (see e.g., World Wide Web at (www).cdc.gov/ARIsolateBank/) and the New York State Department of Health. MICs reported from those laboratories were validated by standard broth microdilution assays (Wiegand, Hilpert and Hancock 2008) in Mueller-Hinton broth; any discrepancies of >1 doubling from reported values were resolved by repeating in triplicate.

RNA-Seq experimental conditions

For each bacteria-antibiotic pair, selected clinical isolates (**Table 7**), two susceptible and two resistant, were grown at 37°C in Mueller-Hinton broth to early logarithmic phase, then treated with the relevant antibiotic at breakpoint concentrations set by the Clinical Laboratory Standards Institute (CLSI): 2 mg/L for meropenem, 1 mg/L for ciprofloxacin, and 4 mg/L for gentamicin. Total RNA was harvested from paired treated and untreated samples at 0, 10, 30, and 60 minutes. cDNA libraries were made using a variant of the previously described RNAtag-Seq protocol (Shishkin *et al.* 2015) and sequenced on either an Illumina™ HiSeq or NextSeq. Sequencing reads were aligned using BWA (Li and Durbin 2009) and tabulated as previously described (Shishkin *et al.* 2015).

Differential gene expression analysis and selection of responsive and control transcripts

Differentially expressed genes were determined using the DESeq2 package (Love, Huber and Anders 2014), comparing treated vs untreated samples at each timepoint. Fisher's combined probability test was used to select only those genes whose expression after antibiotic treatment was statistically distinguishable from its expression at any timepoint in the untreated samples. Gene ontology (GO) terms were assigned using blast2GO (version 1.4.4), with hypergeometric testing for enrichment. For each pathogen-antibiotic pair, the fold-change threshold in DESeq2 used to test statistical significance was increased to select 60-100 antibiotic-responsive transcripts with maximal stringency, a number readily accommodated by the NanoString® assay format. Control transcripts were also determined with DESeq2 using an inverted hypothesis test as described (Love, Huber, and Anders 2014) to select genes whose expression was expected to be unaffected by antibiotic exposure or growth in both susceptible and resistant isolates, at all timepoints and treatment conditions. As with responsive genes, the fold-change threshold was varied in order to select the top 10-20 control transcripts. The resulting control and responsive gene lists for each pathogen-antibiotic pair, and the fold-change thresholds used to generate them, are shown in **Table 9**. See Supplemental Methods sections below for further details.

Targeted transcriptional response to antibiotic exposure

After using BLASTn to identify regions of targeted transcripts with maximal conservation across all RefSeq genomes from that species (see Supplemental Methods), NanoString® probes were designed per manufacturer's standard process (Geiss et al. 2008) to these conserved regions. Strains treated with antibiotic at the CLSI breakpoint concentration, and untreated controls, were lysed via bead-beating at the desired timepoint. The resulting crude lysates were used as input for standard

NanoString® (Seattle, WA) assays, which were performed on the nCounter® Sprint platform with variations on the manufacturer's protocol to enhance speed, detailed in Supplemental Methods. Raw counts for each target were extracted and processed as described in Supplemental Methods. Briefly, for each sample, each responsive gene was normalized by control gene expression as a proxy for cell loading using a variation on the geNorm algorithm (Vandesompele *et al.*), then converted to fold-induction in treated compared with untreated strains. Pilot NanoString® Hyb & Seq™ assays (**FIGS. 12A and 12B**) were performed on a prototype Hyb&Seq instrument at NanoString®, with 20 minute hybridization time and 5 imaging cycles to detect hybridization probes with two-segment 10-plex barcodes. See Supplemental Methods for more details.

Machine learning: feature selection and susceptibility classification

For each pathogen-antibiotic pair, the normalized data were first partitioned, grouping hal the strains into a derivation cohort on which the algorithm was trained, reserving the other half fo validation (**FIGS. 14A-14F**), ensuring equivalent representation of susceptible and resistant isolate in each cohort.

In phase 1, implemented for all pathogen-antibiotic pairs, normalized fold-induction data o responsive genes from strains in the training cohort, along with CLSI susceptibility classification fo each training strain, were input to the ReliefF algorithm using the CORElearn package (versio 1.52.0) to rank the top 10 responsive transcripts that best distinguished susceptible from resistan strains. These 10 features were then used to train a random forest classifier using the caret packag (version 6.0-78) in R (version 3.3.3) on the same training strains. Performance of this classifier wa then assessed on the testing cohort, to which the classifier had yet to be exposed.

In phase 2, implemented for *K. pneumoniae* + meropenem and ciprofloxacin, all 18-2 strains from phase 1 were combined into a single, larger training set. For each antibiotic, Relief was again used to select the 10 most informative responsive transcripts, which were then used t train a random forest classifier on the same larger training set. Transcriptional data were the collected on a test set of 25-30 new strains using a trimmed NanoString® nCounter® Elements™ probeset containing only probes for these 10 selected transcripts, plus 8-13 control probes Susceptibility of each strain in this test set was predicted using the trained classifier. Se Supplemental Methods for further detail on machine learning strategy and implementation.

For classification of simulated blood cultures, NanoString® data were collected for the to 10 transcripts (selected in phase 1) from 12 strains for each pathogen-antibiotic pair, and analyze

using a leave-one-out cross-validation approach (Efron & Gong), training on 11 strains and classifying the 12th, then repeating with each strain omitted once from training and used for prediction.

Blood culture processing

Bacteria were isolated from real or simulated blood cultures in a clinical microbiology laboratory, isolated by differential centrifugation, resuspended in Mueller-Hinton broth, and immediately split for treatment with the indicated antibiotics. Lysis and targeted RNA detection were performed as above. Specimens were blinded until all data acquisition and analysis was complete. See Supplemental Methods for more detail. Samples were collected under waiver o patient consent due to experimental focus only on the bacterial isolates, not the patients from whicl they were derived.

Data availability

All RNA-Seq data generated and analyzed during this study, supporting the analyses i FIGS. 2A-2D, have been deposited as aligned bam files in the NCBI Sequencing Read Archiv under study ID PRJNA518730. All other datasets obtained herein, including raw and processe NanoString® data, are available upon reasonable request.

Code availability

Custom scripts for transcript selection from RNA-Seq data are available at the World Wid Web at (www)github.com/broadinstitute/gene_select_v3/. Custom scripts for feature selection an strain classification from NanoString® data are available at World Wide Web a (www)github.com/broadinstitute/DecisionAnalysis/.

Example 10: Supplemental Methods

RNA extraction for RNA-Seq:

After antibiotic treatment as described in the above Materials and Methods section, cell were pelleted, resuspended in 0.5 mL Trizol reagent (ThermoFisher Scientific), transferred to 1. mL screw-cap tubes containing 0.25 mL of 0.1 mm diameter Zirconia/Silica beads (BioSpe Products), and lysed mechanically via bead-beating for 3-5 one-minute cycles on a Minibeadbeater 16 (BioSpec) or one 90-second cycle at 10 m/sec on a FastPrep (MP Bio). After addition of 0.1 ml chloroform, each sample tube was mixed thoroughly by inversion, incubated for 3 minutes at roon temperature, and centrifuged at 12,000 xg for 15 minutes at 4°C. The aqueous phase was mixed wit

an equal volume of 100% ethanol, transferred to a Direct-zol spin plate (Zymo Research), and RNA was extracted according the Direct-zol protocol (Zymo Research).

Library construction and RNA-Seq data generation:

Illumina cDNA libraries were generated using a modified version of the RNAtag-Seq protocol (Shishkin et al. 2015), RNAtag-Seq-TS, developed during the course of work for the instant disclosure, in which adapters are added to the 3' end of cDNAs by template switching (Zhu et al. 2001) rather than by an overnight ligation, markedly decreasing the time, cost, and minimum input of library construction. Briefly, 250-500 ng of total RNA was fragmented, DNase treated to remove genomic DNA, dephosphorylated, and ligated to DNA adapters carrying 5'-AN_8-3' barcodes of known sequence with a 5' phosphate and a 3' blocking group. Barcoded RNAs were pooled and depleted of rRNA using the RiboZero rRNA depletion kit (Epicentre). Pools of barcoded RNA were converted to Illumina cDNA libraries in 2 main steps: with template switching, then library amplification. RNA was reverse transcribed using a primer designed to the constant region of the barcoded adaptor with addition of an adapter to the 3' end of the cDNA by template switching using SMARTScribe (Clontech). Briefly, two primers were added to the reverse transcription reaction to facilitate template switching: primer AR2 (Shishkin *et al.* 2015), which primes SMARTScribe reverse transcriptase off of the ligated adapter, and primer 3Tr3 (Shishkin *et al.* 2015), which contains 3 protected G's at the 3' terminus to complement the C's added to the 3' end of newly synthesized cDNA by SMARTScribe and also contains a 5' blocking group to prevent multiple template-switching events. These primers were pre-incubated with rRNA-depleted, adapter-ligated RNA (at 8.33 uM of each primer) at 72°C x 3 min, then 42°C x 2 min, then added directly to a master mix containing SMARTScribe buffer (1x), DTT (2.5 mM), dNTPs (1mM each; NEB), SUPERase In RNase inhibitor (1 unit; Invitrogen), and SMARTScribe reverse transcriptase enzyme (final primer concentration in reaction mixture: 5 uM each). This reaction mixture was incubated at 42°C x 60 min, then 70°C x 10 min, followed by addition of Exonuclease I (1 μL) and incubation at 37°C x 30 min. After 1.5x SPRI cleanup, the resulting cDNA library was PCR amplified using primers whose 5' ends target the constant regions of the ligated adapter (3' end of original RNA) and the template-switching oligo (5' end of original RNA) and whose termini contain the full Illumina P5 or P7 sequences. cDNA libraries were sequenced on the Illumina NextSeq 2500 or HiSeq 2000 platform to generate paired end reads.

RNA-Seq data alignment:

Sequencing reads from each sample in a pool were demultiplexed based on their associated barcode sequence. Barcode sequences were removed from the first read, as were terminal G's from the second read that may have been added by SMARTScribe during template switching. The resulting reads were aligned to reference sequences using BWA (Li and Durbin 2009), and read counts were assigned to genes and other genomic features as described (Shishkin *et al.* 2015). For each pathogen-antibiotic pair, a single reference genome was chosen for analysis of all four clinical isolates. This reference genome was selected by aligning a subset of RNA-Seq reads from each of the four isolates to all RefSeq genomes from that species and identifying the genome to which the highest percentage of reads aligned on average across all isolates. Since none of the isolates used fo RNA-Seq have reference-quality genome assemblies themselves, and since four different isolate were used, not all genes in each isolate will be represented in the alignment. Yet for this application any reads omitted due to the absence of a homologue in the reference genome used for alignmen (i.e., accessory genes not shared by the reference) were assumed to be unlikely to be generalizabl enough for diagnostic use. Using these criteria, the following reference genomes were chosen fo alignment of RNA-Seq data for each of the following pathogen-antibiotic pairs: *K. pneumoniae* = NC_016845 for meropenem and ciprofloxacin, and NC_012731 for gentamicin; *E. coli* = NC_020163 for meropenem, and NC_008563 for ciprofloxacin and gentamicin; *A. baumannii* = NC_021726 for meropenem, and NC_017847 for ciprofloxacin and gentamicin. Note that fo display purposes in FIGS. 5, 6, 10, 12A, 12B and 14A-14F, all responsive genes were name according to their homologues in the best-annotated reference available (NC_016845 for *K pneumoniae*, NC_000913 for *E. coli*, and NC_017847 for *A. baumannii*) in order to convey gen names that were as meaningful as possible, instead of simply gene identifiers. Read tables wer generated, quality control metrics examined, and coverage plots from raw sequencing reads in th context of genome sequences and gene annotations were visualized using GenomeView (Abeel *e al.* 2012). Aligned bam files were deposited to the Sequence Read Archive (SRA) under study II PRJNA518730.

Selecting candidate responsive genes from RNA-Seq data:

The DESeq2 package (Love, Huber, and Anders 2014) was used to identify differentiall expressed genes in treated vs untreated samples at each timepoint, in both susceptible and resistan strains. Analyses from select timepoints are displayed as MA plots in FIGS. 2A-2D. Since no

statistically significant changes in transcription were observed in resistant strains, responsive gene selection was only carried out on susceptible isolates.

It was expected that the resulting list of differentially expressed genes would represent both genes that respond primarily to antibiotic exposure, and genes that respond to ongoing growth that may be prevented by antibiotic treatment in susceptible strains, i.e. whose differential expression upon antibiotic exposure is more a secondary effect. As an example of this type secondary effect, consider a gene whose expression is repressed by increasing cell density, or nutrient depletion from the medium, as cells grow. In the presence of antibiotic, cells may never reach that cell density; therefore, this gene would exhibit higher expression in the antibiotic-treated culture (where it is not repressed) than in the untreated culture (where it is repressed). Without any correction, this gene would appear indistinguishable from one whose expression is induced by antibiotic, although this may be entirely a secondary effect. Such "secondarily" regulated genes were reasoned to be more dependent upon precise growth conditions (media type, temperature, cell density, cell state, etc. – in other words, transcripts upregulated by progression towards stationary phase in minimal media will likely look different than that in rich media, etc.), some of which may vary across clinical samples. By contrast, since antibiotics target core cellular processes, it was hypothesized that the "direct" transcriptional response to antibiotic exposure would be more likely to be conserved across strains which is critical for their success in a diagnostic assay. Therefore, a focus was placed on transcripts whose expression appeared to be a direct result of antibiotic exposure, rather than this indirect result of the effects of an antibiotic on the progression of the strain to different culture densities.

To identify such genes, additional differential expression analyses were carried out using DESeq2 to identify genes whose expression varied in untreated samples over the timecourse of the experiment. Such genes were very common: >10% of the transcriptome was differentially regulated at some timepoints compared with others in the timecourses of *K. pneumoniae* and *E. coli* (though considerably fewer in *A. baumannii* cultures). Therefore, the additional requirement that any candidate responsive gene exhibit a greater degree of differential expression in time-matched antibiotic-treated vs untreated samples at ≥1 timepoint, than it did in any untreated timepoint – in other words, that antibiotics induce a degree of induction or repression that exceeds that which was achieved at any timepoint in the absence of antibiotics – was imposed. To implement this, Fisher's combined probability test was imposed to combine p-values from each pairwise comparison selecting those genes whose differential expression upon antibiotic treatment at a given timepoin

exceeds their differential expression between any pair of points in the untreated timecourse, with adjusted p-value <0.05. As an additional filter for gene selection, in order to be sure to target genes with sufficient abundance to be readily detected in the hybridization assay, only genes in the upper 50% of expression in each condition were considered.

For most pathogen-antibiotic pairs, this analysis resulted in the identification of hundreds of candidate antibiotic-responsive genes. This process (differential expression analysis + Fisher's method) was repeated using progressively higher thresholds for the fold-change threshold used in the statistical test for differential expression, by increasing the lfcThreshold parameter in DESeq2 (for all comparisons, i.e. antibiotic treatment and each pair of untreated timepoints used in Fisher's method) until the resulting list of candidate responsive genes was 60-100 long, the size that wa intended to target in phase 1 NanoString® assays. **Table 9** shows the fold-change thresholds used t generate the final candidate responsive transcript list for each pathogen-antibiotic pair. This proces was executed using custom scripts, available at World Wide Web a (www)github.com/broadinstitute/gene_select_v3/.

Selecting candidate control genes from RNA-Seq data

To quantitatively compare the transcription of key antibiotic-responsive genes, it is importan to normalize for cell loading, lysis efficiency, and other experimental factors that may systematicall affect absolute transcript abundance from a given sample. Such invariant transcripts (often referre to as "housekeeping" transcripts in qPCR) are important for scaling candidate responsive genes fo comparison across samples, e.g. for comparing treated vs untreated samples. Control transcript were therefore included in the NanoString® assay in order to normalize for these factors. Candidat control genes were identified by seeking transcripts whose expression did not change in the RNA Seq timecourses, either upon antibiotic treatment or with over the untreated timecourse. To find sucl genes, a statistical test was imposed to find transcripts whose expression did not change by mor than a certain fold-change threshold in any of the treated or untreated samples by re-running DESeq using an inverted hypothesis test (altHypothesis = "lessAbs"), tuning the lfcThreshold paramete until the 10-20 best control genes were identified. **Table 9** shows the fold-change thresholds used t generate the final candidate control transcript list for each pathogen-antibiotic pair.

Gene Ontology (GO) term enrichment:

For GO enrichment analysis, the same protocol was followed for responsive gene selection using DESeq2 and Fisher's method (see "*Selecting candidate responsive genes from RNA-Seq data*", above), with two exceptions. First, the lfcThreshold parameter (log2 fold change threshold) was set to 0, in order to capture all differentially expressed genes. Second, genes of any expression level were considered, since sensitivity of detection was not a concern. This process produced a list of all genes that were differentially expressed upon antibiotic exposure to a greater extent than at any timepoint in the absence of antibiotic, over the full timecourse tested (0, 10, 30, and 60 min). These differentially expressed genes were named according to the reference genome that best matched the four strains used for RNA-Seq, as described (see "*RNA-Seq analysis*", above). GO terms were assigned to annotated genes from each reference genome by blasting the peptide sequences for each ORF from that reference genome against a local database of ~120 well-annotated reference strains from NCBI using blast2GO (version 1.4.4; Gotz *et al.* 2008). GO terms associated with the list of differentially expressed genes was then compared with all GO terms associated with the genome and hypergeometric testing was deployed to identify GO terms that were enriched to a statistically significant extent among the differentially expressed genes, using the Benjamini-Hochberg correction for multiple hypothesis testing. A false discovery rate threshold of 0.05 was used to generate the list of enriched GO terms in **Table 8**.

Homology masking of selected responsive and control transcripts

Within each candidate responsive or control gene, regions of highest homology to target with NanoString® probes were identified. For each species, all complete reference genomes from RefSeq as of January 1, 2016 were compiled, and BLASTn was run to identify the closest homologue of each desired target from each reference genome, and eliminated targets without an annotated homologue in at least 80% of genomes. A multi-sequence alignment was then constructed and queried each sliding 100mer window to keep only those windows with at least one 100mer region of >97% nucleotide identity across all reference genomes; all sequences failing to meet this homology threshold were "masked", i.e., removed from consideration as targets for probe design. If no such region was found, the homology threshold was relaxed to >95% identity, then to >92% identity; if no region with at least 92% identity was found, the transcript was deemed too variable to reliably target and thus eliminated from consideration entirely. The window size of 100 nucleotides was chosen because NanoString® detection involves targeting with two ~50mer probes that bind consecutive regions (Geiss *et al.* 2008). The resulting homology-masked sequences, retaining only

those regions of intended target transcripts with sufficient homology, were then provided to NanoString® for their standard probe design algorithms (Geiss *et al.* 2008).

Design of NanoString® probes for carbapenemase and extended-spectrum betalactamase gene families:

All gene sequences representing each targeted antibiotic resistance gene family (carbapenemases: KPC, NDM, OXA-48, IMP, VIM; ESBLs: CTX-M-15, OXA-10) were collected from representatives reported in three databases of antibiotic resistance genes: Resfinder (Zankari *et al.* 2012), ArDB (Liu and Pop 2009), and the Lahey Clinic catalog of beta-lactamases on the World Wide Web at (www)lahey.org/Studies. Additional representatives of each family were identified by homology search (BLASTp, E-value < 10-10, >80% similarity) against the conceptual translation of genes identified in the genomes of isolates collected as part a multi-institute analysis o carbapenem-resistant Enterobacteriaceae specimens (Cerqueira *et al.* 2017). All other genes in th pan-genome of that cohort that did not meet the homology search criterion for inclusion as one o the targeted families were consolidated in an outgroup sequence database, which was used to scree for cross-reactivity. This outgroup contains many other non-targeted beta-lactamases, as well as th complete genomes of hundreds of Enterobacteriaceae isolates (Cerqueira *et al.* 2017). For eacl targeted antibiotic resistance gene family, target regions for NanoString® probe design wer identified as described above (see above section entitled Homology masking of selected responsiv and control transcripts) by identifying regions with >95% sequence homology across 15(nucleotides in >90% of homologues within that family. In order to minimize risk of cross-reactivity with undesired targets, these conserved regions of the desired targets were then compared by BLASTn to the outgroup database, and any regions with E-value < 10 were discarded. For the IMI gene family, no region of sufficient conservation could be identified due to sequence diversity withi the family, consistent with reports that it is difficult to uniformly target by PCR (Kaase *et al.* 2012) Four different regions were identified that together were predicted to cover all IMP homologs fron these databases, i.e., where each IMP homolog contained a stretch of sufficient homology to one o more of the four regions. These regions were submitted to NanoString® for probe design by thei standard algorithms (Geiss *et al.* 2008), including four separate probe pairs for IMP (**Table 9**). Signa from each of these four IMP probes was combined to yield a single combined total IMP signal (se section entitled "NanoString® data processing, normalization, and visualization" below).

Lysate preparation for NanoString® transcriptional profiling assays:

Each strain to be tested was grown at 37˚C in Mueller-Hinton broth to mid-logarithmic phase, and split into a treated sample, to which antibiotic was added at the CLSI breakpoint concentration, and an untreated control. Both samples were grown for the specified time (30-60 min), then a 100 uL aliquot of culture was added to 100 uL of RLT buffer (Qiagen) plus 1% beta-mercaptoethanol and mechanically lysed using either the MiniBeadBeater-16 (BioSpec) or the FastPrep (MP Biomedicals). This crude lysate was either used directly for hybridization, or frozen immediately and stored at -80˚C, then thawed on ice prior to use.

NanoString® nCounter® assays:

All Phase 1 and Phase 2 NanoString® experiments (see FIG. 5) were performed on a NanoString® nCounter® Sprint instrument, with hybridization conditions as per manufacturer' recommendations, including a 10% final volume of crude lysate as input. Phase 1 experiments used probesets made with XT barcoded probe pools and were hybridized for 2 hours at 65˚C, while Phase 2 experiments used probesets made with nCounter® Elements™ probe pools plus cognate barcoded TagSets (ref?) and were hybridized for 1 hour at 67˚C, rather than the 16-24 hour hybridizations as recommended by the manufacturer's protocol. Including 30-60 min for antibiotic exposure and these hybridizations, plus a 6 hour run for 12 samples, the total run time was under 8 hours for phase 2. Technical replicates for five strains run on separate days resulted in Pearson correlations of 0.95-0.99 for normalized data, consistent with expectations for this assay platform (Geiss *et al.* 2008) indicating that the shorter hybridization time did not affect reproducibility.

Phylogenetic analysis of strains included in this study:

The Genome Tree report was downloaded for each species from the National Center for Biotechnology Information (NCBI; ncbi.nlm.nih.gov) in Newick file format and uploaded to the Interactive Tree of Life (iTOL; itol.embl.de; Letunic *et al.* 2019) for visualization and annotation. Strains from the instant disclosure that were available on NCBI were identified using strain name or other identifying metadata from the NCBI Tree View file, cross-referencing the NCBI ftp server (ftp.ncbi.nlm.nih.gov/pathogen/Results/) as needed to confirm strain identity.

Rapid transcriptional profiling with pilot NanoString® Hyb & Seq™ assay platform

For the rapid pilot GoPhAST-R experiment on a prototype Hyb & Seq™ instrument a NanoString® (FIGS. 12A and 12B), pairs of capture probes (Probe A and Probe B) were constructed

for all targets of interest such that each pair could uniquely bind to one target transcript. For Hyb & Seq™ chemistry (FIG. 12A), each Probe A contained a unique target binding region, a universal purification sequence, and an affinity tag for surface immobilization. Each Probe B contained another unique target binding region, a barcoded sequence for downstream signal detection, and a common purification sequence that was different from that of Probes A. For multiplexed RNA profiling, crude lysates were mixed with all capture and reporter probes in a single hybridization reaction and incubated on a thermocycler with heated lid at 65°C for 20 min. This hybridization reaction enables formation of unique trimeric complexes between target mRNA, Probe A, and Probe B for each target.

Three sequential steps of post-hybridization purification were then performed to ensur minimal background signal. Briefly, the hybridization product was first purified over magnetic bead coupled to oligonucleotides complementary to the universal sequence contained on every Probe B The hybridization product was first incubated with the beads in 5x SSPE/60% formamide/0.1% Tween20 at room temperature for 10min in order to bind all target complexes containing Probes B along with the free (un-hybridized) Probes B, onto the beads. Bead complexes were then washe with 0.1x SSPE/0.1% Tween20 to remove unbound oligos and complexes without Probes B. Th washed beads were then incubated in 0.1x SSPE/0.1% Tween20 at 45°C for 10 min to elute th bound hybridized complexes off the beads. This second purification was carried out pe manufacturer's instructions using Agencourt AMPure XP beads (Beckman Coulter) at a 1.8: volume ratio of beads to sample, in order to remove oligos shorter than 100 nt. This size-selectiv purification recovers the bigger hybridization complexes while removing smaller free capture Probe A and B. Eluates from these AMPure beads were purified over a third kind of magnetic bead coupled to oligonucleotides complementary to the common purification sequence contained o every Probe A, similar to the first bead purification, then eluted at 45°C. These triple-purifie samples were driven through a microfluidic flow cell on a readout cartridge by hydrostatic pressur within 20 min. The flow cell was enclosed by a streptavidin-coated glass slide that can specifically bind to the affinity tag (biotin) of each Probe B, allowing the immobilization of purified complexe on the glass surface.

The cartridge with samples loaded was mounted on a Hyb & Seq™ prototype instrumen equipped with an LED light source, an automated stage, and a fluorescent microscope. The barcode region of each Probe A consisted of two short nucleic acid segments, each of which can bind to on

of ten available fluorescent bi-colored DNA reporter complexes as dictated by complementarity to the exact segment sequences. To detect each complex captured on the glass surface (**FIG. 12B**), photocleavable fluorescent color-coded reporters were grouped by their target segment location and introduced into the flow cell one pool at a time. Following each reporter pool introduction, the flow cell was washed with non-fluorescent imaging buffer to remove unbound reporter complexes and scanned by the automated Hyb & Seq prototype. Each field of view (FOV) was scanned at different excitation wavelengths (480, 545, 580 and 622 nm) to generate four images (one for each wavelength) and then exposed to UV (375nm) briefly to remove the fluorophore on surface-bound reporter probes by breaking a photocleavable linker. The flow cell was then subjected to a second round of probing with a new reporter pool targeting the second segment location on each Probe A. Thus, two rounds of probing, washing, imaging and cleavage completed one Hyb & Seq barcode readout cycle (FIG. 12B). In order to improve signal-to-noise ratio, 5 such cycles were completed for each assay. Between each cycle, the flow cell was incubated with low salt buffer (0.0033x SSPE/0.1% Tween20) to remove all bound reporter complexes without disrupting the ternary complex between Probe A, target mRNA, and Probe B.

A custom algorithm was implemented to process the raw images for each FOV on a FOV by-FOV basis. This algorithm can identify fluorescent spots and register images between each wavelengths and readout cycles. A valid feature is defined as a spot showing positive fluorescence readout for all barcoded segment locations in the same spatial position of each image after image registration. The molecular identity of each valid feature is determined by the permutation of color codes for individual rounds of barcode segment readout. In this implementation, the maximal degree of available multiplexing for a single assay using 10-plex reporter pools was $10^2 = 100$ kinds for two-segment barcodes, but up to four-segment barcodes are available, permitting up to $10^4 = 10{,}000$ distinct barcodes. This algorithm provides tabulated results for the total raw count of each reported barcode of interest identified in a single assay. These raw counts are used as input for subsequent data processing, visualization, and further analysis.

NanoString® data processing, normalization, and visualization:

For each sample, read counts from each targeted transcript were extracted using nSolver Analysis Software (v4.070, NanoString®, Seattle WA). Raw read counts underwent the following processing steps, all executed in R (version 3.3.3), utilizing the packages dplyr (version 0.7.4), xlsx (version 0.5.7), gplots (version 3.0.1), and DescTools (version 0.99.23):

1. Data aggregation: all data for a given pathogen-antibiotic pair, for a given phase of analysis (eg phase 1 or phase 2), was read in to a single data object so that all subsequent data processing steps were done together.

2. Positive control correction: per manufacturer's protocol, ERCC spike-ins were included in every hybridization at known concentrations, spanning the range of expected target RNA concentrations. For each sample, the geometric mean of counts from positive control probes targeting these ERCC spike-ins was calculated. This geometric mean was used to scale each remaining probe in the sample, in order to standardize across lanes for any systematic variation.

3. Negative control subtraction: per manufacturer's protocol, for each sample the mean of negative control probes targeting ERCC spike-ins not present in the hybridization reaction were subtracted from the raw read counts for each target.

4. Failed probe removal: any control probe with fewer than 10 reads, or any responsive control with negative reads, after negative control subtraction in any sample was removed from all samples for a given pathogen-antibiotic pair, in order to omit transcripts whose content, sequence, or expression was too variable across strains.

5. Selection of optimal control probes: among the set of candidate control probes, across all strains in a given phase of analysis, the subset of these control probes that performed most consistently across samples was selected using a variation on the geNorm algorithm (Vandesompele *et al.* 2002). The principle behind this algorithm is that the per cell expression of ideal control probes will not vary under any experimental conditions, and therefore, the ratio between expression levels of a set of ideal control probes will be constant (reflecting only the difference in cell number in each sample). Accordingly, the coefficient of variation of each control probe with the geometric mean of all control probes was calculated. In the ideal case, this coefficient of variation will be zero. The candidate control probe with the highest coefficient of variation is removed, and the process is repeated with the remaining control probes until the highest coefficient of variation is less than a threshold set to yield an acceptable number of non-operonic control transcripts, typically 4-8. For these experiments, this threshold was adjusted from 0.2 to 0.3 depending on the bacteria-antibiotic pair. Thresholds chosen, and the optimal control probes used at this threshold, are noted in **Table 9**.

6. Control transcript normalization: the geometric mean of the optimal control probes was calculated for each sample and used to normalize all remaining read counts from that sample, i.e. for candidate responsive transcripts, and for carbapenemase or ESBL genes (if applicable), by dividing these corrected read counts by this geometric mean for each sample.

7. Calculation of fold-induction of normalized responsive transcripts by antibiotic: for each candidate responsive transcript, normalized counts from each antibiotic-treated strain were divided by normalized counts from untreated samples of the same strain. These fold-inductions of normalized expression for each candidate responsive transcript were used as input into machine learning algorithms, both reliefF for feature selection and the caret package for random forest classification.

8. Log-transformation of fold-induction data for responsive transcripts: for visualization, the natural logarithm of fold-inductions of normalized expression for each candidate responsive transcript was calculated and displayed using the heatmap.2 function of the gplots R package (version 3.0.1). For each set of strains, ln(fold induction) for each transcript was clustered using the default hclust function, and strains were ordered by MIC.

9. Combination of IMP probes: because of the variability of gene sequences in the IMP family, four separate IMP probes were designed, one or more of which was expected to recognize all sequenced members of this gene family. Following control gene normalization, signal from the four separate probes was added together to give a single IMP score.

10. Background subtraction for carbapenemase/ESBL gene detection: For each species, the subset of tested strains was identified for which whole-genome-sequencing (WGS) data was available and none of the target beta-lactamase genes was found. From this subset, the arithmetic mean plus two standard deviations of the normalized signal from each probe (step 6) was calculated, and this mean + two standard deviations was subtracted from the normalized signal from each probe across all tested samples. All carbapenemase identified by WGS were detected above background, though the two *A. baumannii* isolates expressing bla_{NDM} were only detected at very low levels. Background-subtracted data were log-transformed for visualization (any probe with a negative value after background

subtraction was set to 0.1 normalized counts for all standard nCounter experiments, or to 0.25 normalized counts for Hyb & Seq experiments, prior to log-transformation).

One-dimensional projection of transcriptional data via squared projected distance (SPD) metric:

Normalized, log-transformed fold-induction data from the ~60-100 responsive were collapsed into a one-dimensional projection referred to as a squared projected distance (SPD), essentially as described (Barczak *et al.* 2012).. Conceptually, the transcriptional response of a test strain is placed on a vector in N-dimensional transcriptional space (where N = number of responsive genes, here ~60-100 per probeset) between the average position (i.e. centroid in transcriptional space) of a derivation set of susceptible strains (defined as SPD = 0) and the average position of a derivation set of resistant strains (defined as SPD = 1). All vector math was performed exactly as described (Barczak *et al.* 2012) and implemented in R (version 3.3). For each pathogen-antibiotic pair, the same strains used for RNA-Seq were also used as the derivation set of two susceptible and two resistant strains, in order to ensure that the resulting projections of the remaining strains were not self-determined. In other words, only the strains used to select the transcripts to be used in the NanoString® experiments (based on RNA-Seq) were used to set the average position of susceptible or resistant isolates; any tendency of other isolates to cluster at a similar SPD as these derivation strains, either susceptible or resistant, is thus due to a similarity in their transcriptional profiles. These derivation strains are labeled in **Table 7** as "deriv_S" and "deriv_R" for susceptible and resistant strains, respectively. SPD data are plotted by CLSI class (FIG. 4A) and by MIC (FIG. 4B) showing a proportional relationship between MIC and this summative metric of transcriptional response to antibiotic exposure upon treatment at the breakpoint concentration (vertical dashed line).

Approach to strain classification based on NanoString® data:

In order to select the most distinguishing features and to classify isolates as susceptible or resistant, machine learning algorithms were utilized and implemented in two phases (FIG. 5).

In phase 1, NanoString® XT probesets were designed targeting dozens (60-100) of antibiotic responsive transcripts (**Table 9**) selected from RNA-Seq data as described and used to quantify target gene expression from 18-24 isolates of varying susceptibility, both treated and untreated with the antibiotic in question, from which normalized fold-induction data for each responsive gene candidate was determined as described above. These isolates are partitioned into 50% training strains and 50% testing strains, randomly but informed by MIC: isolates are sorted in order of MIC and

then alternately assigned to training and testing sets in order to ensure a balanced mix of isolates in each cohort across the full range of MICs represented by the strains in question. The only exceptions to random strain assignments to training vs testing sets in Phase 1 were: (1) intermediate isolates were not used for training, but were assigned to the validation cohort (and were grouped with resistant isolates for accuracy reporting, i.e., "not susceptible"), and (2) the two *E. coli* isolates with large meropenem inoculum effects were noted prior to randomization and deliberately assigned to the validation cohort, given the physiological basis for their discrepant transcriptional response from that of a conventional susceptible strain. From the training (derivation) cohort, the top 10 features were first selected using reliefF (see details below, "*Feature selection from NanoString® data*") then a random forest model was trained on this derivation cohort using the caret package, ther implemented on the testing (validation) cohort, using only data from these top 10 selected feature (see details below, "*Random forest classification of strains from NanoString® data*"). Accuracy o GoPhAST-R in this phase was assessed by comparing predictions of the random forest model fo the strains in the testing cohort, which it had never previously seen, with known susceptibility dat for these strains (FIG. 7A; **Table 10**).

In phase 2, the training and testing cohorts from phase 1 were first combined into a single larger training set, and selection of the top 10 responsive features were repeated using the sam algorithms (reliefF). These represent the best-informed prediction of the 10 responsive probes tha most robustly discriminate between susceptible and resistant isolates, and are highlighted in **Tabl 9** for each pathogen-antibiotic combination (column F = either "Phase 2" or "Top feature"). A nev NanoString® nCounter® Elements™ probeset was then designed for each pathogen-antibiotic pai targeting only these 10 transcripts as well as ~10 control probes that performed best in phase 1 (i.e had the lowest coefficients of variation compared with the geometric mean of all control probes using the variation on the geNorm algorithm described above; also indicated in **Table 9**, column F) For *K. pneumoniae* + meropenem and ciprofloxacin, an additional 25-30 strains were tested usin these focused phase 2 probesets, again quantifying target gene expression and normalized fold induction of these responsive genes with and without antibiotic exposure. These data were supplie to the random forest classifier trained on all data from phase 1, and the resulting classifications o phase 2 strains were compared with known susceptibility data for these strains (FIG. 7B; **Table 10**) Of note, phase 2 deploys GoPhAST-R in exactly the way it was envisioned being deployed on tru

unknown samples: each of the phase 2 strains was an unknown, considered independently and not used at any point to train the model, only to assess its performance one strain at a time.

Every strain tested was an independent clinical isolate, with two minor exceptions. First, in the case of *A. baumannii* + ciprofloxacin, there were not sufficient numbers of independent ciprofloxacin-susceptible *A. baumannii* isolates to train and test a classifier (only five out of 22 *A. baumannii* isolates). For this bacteria-antibiotic pair, biological replicates of the two susceptible strains used for RNA-Seq, RB197 (three replicates) and RB201 (two replicates) were run. These biological replicates were grown from separate colonies in separate cultures, each split into treated and untreated samples. All three RB197 replicates ended up randomized to the phase 1 training set while both RB201 replicates were randomized to the phase 1 testing set. Since there was not training on one biological replicate and testing on another, the reported categorical agreement should not be confounded by excessive similarity between replicates. One additional linkage between isolates was that one *A. baumannii* isolate, RB197, exhibited two distinct colony morphotypes upon streaking onto LB plates: a dominant, larger morphotype, and a less abundant, smaller morphotype. The smaller morphotype was renamed RB197s and tested in both the meropenem and ciprofloxacin datasets, randomized to the testing (validation) cohort in both cases.

Feature selection from NanoString® data:

For feature selection in both phase 1 and phase 2, the reliefF algorithm (Robnik-Šikonja and Kononenko 2003) was employed using the CORElearn package (version 1.52.0) in R (version 3.3.3) to generate a list of features ranked in order of importance in distinguishing susceptible from resistant strains within the training set. The input to the reliefF algorithm was normalized fold induction data from all responsive probes, and the CLSI classification, for each training isolate. (For this analysis, CLSI classification was simplified into two classes by grouping intermediate strains with resistant strains, in keeping with common clinical practice to avoid an antibiotic for which an isolate tests intermediate.)

The process by which reliefF generates its ranking has been well-described elsewhere (Robnik-Šikonja and Kononenko 2003). The specific estimator algorithm (lEst parameter "ReliefFexpRank", which considers the k nearest hits and misses, was chosen with the weight of each hit and miss exponentially decreasing with decreasing rank. This was iterated five times (ltime parameter = 5), with a separate 80% partition of the training data for each iteration, then averaged feature weight across each of these five iterations to generate the final ranked list. The output from

this reliefF algorithm is a ranked list of features that best distinguish susceptible from resistant isolates; from this list, and the top 10 features (featureCount parameter = 10) were kept. The same parameter values were chosen for feature selection for both phase 1 (i.e., on the half of the phase 1 data assigned to the training set) and phase 2 (i.e., using all of the phase 1 data, for use in designing new probesets for *de novo* data acquisition in phase 2)..

Random forest classification of strains from NanoString® data:

To build a random forest classifier, the caret (*c*lassification *a*nd *re*gression *t*raining) package (version 6.0-78) in R (version 3.3.3) was employed to classify strains in the testing cohort. Input data for this algorithm are normalized fold-inductions of the top 10 responsive genes selected by reliefF for both training and testing strains, and CLSI classifications for each training strain (again with intermediate and resistant isolates grouped together). This random forest model is a common example of an ensemble classifier (Liaw *et al.* 2001) that embeds feature selection and weighting in building its models, which should mitigate risk for overtraining from including additional features from reliefF, since features not required for accurate classification need not be considered. It enacts 5-fold cross-validation on the training set, i.e. 80% sampling of the testing data, run 5 times, to optimize parameters including "mtry", "min.node.size", and "splitrule", to build 500 trees (parameter "ntree" set to 500) based on prediction of the omitted training strains. After these hyperparameters are optimized through this cross-validation, an additional 500 trees are built using all of the training data and used to classify strains from the test set, one strain at a time. The resulting output is this classifier model that generates predictions for the classification of each test strain reported as "probability of resistance" (probR) based on what fraction of trees ended up classifying the strain as resistant. (For instance, a strain with probR of 0.2 was classified as susceptible in 100 trees and as resistant in 400.) For quantitative assessment of accuracy, the prediction of the most likely class as the ultimate classification (i.e., if probR > 0.5, the classifier is predicting resistant; if probR < 0.5, the classifier is predicting susceptible) was used. One might ultimately choose to set this threshold somewhere other than 0.5: since the cost of misclassifying a resistant isolate as susceptible (a "very major error" in the parlance of the FDA) is greater than the cost of misclassifying a susceptible isolate as resistant, one might wish to label an isolate resistant if its probR is, say, 0.3. However, for simplicity, and to avoid overtraining on the relatively limited number of samples in this manuscript, the default threshold of 0.5 was chosen, accepting the classifier's prediction as to which state is more likely.

Reproducibility of GoPhAST-R classification:

Phase 2 probesets for meropenem susceptibility were combined with probes for carbapenemase and ESBL gene detection (**Table 9**). For *K. pneumoniae* + meropenem, in addition to testing all phase 2 strains simultaneously for phenotypic AST and genotypic resistance determinants, 23 of 24 phase 1 strains were retested using the phase 2 probeset in order to capture their carbapenemase and ESBL gene content. This provides a set of effective technical replicates for assessing the robustness of the classifier, since all phase 2 genes are included as a subset of the phase 1 probeset, but all data were regenerated in a new NanoString® experiment using the phase 2 probeset with added genotypic probes.

All 23 retested strains (11 susceptible, 12 resistant) were classified correctly based upon dat from the phase 2 probeset; of these 23 strains, 12 (6 susceptible, 6 resistant) were phase 1 trainin strains (that were therefore not previously classified in phase 1), and 11 (5 susceptible, 6 resistant were phase 1 testing strains that were classified the same way based upon data from the phase 2 probeset as they had been in phase 1 testing. The probability of resistance (probR) parameters fo these 23 replicates from phase 1 (**Table 10**) versus those from "re-classification" using data fron the phase 2 probeset were highly correlated (Pearson correlation coefficient = 0.95). Note tha because these same strains were used in training the random forest classifier, the results of re classification of these retested strains are not included in the accuracy statistics reported elsewher in this manuscript. The 100% concordance observed for re-classification of these 23 strains is thu not a reflection of GoPhAST-R's accuracy, but does speak to its reproducibility.

Blood culture processing:

Under Partners IRB 2015P002215, 1 mL aliquots from blood cultures in the MGH clinica microbiology laboratory whose Gram stain demonstrated gram-negative rods were removed fo processing. For simulated blood cultures, consistent with clinical microbiology laboratory protoco (Clark *et al.* 2009), blood culture bottles were inoculated with individual isolates of each pathoge suspended in fetal bovine serum at <10 cfu/mL to simulate clinical samples and incubated in a BI BacTec FX instrument (BD Diagnostics; Sparks, MD) in the clinical microbiology laboratory a Massachusetts General Hospital, or on a rotating incubator at 37°C in the research laboratory at th Broad Institute. Once the BacTec instrument signaled positive (after 8.5-11.75 hours of growth), o after an equivalent time to reach the same culture density in the research laboratory (confirmed b enumeration of colony-forming units), 1 mL aliquots were removed for processing. Bacteria wer

isolated by differential centrifugation: 100 xg x 10 min to pellet RBCs, followed by 16,000 xg x 5 min to pellet bacteria. The resulting pellet was resuspended in 100 uL of Mueller-Hinton broth and immediately split into 5 x 20 uL aliquots for treatment with the indicated antibiotics (three antibiotics, plus two untreated samples, one for harvesting at 30 min to pair with the ciprofloxacin-treated aliquot and one at 60 min to pair with both meropenem- and gentamicin-treated aliquots). After the appropriate treatment time, 80 uL of RLT buffer + 1% beta-mercaptoethanol was added to 20 uL of treated bacterial sample, and lysis via bead-beating followed by NanoString® detection were carried out as above (see "*Lysate preparation for NanoString® transcriptional profiling assays*" section). For real blood cultures, lysates were stored at -80 °C until organisms were identified in the laboratory by conventional means; only samples containing *E. coli* or *K. pneumoniae* were run on NanoString®. GoPhAST-R results were compared with standard MIC testing in the MGH clinical microbiology laboratory, which were also run on simulated cultures. Specimens were blinded until all data acquisition and analysis was complete. For head-to-head time trial compared with gold standard AST testing in the MGH clinical microbiology laboratory (subculture + VITEK-2), blood culture processing steps were timed in the research laboratory (Boston, MA, USA), then frozen and shipped to NanoString®for transcript quantification on the prototype Hyb & Seq™ platform at NanoString® (Seattle, WA, USA). A timer was restarted when lysates were thawed, and the total time at each site was combined to estimate the complete assay duration.

Blood culture AST classification:

Simulated blood cultures were classified using the same random forest approach as cultured strains, using the top 10 features selected during Phase 1 for each pathogen-antibiotic pair. This was implemented using leave-one-out cross-validation (Efron *et al.* 1983) rather than an even partitioning into training and testing because (1) feature selection was already complete, allowing multiple rounds of classifier training without requiring one unified model, and (2) given this, leave-one-out cross-validation (i.e., iteratively omit each strain once from training, test on the omitted strain, repeat with each strain omitted) allowed for training on the maximum number of strains.

Table 7: Strains used in this study (including origin, and which assay(s) they were used in), with MIC measurements. Highlight those used for RNA-Seq, and which were used for which NSTG assay, and which were used as "derivation" or "validation" in ML algorithms and for SPD.

			KpMero			CRE				
STRAIN	Alt name 1	Alt name 2	Phase 1	Phase 2	mero MIC (mg/L)	Known gene(s) in probeset	Other known bla gene(s)	Source	Comments
AR0034	CarbaNP-03			x	2	IMP-4	TEM-1B; SHV-11	CDC	ARBank
AR0040	CarbaNP-09	RB408	x	(x)	>32	VIM-27; CTX-M-15	SHV-11; OXA-1	CDC	ARBank
AR0041	CarbaNP-10	RB826		x x	16	NDM-1; CTX-M-15; OXA-10	CMY-4; SHV-11	CDC	ARBank
AR0042	CarbaNP-11	RB410	x	(x)	≤0.5	CTX-M15; OXA-10	TEM-1B; SHV-1; OXA-1	CDC	ARBank
AR0043	CarbaNP-12	RB411	x		2		SHV-12	CDC	ARBank
AR0044	CarbaNP-13			x	4	CTX-M-15	OXA-9; TEM-1A; SHV-12; OXA-1	CDC	ARBank
AR0047	CarbaNP-16			x	4		TEM-1A	CDC	ARBank
AR0075	CarbaNP-44	RB414	x	(x)	8	CTX-M15	OXA-232; SHV-1; OXA-1	CDC	ARBank
AR0087	CarbaNP-56	RB417	x	(x)	1		SHV-12	CDC	ARBank
AR0135	CRE-24			x	8	VIM-1	OXA-9; TEM-1A; SHV-12	CDC	ARBank
AR0139	CRE-28			x x	32	NDM-1; CTX-M-15; OXA-10	CMY-4; SHV-11	CDC	ARBank
BAA2524	RB554			x	0.5*	OXA-48		ATCC	
BIDMC_14	RB289			x	16	KPC-3	SHV-134; TEM-1	BIDMC	Cerqueira et al, PNAS 2017

BIDMC_21	RB563							BIDMC	Cerqueira et al. PNAS 2017
BIDMC_22	RB564		x	0.25		SHV-134	BIDMC	Cerqueira et al. PNAS 2017
BIDMC_31	RB565		x	0.125		SHV-38	BIDMC	Cerqueira et al. PNAS 2017
BIDMC_35	RB552	x	(x)	>32	OXA-10	SHV-134	BIDMC	Cerqueira et al. PNAS 2017
BIT-03	RB400	x	(x)	8	KPC (unknown type)		CDC	precursor to ARBank strain collection, shared by J. Patel
BIT-04	RB401	x (deriv. R)	x (deriv. R)	32	KPC (unknown type)		CDC	precursor to ARBank strain collection, shared by J. Patel
BIT-05	RB402	x	(x)	>32	KPC (unknown type)		CDC	precursor to ARBank strain collection, shared by J. Patel
BIT-12	RB404	x	(x)	≤0.5			CDC	precursor to ARBank strain collection, shared by J. Patel

BIT-16	RB405	x	(x)	≤0.5			CDC		precursor to ARBank strain collection, shared by J. Patel
BWH_15	RB268	x	(x)	8	KPC-4	SHV-134; TEM-1	BWH		Cerqueira et al. PNAS 2017
BWH_2	RB551		x	16	CTX-M-15; OXA-48	OXA-30; OXA-9; SHV-38; TEM-1	BWH		Cerqueira et al. PNAS 2017
BWH_30	RB270	x	(x)	≤0.5		SHV-134	BWH		Cerqueira et al. PNAS 2017
BWH_36	RB271	x	(x)	16	KPC-3	SHV-134; TEM-1	BWH		Cerqueira et al. PNAS 2017
CDC_1500610	RB419	x	(x)	≤0.5			CDC		precursor to ARBank strain collection, shared by J. Patel
IDR1200023303	RB596	x	(x)	>32		SHV-38	NYDOH		shared by K. Musser
IDR1600031102-01-00	RB579	x	(x)	>32	NDM-1; CTX-M15		NYDOH		shared by K. Musser
IDR1600037310	RB587	x	(x)	1	CTX-M-15		NYDOH		shared by K. Musser
IDR1600057468-01-00	RB584		x	4	CTX-M-15		NYDOH		shared by K. Musser
MGH_17	RB273		x	≤0.5		SHV-134	MGH		Cerqueira et al. PNAS 2017
MGH_18	RB274	x (deriv. S)	x (deriv. S)	≤0.5		SHV-134	MGH		Cerqueira et al. PNAS 2017

MGH_19	RB275		x	(x)	≤0.5		SHV-134	MGH	Cerqueira et al. PNAS 2017
MGH_20	RB276			x	≤0.5		SHV-134	MGH	Cerqueira et al. PNAS 2017
MGH_31	RB291			x	8		SHV-134	MGH	Cerqueira et al. PNAS 2017
MGH_35	RB543			x	2	CTX-M-15	OXA-30; SHV-134; TEM-1	MGH	Cerqueira et al. PNAS 2017
MGH_36	RB280			x	≤0.5		SHV-38	MGH	Cerqueira et al. PNAS 2017
MGH_39	RB780			x	2	KPC-3	OXA-9; SHV-38; TEM-1	MGH	Cerqueira et al. PNAS 2017
MGH_48	RB284			x	≤0.5		SHV-134	MGH	Cerqueira et al. PNAS 2017
MGH_71	RB462			x	32	KPC-2; OXA-10	SHV-134; TEM-1	MGH	Cerqueira et al. PNAS 2017
RB039			x (deriv_S)	x (deriv_S)	≤0.5			BWH	this paper
RB041				x	≤0.5			BWH	this paper
RB042				x	≤0.5			BWH	this paper
UCI_19	RB285		x (deriv_R)	x (deriv_R)	>32	KPC-2	SHV-134; TEM-1	UCI	Cerqueira et al. PNAS 2017
UCI_37	RB290		x	(x)	32	KPC-3	OXA-9; SHV-38; TEM-1	UCI	Cerqueira et al. PNAS 2017
UCI_38	RB288		x	(x)	≤0.5		SHV-134	UCI	Cerqueira et al. PNAS 2017
UCI_44	RB483			x	0.25		OXA-9; TEM-1	UCI	Cerqueira et al. PNAS 2017

UCI_61	RB480			x	32	KPC-2	SHV-134; TEM-1	UCI	Cerqueira et al, PNAS 2017
UCI_64	RB541			x	0.25		SHV-134	UCI	Cerqueira et al, PNAS 2017
UCI_7	RB540			x	0.25		SHV-134	UCI	Cerqueira et al, PNAS 2017

			Kp.Cip					
STRAIN	Alt name 1	Alt name 2	Phase 1	Phase 2	cip MIC (mg/L)	Source	Comments	
AR0034	CarbaNP-03			x	1	CDC	ARBank	
AR0040	CarbaNP-09	RB408		x	128	CDC	ARBank	
AR0076	CarbaNP-45	RB415	x		0.5	CDC	ARBank	
AR0080	CarbaNP-49	RB416	x		<0.03	CDC	ARBank	
AR0126	CRE-15			x	0.125	CDC	ARBank	
AR0160	CRE-49			x	0.06	CDC	ARBank	
BAC080060595O	RB592		x		0.25	NYDOH	shared by K. Musser	
BIDMC_21	RB563			x	64	BIDMC	Cerqueira et al, PNAS 2017	
BIDMC_22	RB564			x	0.03	BIDMC	Cerqueira et al, PNAS 2017	
BIDMC_31	RB565			x	0.125	BIDMC	Cerqueira et al, PNAS 2017	
BIT-03	RB400		x		32	CDC	precursor to ARBank strain collection, shared by J. Patel	

BIT-04	RB401	x		16	CDC		precursor to ARBank strain collection, shared by J. Patel
BIT-05	RB402	x		128	CDC		precursor to ARBank strain collection, shared by J. Patel
BIT-10	RB403	x			CDC		precursor to ARBank strain collection, shared by J. Patel
BIT-16	RB405	x		0.5	CDC		precursor to ARBank strain collection, shared by J. Patel
BWH_15	RB268	x		0.125	BWH		Cerqueira et al, PNAS 2017
BWH_22	RB287		x	64	BWH		Cerqueira et al, PNAS 2017
CDC_1500476	RB418	x		1	CDC		precursor to ARBank strain collection, shared by J. Patel
CDC_1500610	RB419		x	16	CDC		precursor to ARBank strain collection, shared by J. Patel
IDR12000022727	RB595	x		>32	NYDOH		shared by K. Musser
IDR16000031102-01-00	RB579		x	64	NYDOH		shared by K. Musser

IDR160003719-01-00	RB582			x	>32	NYDOH	shared by K. Musser
IDR160003951 1-01-00	RB578	x			>32	NYDOH	shared by K. Musser
IDR160005336 3-01-00	RB583			x	16	NYDOH	shared by K. Musser
MGH_18	RB274			x	0.125	MGH	Cerqueira et al, PNAS 2017
MGH_21	RB277			x	0.125	MGH	Cerqueira et al, PNAS 2017
MGH_35	RB543			x	64	MGH	Cerqueira et al, PNAS 2017
MGH_39	RB780			x	0.06	MGH	Cerqueira et al, PNAS 2017
MGH_74	RB572			x	0.03	MGH	Cerqueira et al, PNAS 2017
RB013		x (deriv_R)		x (deriv_R)	128	BWH	this paper
RB039		x (deriv_R)		x (deriv_R)	128	BWH	this paper
RB040		x (deriv_S)		x (deriv_S)	<0.03	BWH	this paper
RB041		x (deriv_S)		x (deriv_S)	<0.03	BWH	this paper
RB122		x			2	BWH	this paper
RB123		x			<0.03	BWH	this paper
UCI_20	RB568			x	0.06	UCI	Cerqueira et al, PNAS 2017
UCI_22	RB569			x	64	UCI	Cerqueira et al, PNAS 2017
UCI_37	RB290			x	64	UCI	Cerqueira et al, PNAS 2017
UCI_56	RB571			x	0.125	UCI	Cerqueira et al, PNAS 2017

			Antigen			
STRAIN	Alt name 1	Alt name 2	Phase 1	gent MIC (mg/L)	Source	Comments
AR0042	CarbaNP-11	RB410	x	32	CDC	ARBank
AR0043	CarbaNP-12	RB411	x	1	CDC	ARBank
AR0076	CarbaNP-45	RB415	x	32	CDC	ARBank
AR0080	CarbaNP-49	RB416	x	2	CDC	ARBank
ATCC 700721	RB435		x	>32	ATCC	
BAC08000007138	RB594		x	0.5	NYDOH	shared by K. Musser
BIDMC_2A	RB469		x	2	BIDMC	Cerqueira et al, PNAS 2017
BIDMC_34	RB456		x	32	BIDMC	Cerqueira et al, PNAS 2017
BIT-10	RB403		x	4	CDC	precursor to ARBank strain collection, shared by J. Patel
BWH_15	RB268		x	4	BWH	Cerqueira et al, PNAS 2017
IDR16000031102-01-00	RB579		x	>32	NYDOH	shared by K. Musser
IDR16000039511-01-00	RB578		x	0.5	NYDOH	shared by K. Musser
MGH_30	RB278		x	1	MGH	Cerqueira et al, PNAS 2017
MGH_35	RB543		x	>16	MGH	Cerqueira et al, PNAS 2017
MGH_63	RB545		x	>16	MGH	Cerqueira et al, PNAS 2017
RB012			x (deriv_R)	32	BWH	this paper
RB040			x (deriv_S)	0.5	BWH	this paper

RB042			x	2	BWH	this paper							
RB121			x (deriv_S)	1	BWH	this paper							
RB122			x (deriv_R)	128	BWH	this paper							
UCI_13	RB487		x	0.5	UCI	Cerqueira et al, PNAS 2017							
UCI_37	RB290		x	16	UCI	Cerqueira et al, PNAS 2017							
UCI_63	RB481		x	4	UCI	Cerqueira et al, PNAS 2017							
UCI_67	RB484		x	8	UCI	Cerqueira et al, PNAS 2017							
UCI_7	RB540		x	0.5	UCI	Cerqueira et al, PNAS 2017							
			EdMero				CRE						
STRAIN	Alt name 1	Alt name 2	Phase 1	mero MIC (mg/L)	Known gene(s) in probeset					Other known bla gene(s)	Source	Comments	
AR0048	CarbaNP-17	RB420	x (deriv_R)	32	NDM-1; CTX-M-15					TEM-1B; CMY-6; OXA-1	CDC	ARBank	
AR0055	CarbaNP-24		x	8	NDM-1					CMY-6; OXA-1	CDC	ARBank	
AR0058	CarbaNP-27		x	0.25	KPC-3					TEM-52B	CDC	ARBank	
AR0061	CarbaNP-30		x	8						OXA-9; TEM-1A	CDC	ARBank	
AR0069	CarbaNP-38	RB421	x (deriv_R)	16	NDM-1					TEM-1B; CMY-6	CDC	ARBank	
AR0077	CarbaNP-46		x	0.5							CDC	ARBank	
AR0089	CarbaNP-58		x	0.5						CMY-2	CDC	ARBank	
AR0104	CarbaNP-73		x	1*	KPC-4					TEM-1A	CDC	ARBank	
BAA2469	RB557		x	16	NDM-1						ATCC		
BAA2523	RB553		x	0.5*	OXA-48						ATCC		
BIDMC_77	RB827		x	0.5	CTX-M-15					CFE-1; OXA-30	BIDMC	Cerqueira et al, PNAS 2017	
IDR1200024571	RB597		x	>32						CMY-2	NYDOH	shared by K. Musser	

IDR1200039757	RB598	x	>32		CMY-2	NYDOH	shared by K. Musser
IDR1300027657	RB602	x	1		CMY-2	NYDOH	shared by K. Musser
IDR1600029769	RB585	x	8	OXA-48		NYDOH	shared by K. Musser
IDR1600035372	RB586	x	0.5	CTX-M-15		NYDOH	shared by K. Musser
IDR1600043633	RB589	x	2	CTX-M-15		NYDOH	shared by K. Musser
MGH_57	RB544	x	4	CTX-M-15	CFE-1; TEM-1	MGH	Cerqueira et al, PNAS 2017
RB001		x (deriv_S)	0.25			BWH	this paper
RB002		x (deriv_S)	0.25			BWH	this paper
RB076		x	≤0.5			BWH	this paper
RB156		x	1			BWH	this paper
RB765		x	>32	NDM; KPC		MGH	this paper
RB767		x	>32	NDM		MGH	this paper
UCI_51	RB828	x	4	CTX-M-15	bl1_ec; OXA-30; TEM-1	UCI	Cerqueira et al, PNAS 2017

ExCip

STRAIN	Alt name 1	Alt name 2	Phase 1	cip MIC (mg/L)	Source	Comments
AR0061	CarbaNP-30		x	0.25	CDC	ARBank
AR0081	CarbaNP-50		x	16	CDC	ARBank
AR0085	CarbaNP-54		x	16	CDC	ARBank
AR0089	CarbaNP-58		x	0.25	CDC	ARBank
AR0104	CarbaNP-73		x	32	CDC	ARBank
BAA2469	RB557		x	64	ATCC	
BAA2523	RB553		x	0.5	ATCC	
BAC080000005647	RB591		x	64	NYDOH	shared by K. Musser
IDR1200024571	RB597		x	0.5	NYDOH	shared by K. Musser

IDR1300034680	RB603	x	0.03	NYDOH	shared by K. Musser
RB001		x (deriv_S)	0.03	BWH	this paper
RB025		x	0.25	BWH	this paper
RB051		x (deriv_R)	64	BWH	this paper
RB057		x (deriv_R)	64	BWH	this paper
RB075		x (deriv_S)	0.03	BWH	this paper
RB077		x	1	BWH	this paper
RB086		x	64	BWH	this paper
RB110		x	8	BWH	this paper

			Lot Cost			
STRAIN	Alt name 1	Alt name 2	Phase 1	gent MIC (mg/L)	Source	Comments
AR0055	CarbaNP-24		x	64	CDC	ARBank
AR0061	CarbaNP-30		x	32	CDC	ARBank
AR0081	CarbaNP-50		x	0.5	CDC	ARBank
AR0084	CarbaNP-53		x	0.5	CDC	ARBank
AR0085	CarbaNP-54		x	2	CDC	ARBank
BAA2469	RB557		x	64	ATCC	
BAC08000005647	RB591		x	1	NYDOH	shared by K. Musser
IDR1300027657	RB602		x	64	NYDOH	shared by K. Musser
IDR1300034680	RB603		x	1	NYDOH	shared by K. Musser
IDR1600047120	RB590		x	64	NYDOH	shared by K. Musser
MGH_57	RB544		x	0.5	MGH	Cerqueira et al., PNAS 2017
RB001			x (deriv_S)	1	BWH	this paper
RB051			x (deriv_R)	256	BWH	this paper
RB057			x (deriv_R)	256	BWH	this paper
RB075			x (deriv_S)	0.5	BWH	this paper
RB076			x	1	BWH	this paper
RB765			x	64	MGH	this paper

AbMero

CRO

STRAIN	Alt name 1	Alt name 2	Phase 1	mero MIC (mg/L)	Known gene(s) in probeset	Other known bla gene(s)	Source	Comments
ATCC 17978	RB651		x	≤0.5		OXA-95	ATCC	
AR0033	CarbaNP-02	RB389	x	>32	NDM-1	OXA-94	CDC	ARBank
AR0035	CarbaNP-04	RB390	x	>32		TEM-1D; ADC-25; OXA-66; OXA-72	CDC	ARBank
AR0036	CarbaNP-05	RB425	x	16		OXA-65; OXA-24	CDC	ARBank
AR0037	CarbaNP-06	RB391	x	>32	NDM-1	OXA-94	CDC	ARBank
AR0045	CarbaNP-14	RB392	x	32		TEM-1D; OXA-23; OXA-69	CDC	ARBank
AR0052	CarbaNP-21	RB393	x	2		OXA-58; OXA-100	CDC	ARBank
AR0056	CarbaNP-25	RB394	x	>32		OXA-23; OXA-66	CDC	ARBank
AR0063	CarbaNP-32	RB395	x	4		OXA-23; OXA-24; OXA 65	CDC	ARBank
AR0070	CarbaNP-39	RB396	x	16		OXA-58; OXA-100	CDC	ARBank
AR0078	CarbaNP-47	RB397	x	>32		ADC-25; SHV-5; OXA-71	CDC	ARBank
AR0101	CarbaNP-70	RB398	x	>32		OXA-65; OXA-24	CDC	ARBank
AR0102	CarbaNP-71	RB399	x	4		ADC-25; OXA-66	CDC	ARBank
RB197			x (deriv_S)	≤0.5			BWH	this paper
RB197s			x	≤0.5			BWH	this paper; small colony morphotype of RB197
RB198			x	8			BWH	this paper
RB200			x (deriv_R)	>32			BWH	this paper
RB201			x (deriv_S)	0.25			BWH	this paper
RB202			x	32			BWH	this paper
RB203			x (deriv_R)	>32			BWH	this paper
RB204			x	16			BWH	this paper
RB205			x	1			BWH	this paper

RB206			x	1		BWH	this paper
			AbCp				
STRAIN	Alt name 1	Alt name 2	Phase 1	cip MIC (mg/L)	Source	Comments	
ATCC 17978	RB651		x	0.5	ATCC		
AR0033	CarbaNP-02	RB389	x	>32	CDC	ARBank	
AR0035	CarbaNP-04	RB390	x	>32	CDC	ARBank	
AR0036	CarbaNP-05	RB425	x	>32	CDC	ARBank	
AR0037	CarbaNP-06	RB391	x	>32	CDC	ARBank	
AR0045	CarbaNP-14	RB392	x	>32	CDC	ARBank	
AR0052	CarbaNP-21	RB393	x	4	CDC	ARBank	
AR0056	CarbaNP-25	RB394	x	>32	CDC	ARBank	
AR0063	CarbaNP-32	RB395	x	8	CDC	ARBank	
AR0070	CarbaNP-39	RB396	x	8	CDC	ARBank	
AR0078	CarbaNP-47	RB397	x	>32	CDC	ARBank	
AR0101	CarbaNP-70	RB398	x	>32	CDC	ARBank	
AR0102	CarbaNP-71	RB399	x	>32	CDC	ARBank	
RB197			x x x (deriv_S)	0.25	BWH	this paper	
RB197s			x	0.25	BWH	this paper; small colony morphotype of RB197	
RB198			x (deriv_R)	>32	BWH	this paper	
RB201			x x (deriv_S)	0.25	BWH	this paper	
RB202			x (deriv_R)	>32	BWH	this paper	
RB203			x	>32	BWH	this paper	
RB204			x	>32	BWH	this paper	

RB205			x	1	BWH	this paper
RB206			x	>32	BWH	this paper

			AbGent			
STRAIN	Alt name 1	Alt name 2	Phase 1	gent MIC (mg/L)	Source	Comments
ATCC 17978	RB651		x	≤0.5	ATCC	
AR0033	CarbaNP-02	RB389	x	32	CDC	ARBank
AR0035	CarbaNP-04	RB390	x	16	CDC	ARBank
AR0037	CarbaNP-06	RB391	x	>32	CDC	ARBank
AR0045	CarbaNP-14	RB392	x	>32	CDC	ARBank
AR0052	CarbaNP-21	RB393	x	32	CDC	ARBank
AR0056	CarbaNP-25	RB394	x	>32	CDC	ARBank
AR0063	CarbaNP-32	RB395	x	4	CDC	ARBank
AR0070	CarbaNP-39	RB396	x	>32	CDC	ARBank
AR0078	CarbaNP-47	RB397	x	>32	CDC	ARBank
AR0101	CarbaNP-70	RB398	x	8	CDC	ARBank
AR0102	CarbaNP-71	RB399	x	>32	CDC	ARBank
RB197			x (deriv_S)	≤0.5	BWH	this paper
RB198			x	>32	BWH	this paper
RB200			x (deriv_R)	>32	BWH	this paper
RB201			x	1	BWH	this paper
RB202			x	>32	BWH	this paper
RB203			x	4	BWH	this paper
RB204			x (deriv_R)	>32	BWH	this paper
RB205			x (deriv_S)	2	BWH	this paper
RB206			x	>32	BWH	this paper

STRAIN	KpMero			CRE				KpGent		
	Phase 1	Phase 2	mero MIC (mg/L)	Run?	Known gene(s) in probeset	Other known bla gene(s)	Found by	Phase 1	gent MIC (mg/L)	Used in bloo cultures?
AR0034		x	2	+	IMP-4	TEM-1B; SHV-11	WGS			
AR0040	x	(x)	>32	+	VIM-27; CTX-M-15	SHV-11; OXA-1	WGS			
AR0041		x x	16	+	NDM-1; CTX-M-15; OXA-10	CMY-4; SHV-11	WGS			

AR0042	x	(x)	≤0.5	+	CTX-M15; OXA-10	TEM-1B; SHV-1; OXA-1	WGS	x	32		
AR0043	x		2	-		SHV-12 OXA-9; TEM-1A; SHV-12; OXA-1	WGS	x	1		
AR0044		x	4	+	CTX-M-15	TEM-1A	WGS				
AR0047		x	4	+		OXA-232; SHV-1; OXA-1	WGS				
AR0075	x	(x)	8	+	CTX-M15	SHV-12	WGS			x	
AR0076						OXA-9; TEM-1A; SHV-12		x	32		
AR0080								x	2	x	
AR0087	x	(x)	1	+		SHV-12	WGS				
AR0126						OXA-9; TEM-1A; SHV-12					
AR0135		x	8	+	VIM-1 NDM-1; CTX-M-15; OXA-10		WGS				
AR0139		x x	32	+		CMY-4; SHV-11	WGS				
AR0160								x	>32		
ATCC 700721											
BAA2524		x	0.5*	+	OXA-48		unknown				
BAC0800005950								x	0.5		
BAC0800007138											
BIDMC_14		x	16	+	KPC-3	SHV-134; TEM-1	WGS				
BIDMC_21											
BIDMC_22		x	0.25	+		SHV-134	WGS				
BIDMC_2A								x	2		
BIDMC_31		x	0.125	+		SHV-38	WGS				
BIDMC_34								x	32		
BIDMC_35	x	(x)	>32	+	OXA-10	SHV-134	WGS				
BIT-03	x	(x)	8	+	KPC (unknown type)		unknown				
BIT-04	x (deriv_R)	x (deriv_R)	32	+	KPC (unknown type)		unknown				
BIT-05	x	(x)	>32	-			unknown				
BIT-10								x	4		
BIT-12	x	(x)	≤0.5	+			unknown				

BIT-16	x	(x)	≤0.5	+	KPC-4	SHV-134; TEM-1	unknown			x
BWH_15	x	(x)	8	+	CTX-M-15; OXA-48	SHV-134; TEM-1 OXA-30; OXA-9; SHV-38; TEM-1	WGS	x	4	
BWH_2		x	16	+			WGS			x
BWH_22				-		SHV-134	WGS			
BWH_30	x	(x)	≤0.5	+	KPC-3	SHV-134; TEM-1	WGS			
BWH_36	x	(x)	16				(no data)			
CDC_1500476				+						
CDC_1500610	x	(x)	≤0.5	+	NDM-1; CTX-M15	SHV-38	WGS			
IDR1200022727										
IDR1200023303	x	(x)	>32	+			WGS	x	>32	
IDR1600031102-01-00	x	(x)	>32	+	CTX-M-15	SHV-134	WGS			
IDR1600037310	x	(x)	1	+			WGS			
IDR1600037319-01-00								x	0.5	
IDR1600039511-01-00										
IDR1600053363-01-00										
IDR1600057468-01-00		x	4	+	CTX-M-15	SHV-134	WGS			
MGH_17		x	≤0.5	+			WGS			
MGH_18	x (deriv_S)	x (deriv_S)	≤0.5	+		SHV-134	WGS			
MGH_19	x	(x)	≤0.5	+		SHV-134	WGS			
MGH_20		x	≤0.5	+		SHV-134	WGS			
MGH_21										
MGH_30								x	1	
MGH_31		x	8	+		SHV-134 OXA-30; SHV-134; TEM-1	WGS			
MGH_35		x	2	+	CTX-M-15		WGS	x	>16	
MGH_36		x	≤0.5	+		SHV-38	WGS			
MGH_39		x	2	+	KPC-3	OXA-9; SHV-38; TEM-1	WGS			
MGH_48		x	≤0.5	+		SHV-134	WGS			
MGH_63								x	>16	
MGH_71		x	32	+	KPC-2; OXA-10	SHV-134; TEM-1	WGS			

MGH_74										x
RB012								x (deriv_R)	32	
RB013										
RB039	x (deriv_S)	x (deriv_S)	≤0.5	+			(no data)			
RB040								x (deriv_S)	0.5	
RB041		x	≤0.5	+			(no data)			x
RB042		x	≤0.5	+			(no data)	x	2	
RB121								x (deriv_S)	1	
RB122								x (deriv_R)	128	
RB123										x
UCI_13								x	0.5	
UCI_19	x (deriv_R)	x (deriv_R)	>32	+	KPC-2	SHV-134; TEM-1	WGS			
UCI_20										
UCI_22										
UCI_37	x	(x)	32	+	KPC-3	OXA-9; SHV-38; TEM-1	WGS	x	16	
UCI_38	x	(x)	≤0.5			SHV-134	WGS			
UCI_44		x	0.25	+		OXA-9; TEM-1	WGS			
UCI_56										
UCI_61		x	32	+	KPC-2	SHV-134; TEM-1	WGS			
UCI_63								x	4	
UCI_64		x	0.25	+		SHV-134	WGS			
UCI_67								x	8	
UCI_7		x	0.25	+		SHV-134	WGS	x	0.5	

	EcCip		EcGent		
STRAIN	Phase 1	cip MIC (mg/L)	Phase 1	gent MIC (mg/L)	Used in blood cultures?
AR0048					
AR0055			x	64	x
AR0058					

AR0061	x	0.25	x	32	x	
AR0069					x	
AR0077						
AR0081	x	16	x	0.5		
AR0084			x	0.5		
AR0085	x	16	x	2		
AR0089	x	0.25			x	
AR0104	x	32				
BAA2469	x	64	x	64		
BAA2523	x	0.5				
BAC08000005647	x	64	x	1	x	
BIDMC_77						
IDR1200024571	x	0.5				
IDR1200039757						
IDR1300027657			x	64		
IDR1300034680	x	0.03	x	1	x	
IDR1600029769						
IDR1600035372						
IDR1600043633						
IDR1600047120			x	64		
MGH_57			x	0.5		
RB001	x (deriv_S)	0.03	x (deriv_S)	1		
RB002						
RB025	x	0.25				
RB051	x (deriv_R)	64	x (deriv_R)	256	x	
RB057	x (deriv_R)	64	x (deriv_R)	256	x	
RB075	x (deriv_S)	0.03	x (deriv_S)	0.5		

RB076				x		1		x		
RB077		x		1						
RB086		x		64				x		
RB110		x		8						
RB156								x		
RB765					x		64			
RB767										
UCI_51										
BAA2471								x		

	AbCip		Argent	
STRAIN ATCC	Phase 1	cip MIC (mg/L)	Phase 1	gent MIC (mg/L)
17978	x	0.5	x	≤0.5
AR0033	x	>32	x	32
AR0035	x	>32	x	16
AR0036	x	>32		
AR0037	x	>32	x	>32
AR0045	x	>32	x	>32
AR0052	x	4	x	32
AR0056	x	>32	x	>32
AR0063	x	8	x	4
AR0070	x	8	x	>32
AR0078	x	>32	x	>32
AR0101	x	>32	x	8
AR0102	x	>32	x	>32
RB197	x x x (deriv_S)	0.25	x (deriv_S)	≤0.5
RB197s	x	0.25		

RB198	x (deriv_R)	>32	x x (deriv_R)	>32	
RB200					
RB201	x x (deriv_S)	0.25	x	1	
RB202	x (deriv_R)	>32	x	>32	
RB203	x	>32	x x (deriv_R)	4	
RB204	x	>32		>32	
RB205	x	1	x (deriv_S)	2	
RB206	x	>32	x	>32	

PacIp

STRAIN	Alt name 1	Phase 1	cip MIC (mg/L)	Source	Comments
BL01	RB918	x	0.125	B&L	eye isolate
BL03	RB919	x	16	B&L	eye isolate
BL08	RB920	x	0.06	B&L	eye isolate
BL11	RB921	x	0.125	B&L	eye isolate
BL17	RB922	x	16	B&L	eye isolate
BL22	RB923	x	0.5	B&L	eye isolate
BWHPSA003	RB924	x	16	BWH	clinical pulmonary isolate
BWHPSA006	RB925	x	16	BWH	clinical pulmonary isolate
BWH029	RB926	x	0.03	BWH	clinical pulmonary isolate
BWH033	RB927	x	0.06	BWH	clinical urinary isolate
BWHPSA041	RB928	x	2	BWH	clinical wound isolate
BWHPSA043	RB929	x	0.06	BWH	clinical wound isolate

BWHPSA046	RB930	x	0.06	BWH	clinical pulmonary isolate
BWHPSA048	RB931	x	8	BWH	clinical urinary isolate
BWH049	RB932	x	16	BWH	clinical urinary isolate
BWH050	RB933	x	0.25	BWH	clinical blood isolate
BWH053	RB934	x	16	BWH	clinical blood isolate
BWH055	RB935	x	0.125	BWH	clinical urinary isolate
CF5	RB936	x	8	Lory lab	respiratory isolate from CF patient from Lory lab via Aussubel lab
CF18	RB937	x	0.06	Lory lab	respiratory isolate from CF patient from Lory lab via Aussubel lab
CF27	RB938	x	1	Lory lab	respiratory isolate from CF patient from Lory lab via Aussubel lab
UDL	RB939	x	0.125	Lory lab	urinary isolate from Lory lab via Aussubel lab
X13273	RB940	x	8	Lory lab	blood isolate from Lory lab via Aussubel lab
X24509	RB941	x	64	Lory lab	urinary isolate from Lory lab via Aussubel lab

	SaLevo			
STRAIN	Phase 1	levo MIC (mg/L)	Source	Comments
RB003	x	0.125	BWH	clinical isolate from BWH
RB004	x	32	BWH	clinical isolate from BWH
RB006	x	0.06	BWH	clinical isolate from BWH Crimson Core
RB007	x	16	BWH	clinical isolate from BWH Crimson Core
RB010	x	>32	BWH	clinical isolate from BWH Crimson Core

				clinical isolate from BWH Crimson
RB045	x	32	BWH	Core
				clinical isolate from BWH Crimson
RB047	x	>32	BWH	Core
				clinical isolate from BWH Crimson
RB064	x	8	BWH	Core
				clinical isolate from BWH Crimson
RB065	x	0.06	BWH	Core
				clinical isolate from BWH Crimson
RB066	x	0.06	BWH	Core
				clinical isolate from BWH Crimson
RB067	x	0.13	BWH	Core
				clinical isolate from BWH Crimson
RB069	x	0.13	BWH	Core
				clinical isolate from BWH Crimson
RB072	x	4	BWH	Core
				clinical isolate from BWH Crimson
RB074	x	32	BWH	Core
				clinical isolate from BWH Crimson
RB090	x	32	BWH	Core
				clinical isolate from BWH Crimson
RB095	x	32	BWH	Core
				clinical isolate from BWH Crimson
RB096	x	0.13	BWH	Core
				clinical isolate from BWH Crimson
RB098	x	0.13	BWH	Core
				clinical isolate from BWH Crimson
RB211	x	16	BWH	Core
				clinical isolate from BWH Crimson
RB219	x	32	BWH	Core

RB221	x	0.13	BWH	clinical isolate from BWH Crimson Core
RB223	x	0.13	BWH	clinical isolate from BWH Crimson Core
RB245	x	0.25	BWH	clinical isolate from BWH
RB247	x	0.5	BWH	clinical isolate from BWH

KEY/ABBREVIATIONS:

*	large inoculum effect for meropenem MIC (RB554: MIC 0.5 at 1e5 cfu/mL , MIC 32 at 1e7 cfu/mL)
ATCC	American Type Culture Collection
BWH	Brigham and Women's Hospital, Boston MA USA
CDC	United States Centers for Disease Control
deriv_S	susceptible strain used in RNA-Seq for derivation of responsive and control genes, and for derivation of "centroid" of susceptible strains for SPD calculations, defined as SPD := 0 (see Barczak, Gomez et al, PNAS 2012).
deriv_R	resistant strain used in RNA-Seq for derivation of control genes, and for derivation of "centroid" of resistant strains for SPD calculations, defined as SPD := 1 (see Barczak, Gomez et al, PNAS 2012).
MGH	Massachusetts General Hospital, Boston MA USA
NYDOH	New York Department of Health (aka Wadsworth laboratories)
UCI	University of California at Irvine, USA
(x)	non-derivation strain from phase 1 that was rerun in phase 2

Table 8: GO term enrichment summary (**bold** = enriched in two bacteria for the same drug; ***bold/red*** = enriched in all three bacteria for the same drug)

KpMero:	category	over_represented_pvalue	under_represented_pvalue	numDEInCat	numInCat	term	ontology	BH.adjusted.pvalue
	GO:0009432	2.30E-07	1	13	30	SOS response	BP	6.75E-05
	GO:0009245	7.11E-05	0.9999908	9	24	lipid A biosynthetic process	BP	0.010445386
	GO:0009103	0.0002335	0.9999686	8	22	**lipopolysaccharide biosynthetic process**	BP	0.022882608
KpCip:								
	GO:0009432	1.20E-11	1	19	30	***SOS response***	BP	3.52E-09
	GO:0009246	7.42E-06	0.9999995	9	15	enterobacterial common antigen biosynthetic process	BP	0.001090988
	GO:0045272	0.0002088	0.9999808	7	13	***plasma membrane respiratory chain complex I***	CC	0.020461935

KpGen1:								
	GO:0005829	4.52E-08	1	354	804	*cytosol*	CC	1.29E-05
	GO:0042802	4.46E-07	1	139	279	**identical protein binding**	MF	6.38E-05
	GO:0003677	1.42E-06	1	162	339	DNA binding	MF	0.0001353
	GO:0006094	3.72E-05	1	12	13	gluconeogenesis	BP	0.0021253
	GO:0045272	3.72E-05	1	12	13	*plasma membrane respiratory chain complex I*	CC	0.0021253
	GO:0006096	0.0004	0.99993	15	20	glycolytic process	BP	0.015156
	GO:0008137	0.0004	0.99993	15	20	**NADH dehydrogenase (ubiquinone) activity**	MF	0.015156
	GO:0009246	0.00042	0.99996	11	13	**enterobacterial common antigen biosynthetic process**	BP	0.015156
	GO:0048038	0.00073	0.99989	13	17	*quinone binding*	MF	0.0232089

					transcription factor activity, sequence-specific DNA binding	MF	0.0232221
	GO:0003700	0.00088	0.99944	116	257		
					protein binding	MF	0.0232221
	GO:0005515	0.00089	0.99935	247	594		
					unfolded protein binding	MF	0.0465668
	GO:0051082	0.00195	0.99955	15	22		
					peptidoglycan biosynthetic process	BP	0.0479236
	GO:0009252	0.00218	0.99921	25	43		
					regulation of transcription, DNA-templated	BP	0.0499734
	GO:0006355	0.00245	0.99838	114	258		
EdMero:	category	over_represented_pvalue	under_represented_pvalue	numDEInCat	numInCat	term	ontology	BH.adjusted.pvalue

	GO:0045228	1.63E-10	1	10	10	slime layer polysaccharide biosynthetic process	BP	4.84E-08
	GO:0009103	1.53E-08	1	18	39	**lipopolysaccharide biosynthetic process**	BP	2.26E-06
	GO:0000160	1.20E-05	0.9999968	21	73	phosphorelay signal transduction system	BP	0.001179541
	GO:0003700	8.05E-05	0.9999668	34	165	transcription factor activity, sequence-specific DNA binding	MF	0.005950885
	GO:0000155	0.0001407	0.9999748	11	30	phosphorelay sensor kinase activity	MF	0.005950885
	GO:0018106	0.0001407	0.9999748	11	30	peptidyl-histidine phosphorylation	BP	0.005950885

	GO:0023014	0.0001407	0.9999748	11	30	signal transduction by protein phosphorylation	BP	0.005950885
	GO:0009408	0.000194	0.9999563	13	41	**response to heat**	BP	0.007176356
	GO:0009242	0.0007007	0.9999106	7	16	colanic acid biosynthetic process	BP	0.023043956
	GO:0042802	0.0010501	0.9994156	51	316	identical protein binding	MF	0.031083956
	GO:0009097	0.0012302	0.9998603	6	13	isoleucine biosynthetic process	BP	0.033102869
	GO:0006355	0.0016	0.9992615	28	149	regulation of transcription, DNA-templated	BP	0.039467343
EcCip:								
	GO:0005829	5.89E-14	1	259	838	cytosol	CC	1.77E-11
	GO:0045272	8.23E-08	1	12	13	*plasma membrane respiratory chain complex I*	CC	8.45E-06

GO:0009432	1.04E-07	1	22	35	*SOS response*	BP	8.45E-06
GO:0048038	1.12E-07	1	13	15	quinone binding	MF	8.45E-06
GO:0005524	4.95E-07	0.9999997	142	468	ATP binding	MF	2.98E-05
GO:0042802	7.52E-06	0.9999959	98	312	identical protein binding	MF	0.000377223
GO:0005515	2.15E-05	0.999986	185	678	protein binding	MF	0.0008179
GO:0008137	2.17E-05	0.9999981	11	15	**NADH dehydrogenase (ubiquinone) activity**	MF	0.0008179
GO:0009060	7.64E-05	0.9999928	10	14	**aerobic respiration**	BP	0.002554494
GO:0009408	0.0001178	0.9999698	19	39	response to heat	BP	0.003544968
GO:0005737	0.0004105	0.9997398	107	379	cytoplasm	CC	0.011232616
GO:0003924	0.0010496	0.9997509	13	26	GTPase activity	MF	0.025792402
GO:0000287	0.001114	0.9993795	56	181	magnesium ion binding	MF	0.025792402
GO:0000049	0.0012322	0.9996029	18	42	tRNA binding	MF	0.026492746
GO:0006281	0.0013993	0.9995073	20	49	DNA repair	BP	0.028079213
GO:0006094	0.0018422	0.9997384	8	13	gluconeogenesis	BP	0.033095829
GO:0005525	0.0019593	0.9992409	22	57	GTP binding	MF	0.033095829

	GO:0008270	0.0019792	0.9989393	45	142	zinc ion binding	MF	0.033095829
EcGene:								
	GO:0005829	1.10E-10	1	292	838	*cytosol*	CC	3.32E-08
	GO:0045272	9.19E-07	1	12	13	*plasma membrane respiratory chain complex I*	CC	0.000138358
	GO:0048038	1.46E-06	0.9999999	13	15	*quinone binding*	MF	0.000146098
	GO:0009408	2.88E-06	0.9999994	24	39	response to heat	BP	0.000216511
	GO:0009060	4.90E-06	0.9999997	12	14	**aerobic respiration**	BP	0.000295219
	GO:0000976	0.0001515	0.9999613	20	36	**transcription regulatory region sequence-specific DNA binding**	MF	0.007180246

	GO:0008137	0.000167	0.9999813	11	15	NADH dehydrogenase (ubiquinone) activity	MF	0.007180246
	GO:0009246	0.0004784	0.9999418	10	14	enterobacterial common antigen biosynthetic process	BP	0.015360219
	GO:0000160	0.0005103	0.9997895	33	75	phosphorelay signal transduction system	BP	0.015360219
	GO:0045893	0.0005103	0.9997895	33	75	positive regulation of transcription, DNA-templated	BP	0.015360219
	GO:0045892	0.000689	0.9996804	40	97	negative regulation of transcription, DNA-templated	BP	0.018272272

	GO:0042802	0.0007285	0.9995352	106	312	**identical protein binding**	MF	0.018272272
	GO:0032993	0.0011444	0.9996019	22	46	protein-DNA complex	CC	0.025110664
	GO:0005524	0.0011679	0.9991888	150	468	**ATP binding**	MF	0.025110664
	GO:0051082	0.0018124	0.9995693	13	23	*unfolded protein binding*	MF	0.036369052
	GO:0001216	0.0024028	0.9994473	12	21	**bacterial-type RNA polymerase transcriptional activator activity, sequence-specific DNA binding**	MF	0.045203227
	GO:0000156	0.0026702	0.9992241	15	29	phosphorelay response regulator activity	MF	0.047278898
AbMero:	category	over_represented_pvalue	under_represented_pvalue	numDEInCat	numInCat	term	ontology	BH.adjusted.pvalue

GO:0003735	6.18E-25	1	38	56	structural constituent of ribosome	MF	9.02E-23
GO:0006412	1.02E-21	1	37	61	translation	BP	7.42E-20
GO:0022625	2.06E-19	1	26	34	cytosolic large ribosomal subunit	CC	1.00E-17
GO:0010124	1.12E-11	1	14	17	phenylacetate catabolic process	BP	4.07E-10
GO:0019843	5.58E-10	1	18	33	rRNA binding	MF	1.63E-08
GO:0000027	1.20E-09	1	15	24	ribosomal large subunit assembly	BP	2.93E-08
GO:0008137	2.95E-07	1	9	12	NADH dehydrogenase (ubiquinone) activity	MF	5.39E-06
GO:0045272	2.95E-07	1	9	12	plasma membrane respiratory chain complex I	CC	5.39E-06
GO:0022627	7.15E-06	0.9999993	10	19	cytosolic small ribosomal subunit	CC	0.000115922

GO:0005515	2.53E-05	0.9999893	43	216	protein binding	MF	0.000368873
GO:0009408	0.000156	0.9999865	7	13	**response to heat**	BP	0.002069898
GO:0009060	0.001353	0.999844	6	13	aerobic respiration	BP	0.016461583
GO:0005887	0.0015257	0.9993957	21	99	integral component of plasma membrane	CC	0.01713523
GO:0006635	0.0032705	0.9995175	6	15	fatty acid beta-oxidation	BP	0.031887682
GO:0000049	0.0032761	0.999218	9	30	tRNA binding	MF	0.031887682
GO:0048038	0.0038197	0.9995601	5	11	quinone binding	MF	0.034855201
Abcp:							
GO:0005887	4.48E-07	0.9999999	27	99	integral component of plasma membrane	CC	6.64E-05
GO:0045272	4.54E-05	0.999997	7	12	*plasma membrane respiratory chain complex I*	CC	0.002664886

					NADH dehydrogenase (ubiquinone) activity	MF	0.002664886
GO:0008137	9.00E-05	0.9999929	7	13			
					aerobic respiration	BP	0.002664886
GO:0009060	9.00E-05	0.9999929	7	13			
					SO3 response	BP	0.002664886
GO:0009432	9.00E-05	0.9999929	7	13			
					ATP hydrolysis coupled cation transmembrane transport	BP	0.038240038
GO:0099132	0.0015503	0.999864	5	10			
AbGen							
					plasma membrane respiratory chain complex I	CC	9.93E-06
GO:0045272	6.71E-08	1	12	12			
					NADH dehydrogenase (ubiquinone) activity	MF	0.000685478
GO:0008137	1.24E-05	0.9999993	11	13			

	GO:0051082	1.39E-05	0.999999	12	15	*unfolded protein binding*	MF	0.000685478
	GO:0005829	8.20E-05	0.999951	118	348	*cytosol*	CC	0.003034026
	GO:0048038	0.0001397	0.999991	9	11	*quinone binding*	MF	0.003461981
	GO:0009060	0.0001404	0.9999876	10	13	**aerobic respiration**	BP	0.003461981
	GO:0051537	0.0006792	0.9998184	17	32	2 iron, 2 sulfur cluster binding	MF	0.014360095
	GO:0005524	0.0011434	0.9993209	76	221	**ATP binding**	MF	0.021153405
	GO:0006099	0.0018825	0.9995827	12	21	tricarboxylic acid cycle	BP	0.030956723
	GO:0051301	0.0027479	0.9992393	14	27	cell division	BP	0.040669255
	GO:0016226	0.0038105	0.999543	7	10	iron-sulfur cluster assembly	BP	0.046996546
	GO:0099132	0.0038105	0.999543	7	10	ATP hydrolysis coupled cation transmembrane transport	BP	0.046996546
PaCip.								
	GO:0005829	1.5411E-10	1	88	596	cytosol	CC	4.6387E-08

	GO:0005515	1.6401E-05	0.999992 56	49	349	protein binding	MF	0.00246842
	GO:0016226	3.2454E-05	0.999998 5	6	10	iron-sulfur cluster assembly	BP	0.00325621
	GO:0005737	0.00011236	0.999944 78	48	365	cytoplasm	CC	0.00845502
	GO:0001896	0.00021704	0.999982 53	6	13	autolysis	BP	0.01306574
	GO:0009432	0.00094306	0.999858 92	7	22	*%0% response*	BP	0.04355305
	GO:0000049	0.00101286	0.999791 12	9	35	tRNA binding	MF	0.04355305
Salevo:								
	GO:0009432	3.67E-05	0.999997 3	7	15	*%0% response*	BP	0.00433248
	GO:0006096	1.51E-04	0.999984 79	7	18	glycolytic process	BP	0.00888559

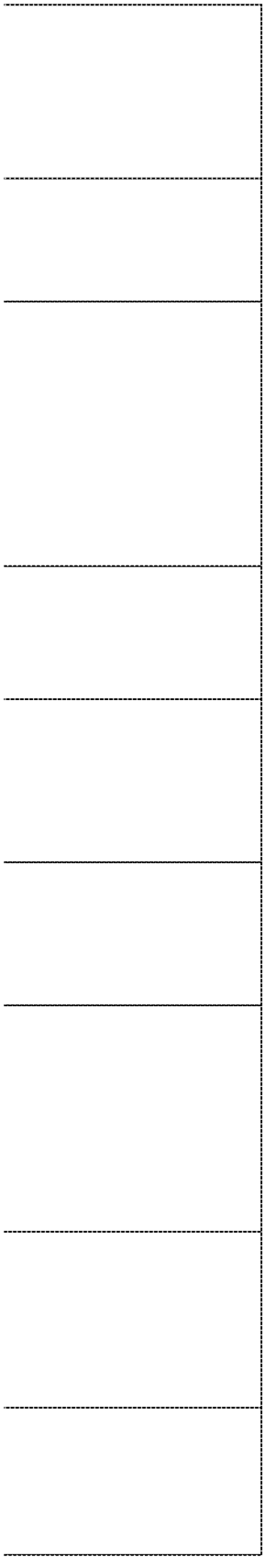


Table 9: displays the initially selected responsive and control genes for each pathogen-antibiotic pair disclosed herein, and all probes for carbapenemase and ESBL gene family detection, including probe sequences, and also l2fc thresholds used to generate each responsive and control gene list for each bug-drug pair. Also append reliefF ranking for the top 10 chosen. Table legend: a = GeneID refers to reference genome as indicated, with alternate GeneID references in parentheses; when GeneID is NC_009648, reference is using what is currently referred to as "old_locus_tag"; b = Position is listed relative to the start codon of that locus; c = 100-mer target selected based on homology masking of full-length gene, used to design hybridization probes. Probe A is complementary to the first half; probe B is complementary to the second half of the target sequence; d = for responsive genes, listing whether they are predicted to be up-regulated ("up") or down-regulated ("dn") based on RNA-Seq results. Note that for all genes selected by reliefF, the direction of change expected from RNA-Seq matched that seen in NanoString® data; e = selected by reliefF as top 10 responsive feature, or by variation on geNorm algorithm as top ~10 control feature, and thus used in phase 2 experiments.

Strain/Ab	GeneID[a]	Position[b]	Target Sequence[c]	SEQ ID NO:	Ctrl/ Resp	Up/ Dn[d]		Phase 2?[e]
Kp_mero GeneID = NC_009648	KPN_00050	1178-1277	AGATCGTGCTTACCGCATGCTGATGAACCGCAAATTCTCTGAAGAAGCGG CAACCTGGATGCAGGAACAGCGCGCCAGTGCGTATGTTAAAATTCTGAGC	SEQ ID NO:140	C			x
Kp_mero	KPN_00098	523-622	GGAACGTTGTGGTCTGAAAGTTGACCAACTTATTTTCGCCGGGTTAGCGG CCAGTTATTCGGTATTAACAGAAGACGAACGTGAGCTGGGCGTCTGCGTT	SEQ ID NO:141	C			x
Kp_mero	KPN_00100	635-734	TCGATTGTGCCATCGTTGTTGACGATTATCGCGTACTGAACGAAGACGGT CTGCGCTTTGAAGACGAATTTGTTCGCCACAAAATGCTGGATGCGATCGG	SEQ ID NO:142	C			x
Kp_mero	KPN_00945	637-736	AGTGCTGTGGTATGGCGAGAAAATCCATGTCGCCGTGGCGGCCGAAGTGC CCGGCACCGGCGTGGATACCCCGGAAGATCTGGAGCGCGTCCGCGCTGAG	SEQ ID NO:143	C			
Kp_mero	KPN_00949	157-256	GTGGATGCGTTCCGCCACGTCAGTGATGCGTTTGAGCAGACCAGCGAAAC CATCAGCCAGCGCGCCAATAACGCGATCAACGATTTGGTGCGCCAGCGTC	SEQ ID NO:144	C			
Kp_mero	KPN_00950	61-160	GTTAAGCTGGCGCAGGCGTTGGCCAATCCGTTATTTCCGGCGCTGGACAG CGCCCTGCGCGCGGGCCGTCATATCGGTCTCGACGAGCTGGATAATCACG	SEQ ID NO:145	C			

Kp_mero	KPN_01276	1-100	ATGCTGGAGTTGTTGTTCTGCTTTACCCGTTGCCGCCGCTTACGGCTG GTACATGGGGCGCAGAAGTGCACAACAGTCCAAACAGGACGATGCGAGCCC	SEQ ID NO:146	C		x
Kp_mero	KPN_02357	679-778	TGATCAAATGTGCGCTGGTCGCCGGGATGGTGGTAATTGCGTTAGTGAAC AGGTATGTTCTGGTACCGCGCATGTCGGCAAGCGGTTCGCAGGCGGAAAG	SEQ ID NO:147	C		
Kp_mero	KPN_02805	81-180	GTTAATGATTGAACGCCTGCGTGCGATCGGCTTTACCGTTGAACCGATGG ATTTCGGCGATACGCAGAATTTCTGGGCCTGGCGCGCCGGCCACGGCGAGACG	SEQ ID NO:148	C		
Kp_mero	KPN_02846	732-831	GCGCAGGATCTGGTGATGAACTTTTCCGCCGACTGCTGGCTGGAAGTGAG CGATGCCACCGGTAAAAAACTGTTCAGCGGCCTGCAGCGTAAAGGCGGTA	SEQ ID NO:149	C		x
Kp_mero	KPN_02864	527-626	CCGTACCCGCTGGTGGACGATCTGGAGCGATTCTACGACCATCTTGAGCA GACGCTGCTGGCGACGGGCTTTATCCGCCCGAATCATCCGGGGCAGGTGA	SEQ ID NO:150	C		
Kp_mero	KPN_03230	100-199	ATCCGCAAAAGCGAAAAAGATACGCGTCAGTATCAGGCGATCCGCCTTGA TAACGACATGGTCGTGCTGCTGGTTTCCGATCCGCAGGCGGTGAAATCGC	SEQ ID NO:151	C		
Kp_mero	KPN_03317	34-133	ATGGCCGGGGAACACGTCATTTTGCTGGATGAGCAGGATCAGCCTGCCGG TATGCTGGAGAAGTATGCCGCCCATACGTTTTGATACCCCTTTACATCTCG	SEQ ID NO:152	C		x
Kp_mero	KPN_03628	256-355	CCGCCGTTAATGCCGGTTTATCCGGTGGCGCGTGGTGAAAGCCGCCTGTA TATGCAACGTATCGAGAAGGACTGGTATTCGCTGATGAACACCATCCAGA	SEQ ID NO:153	C		
Kp_mero	KPN_03634	656-755	AGCAATGACGGCGAAACGCCGGAAGGCATTGGCTTTGCGATCCCGTTCCA GTTAGCGACCAAAATTATGGATAAACTGATCCGCGATGGCCGGGTGATCC	SEQ ID NO:154	C		x
Kp_mero	KPN_04331	423-522	TCTGAAGGAGAATGGCAAAGAGGTGGTGATCAAGGTTATCCGCCCGGATA TTTTGCCGATCATTAAAGCGGACATGAAGCTCATCTACCGCCTGGCGCGC	SEQ ID NO:155	C		
Kp_mero	KPN_04429	49-148	CAGGTGCTGGTAAAAAGCAAGTCTATTCCGGCAGAGCCTGCCCAGGAATT AGGACTCGATACCTCGCGTCCGGTCATGTACGTCCTGCCCTATAATTCGA	SEQ ID NO:156	C		
Kp_mero	KPN_04616	1272-1371	TCATCGTGATGCAGGCCCAGGACGTCTGGATCCGTACCCTCTATGACCGC CACCGCTTTGTGGTGCGCGGCAACCTTGGCTGGATCGAAGCGGACAACTT	SEQ ID NO:157	C		
Kp_mero	KPN_04617	3455-3554	CGATAGCGCCGCGATGACCTCAATGCTTATTGGTATGGGGGTTGCACAAA GTGGTCAGGTTGTGGGTAAAATCGGCGAGACGTTTGGCGTAAGCAACTTG	SEQ ID NO:158	C		
Kp_mero	KPN_04663	1199-1298	ATTCAGTTCGTGCCGAAGCAGTACGAAAAATATGTACTTCTCCTGGATGCG CGATATTCAGGACTGGTGTATCTCCCGTCAGCTGTGGTGGGGTCACCGCA	SEQ ID NO:159	C		
Kp_mero	KPN_04666	450-549	CAGGCCAGCGATGGTAACGCGGTGATGTTTATCGAAAGCGTCAACGGCAA CCGCTTCCATGACGTCTTCCTTGCCCAGCTGCGTCCGAAGGGCAATGCGC	SEQ ID NO:160	C		x

Kp_mero	KPN_00055	496-595	CCCGATGCTGTGCGGCGAAGTGGTCGGCATGCTGGTGGGCATCGGCGTCG GCACGCTGCTGGGCATGGAGCCGTTCCAGGTGTTCTTCTTTATCGTGCTG	SEQ ID NO:161	R	dn		
Kp_mero	KPN_00499	331-430	TCTTCCCAATTTTAAATAACCCGGTGCCAGCAGGTATTGCCTGTATTGCC ATCGTGTGGATCTTTACTTTCGTTAATATGCTCGGCGGGACCTGGGTCAG	SEQ ID NO:162	R	dn		
Kp_mero	KPN_00681	452-551	CTTCTCCGATACCATCTTCGTGGTCGGTACCCGTCTGCTGGTGAAGAAAG GCGGTCCGATCAAAGATTTCCCGGACCTGAAGGATAAAGCGGTCGTCGTC	SEQ ID NO:163	R	dn		
Kp_mero	KPN_00699	295-394	TCCGGCAGAAAATATCAACCTGCTGAATGGTAACGCGCCGGACATCGATG CGGAATGCCGTCGCTATGAAGAAAAATTCGTTCCTACGGTAAAATCCAC	SEQ ID NO:164	R	dn		
Kp_mero	KPN_00840	385-484	GACATCAAAGATGTCAAAGATCTGAACGGTAAAGTGGTCGCGGTGAAGAG CGGCACCGGCTCCGTTGACTACGCGAAAGCCAATATCAAAACCAAAGATC	SEQ ID NO:165	R	dn		
Kp_mero	KPN_00868	110-209	TGCAACTGCGAAAGGCCAAAGGCTACATGTCAGTCAGCGAAAATGACCAT CTGCGTGATAACTTGTTTGAGCTTTGCCGTGAAATGCGTGCGCAGGCGCC	SEQ ID NO:166	R	dn		x
Kp_mero	KPN_00956	570-669	CTTCAGCACCGCAGCCACCTACGCGTTCGACAACGGTATCGCACTGTCTG CAGGCTACTCCAGCTCTAACCGTAGCGTCGATCAGAAAGCTGACGGCAAT	SEQ ID NO:167	R	dn		
Kp_mero	KPN_01105	326-425	AGCGGATTGGTTTTCTGTGCGATATCCGCCAGGCGGTGTTCAATCCAAAC CTGTTTCCGCATGAGAACATGGAAGGCAAAATCGACCGACCGGAAGAGTA	SEQ ID NO:168	R	dn		
Kp_mero	KPN_01164	1059-1158	GGAAGCCTTACAGATTATGGAAGCGGATGTTATAAATGGCGCTCTGGATA GCGATGTCTTCCTCGTTTTGCGCCACCATGCGGAAACGCTACACGCCATC	SEQ ID NO:169	R	dn		
Kp_mero	KPN_01172	834-933	CTGTGCGGCGTCTACTTCCTCGGCGAACAGCGTATCGACTATGAGGGCGC CAGCTTCGGGTGGTCACCTGCGATCCGCAGAGTATCGATGTTGAAGCGG	SEQ ID NO:170	R	dn		
Kp_mero	KPN_01229	3-102	GAACAAAAGCTTAGCAGGAATACTGGGCGTCACCGTCGCGTTAACCTTAC TGGCGGGCTGTACCGCTTACGATCGTACCAAAGACCAGTTTACCCAGCCG	SEQ ID NO:171	R	dn		
Kp_mero	KPN_01529	69-168	AGCGGTGTACCTGCACCAACGGATTGGTGGACGCATCAAGCCTTTTTGC CGATCTATGATTTTTCCTATGAAATGACCACCCTGCTGTCGCCGGACGAG	SEQ ID NO:172	R	dn		
Kp_mero	KPN_01553	610-709	AGGCAGATCGTCAATATGCTGACAACCGGACTCGCCATCCGTGACGGTCG GGTGTACAGCAATTTGCGGGTGGACGTGCAGGCTGACAATTCGCACTGGG	SEQ ID NO:173	R	dn		
Kp_mero	KPN_02241	71-170	GGGTAGGTTACTCCATTCTGAACCAGCTTCCGCAGCTTAACCTGCCACAA TTCTTTGCGCATGGCGCAATCCTAAGCATCTTCGTTGGCGCAGTGCTCTG	SEQ ID NO:174	R	dn		x
Kp_mero	KPN_02411	1592-1691	CGCGATGAATCGCCACGATCATGCGATCTCCGGGCATCGCAAAAAACGGGC GAAAGTGAAGAGCACCAGCTCGCTTGAGACTATCGAGGGGGTGGGGCCGA	SEQ ID NO:175	R	dn		

Kp_mero	KPN_02412	177-276	GTGCCGGGCTAATTCCGCAGATGTCGTCCTGATGGACATGAACATGCCTG GGATCGGTGGTCTTGAAGCGACGCGCAAAATCGCGCGCTCCGTGGCGGGC	SEQ ID NO:176	R	dn	
Kp_mero	KPN_02563	150-249	TCGCCTGCCGCACAAGCTGCTGTGCTACGTCACCTTCTCCATTTCTCTGCA TTATGGGGACCTATTTCGGTCTGCATATCGAAGACTCCATCGCCAACACC	SEQ ID NO:177	R	dn	
Kp_mero	KPN_02725	174-273	GTTAAGCGAAAAAGCCCCGCAATGTCGAATCTGAGCCGTGCCAAATTAACC CAACCTTCACTGACGTTGACGGCGGTGTGCAGCTGGATATCGATTTTGTT	SEQ ID NO:178	R	dn	
Kp_mero	KPN_02907	1176-1275	CGCGCGGTAAATATGTCACCGTGCTGACCAACTGGTGCGGCGAATTTTCC TCGCAGGAAGCGCGACGTTTATTCAGCGATGCCGGCCTCCCTACCTACCG	SEQ ID NO:179	R	dn	
Kp_mero	KPN_02919	100-199	GTCGCAGACCGTCTCGCCAAACTGGATAAGTGGCAAACTCATTTAATCAA CCCGCACATCATTCTGTCTAAGGAGCCGCAGGGTTTTATCGCTGATGCAA	SEQ ID NO:180	R	dn	
Kp_mero	KPN_03396	15-114	GCAGCTCAAAATACTGTCGTTCCTGCAGTTCTGCCTTTGGGGAGCTGGC TCACCACGCTTGGCTCGTACATGTTTGTCACGCTGAAGTTTGACGGCGCG	SEQ ID NO:181	R	dn	
Kp_mero	KPN_04155	512-611	GATCCCGACGCCGGTATGGATCATGGCGATTGTCTTCCTGGCGGCCTGGT ACATGCTGCACCATACTCGCCTGGGCCGTTATATTTATGCCCTGGGCGGT	SEQ ID NO:182	R	dn	
Kp_mero	KPN_04160	539-638	TCATTCGGTCTACCACACCTACTTCACGTCGATTACGCAAAATGAAGTGG TGAAGCTCGATCTCCACCAGGCGATTGTCGATGCCATTCTTATTCAGTGAT	SEQ ID NO:183	R	dn	
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Kp_mero	KPN_04425	402-501	TCATGACCGTTCACATGATCGACTTCTACTACTGGGATATCTCCGGCCCGG GTGCAGGTCTGGAAAACGTTGACCTTGGCTTCGGTAAGCTCTCTCTGGCC	SEQ ID NO:185	R	dn	
Kp_mero	KPN_04553	452-551	CGCTTTGACGAACATTTCGTCCTTGACCTGCTGGTCGATGACGGGCAGGC CCGCGGCCTGGTGGCGATGAATATGATGGAAGGCACCCTGGTGCAGATCC	SEQ ID NO:186	R	dn	
Kp_mero	KPN_04582	56-155	GCGCCCTGCAGGGAACGCCGGAAGCCCCGCCGCCCACCGACCATCCG CAGGAGATCCAGCGCTACCAGACGGCTGGCCTGCAGAAAATGGCCACGGT	SEQ ID NO:187	R	dn	
Kp_mero	KPN_04672	183-282	TTTTGCCAACGCCCTTCGGCTTCAGCGGCTTTAACGAAATGAACACGATGT TCAAGCAACATTTGATGGAAGACGACCGCCAACTATACCGAGCGCGCCCGT	SEQ ID NO:188	R	dn	
Kp_mero	KPN_04814	230-329	CGCAAAAATGTCGATCGCGGCATTAATATGCATGTGGTGACGGAAGTGCA GCACATTGTGATCCTCGCCGAGCATAAGCTGCTGGACTATCGCGACGTCG	SEQ ID NO:189	R	dn	
Kp_mero	KPN_00016	501-600	TGAAGATTTTCCTGATGGCGCTGGCGATTATTGATGACCTCGGGGCTATC GTGATTATCGCGCTGTTTTATACCCACGACCTGTCCATGCTCTCGCTGGG	SEQ ID NO:190	R	up	

Kp_mero	KPN_00017	403-502	TGGAGCAGCTGAGCCAGCATAAGCTCGACATGATTATCTCTGACTGCCCG ATCGACTCGACGCAGCAGGAAGGGCTATTTTCGGTGAAGATCGGCGAGTG	SEQ ID NO:191	R	up		
Kp_mero	KPN_00043	139-238	GCCGCCGAGCAGGCGGCGCTGGCCCGTGCCGATCTGGTTATCTGGCAGCA TCCTATGCAGTGGTATAGCGTACCGCCGCTGCTCAAGCTGTGGATGGACA	SEQ ID NO:192	R	up		
Kp_mero	KPN_00078	682-781	AAAGCGGGCCTGGTCGCGCCGGACGAAACCACCTTCAATTACGTACGCGG CCGTCTGCATGCGCGCGAAGGCAAGATTTTGACGATGCCGTAGCGTACT	SEQ ID NO:193	R	up		
Kp_mero	KPN_00164	208-307	GCTGTGGCTGCTGGTCAAGCTGGGGATTGTCTTCGCGGTGCTGATTGCCG CCTATGGCGTCTACCTCGACCAGAAAATCCGCAGCCGCATTGACGGTAAA	SEQ ID NO:194	R	up		
Kp_mero	KPN_00176	597-696	GCAACCCGTTCGGTCTGGGCGAAACCGTGACCTCCGGGATTGTCTCCGCG CTGGGCCGTAGCGGCCTCAACGTGGAAAACTACGAAAACTTTATCCAGAC	SEQ ID NO:195	R	up		
Kp_mero	KPN_00200	1-100	ATGCTGGGTTTGAAACGGGTTCACCATATTGCCATCATTGCGACCGACTA CGCCCGCAGTAAAGCGTTCTATTGCGATATTCTGGGGTTTACGCTGCAAA	SEQ ID NO:196	R	up		
Kp_mero	KPN_00320	351-450	CATTCCGCCGTTTCTGGTCCATACCGCGCTGAAGATCACCTCGCCAAACG GTAAAAGCTATAGCGACCGTCTGGACAATGTGAAGACGGAAAAGCAGTTG	SEQ ID NO:197	R	up		
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Kp_mero	KPN_00341	205-304	CGCGGCAGTTGGGAGCCGCTGCTGTATGGTCTGCACCAGATGCAGATGCG TAATAAAAAGCGTCGGCGCGAGCTGGGAAGCCTGATTAAACGCTTTCGCA	SEQ ID NO:199	R	up		
Kp_mero	KPN_00560	917-1016	GTGCTGAAGCCGGACCACACCGCCGGGCAGCGTCGTCTGACCCTCGCGGG GCAGCAGGGCAGCAGTTTGCGGTCGAGAAAGGGCTGCAGGCGGGCGAGC	SEQ ID NO:200	R	up		
Kp_mero	KPN_00833	134-233	AACCACTTTAGATGGTCTGGAAGCAAAACTGGCTGCTAAAGCCGAAGCCG CTGGCGCGACCGGCTACAGCATTACTTCCGCTAACACCAACAACAAACTG	SEQ ID NO:201	R	up	x	
Kp_mero	KPN_01006	184-283	CTGATGTTCCTGACCTACAAAACGGCGAATAAACCCACCGGGATTATTTC CGCCTTCGCCTTCACCGGGTTCCTCGGCTATATCCTTGGGCCGATGCTGA	SEQ ID NO:202	R	up		
Kp_mero	KPN_01107	100-199	GCTGTCGCTGGTCTCAACGTGTTGGATCGCGGCCCCGCAGTATGCGCAAGT GGTCTCCAGTACACCGATTAAAGAAACCGTGAAAACGCCGCGTCAGGAAT	SEQ ID NO:203	R	up	x	
Kp_mero	KPN_01111	722-821	GATCAAGGCGTCGGTTGAGCCGGATGGCCGCGTCTGGTTGAGGTCCATC AGCCGCTGTCTGAGCATATCGATGACGACCCGCAGACCCTGCCCATTACG	SEQ ID NO:204	R	up		
Kp_mero	KPN_01183	88-187	GCTCAGGACTATGTTGAGAAGCGAATCGACCTCAACGAGCTGCTGGTGCA GCATCCCAGCGCGACCTATTTGTCAAAGCCGCTGGCGACAGCATGATCG	SEQ ID NO:205	R	up		

Kp_mero	KPN_01184	273-372	CCCGCGCTGCGAAATTTACAGTATCGATGAGGCCTTTTGCGATGTCAGCG GTGTGCGTCATTGCAGAGATCTGACCGATTTTGGCCGCGCGAAATCCGCGCC	SEQ ID NO:206	R	up		
Kp_mero	KPN_01226	253-352	GCGCGATGCACGATCTGATCGCCAGCGACACCTTCGATAAGGCGAAGGCG GAAGCGCAGATCGATAAGATGGAAGCGCAGCATAAAGCGATGGCGCTGTC	SEQ ID NO:207	R	up		x
Kp_mero	KPN_01266	19-118	CGCGAACGCCAGCAGCGGCTGAAAGATAAAGTTGACGCCCGGGTGGCGGC GGCCCAGGACGAGCGCGGCATTGTGATGGTCTTTACCGGCAACGGCAAAG	SEQ ID NO:208	R	up		
Kp_mero	KPN_01448	49-148	TCCGGCTGTGTCTATAACAGTAAGGTGTCCACCGGTGCGGAACAGCTGCA GCATCATCGCTTCGTGCTGACCAGCGTCAACGGCCAGGGCGGTCAACGCCA	SEQ ID NO:209	R	up		
Kp_mero	KPN_01624	130-229	CAACGTATGTTTAAGAAAGAGACCGGCCATTCCCTCGGCCAGTACATCCG CAGCCGCAAGCTGACGGAGATTGCGCAGAAGCTCAAGCAGAGCAATGAGC	SEQ ID NO:210	R	up		
Kp_mero	KPN_01625	65-164	ACCAGAAAAAAGATCGCCTGCTCAATGACTACCTCTCACCTATGGATATT ACCGCGACCCAGTTTCGCGTGCTCTGCTCCATTCGTTGCGAAGTATGTAT	SEQ ID NO:211	R	up		
Kp_mero	KPN_02024	277-376	CACGGGCGCGCTCCCCTTGCCGTGAACTACGGTCTGGTCGGCTATCAGGCG CTGCCGCCCGGGTATCGCCAAAAATGTCGCCCGCGGCAAACCGCTCCCTCC	SEQ ID NO:212	R	up		
Kp_mero	KPN_02342	67-166	TATGGGGTGTTATTTCCACAGTGAGGAAAACGTCGGCGGTCTGGGTCTTAA GTGCCAATACCTCACCGCCCGCGGAGTCAGCACCGCACTTTATGTTCATT	SEQ ID NO:213	R	up		x
Kp_mero	KPN_02345	4-103	ATGCGAATCGCGCTTTTCCTGCTGACGAACCTGGCAGTGATGGTCGTGTT CGGGCTGGTGTTAAGCCTCACGGGGATCCAATCCAGCAGCATGACCGGTC	SEQ ID NO:214	R	up		x
Kp_mero	KPN_02394	556-655	CGGATTATTACTAAACAAAACCACCTTTGGCCGTAATACGCCTGGCTATTG GCGGCAATGAAGAGGCGGCGCCTGGCCGGCGTCCCGGTGGTGCGCACC	SEQ ID NO:215	R	up		
Kp_mero	KPN_02742	97-196	CAAATAGGCGATCGTGACAATTACGGTAACTACTGGGACGGTGGCAGCTG GCGCGACCGTGATTACTGGCGTCGTCACTATGAATGGCGTGATAACCGTT	SEQ ID NO:216	R	up		x
Kp_mero	KPN_02800	75-174	GCAGCGCTTCAACGACTGGCTGGTCACCTGTAACAACCAAAATTTCTGCG TCACCCGTAACGTGGGGCTGCATCATGGCCTGGTGATGACCCTCAGCCGC	SEQ ID NO:217	R	up		
Kp_mero	KPN_02938	121-220	GCGCTGGGCGTGTGCCTCGGCGGCAGAGCGGAAGCCGACATGGTGCGTCG CGGCGCCACCCGTGCCGACCTGTGCGCGCGCTTCGCGCTGAAAGATACCC	SEQ ID NO:218	R	up		
Kp_mero	KPN_03000	89-188	GCCGCGGCGATAATTATGTTTATGTGAACCGCGAAGCGCGCATGGGGCGA ACAGCGTTAGTTATTCATCCN	SEQ ID NO:219	R	up		
Kp_mero	KPN_03270	1-100	ATGCAACAGACCCCCACATCAGCGCAAGACGCTCACCGAACGCGTTATCCA CGCCATCACCTTCGAAGGACTGGCGACGCTGATCCTCGCCCCCTACCGCCG	SEQ ID NO:220	R	up		

Kp_mero	KPN_03358	539-638	GGGCGAAAAACTGGTGAACTCGCAGTTCTCCCAGCGTCAGGAATCGGAAG CGGATGACTACTCTTACGACCTGCTGCGTAAGCGCGGTATCAATCCGTCG	SEQ ID NO:221	R	up	x
Kp_mero	KPN_03458	362-461	CCGCGGGCCAGTTGCTGAACATTTATTACGAAACCGCCGATAACTGGCTG CGTCGTCACGATATGGGGCTGCGCATCCGCGGCGATCAGGGGCGTTATGA	SEQ ID NO:222	R	up	
Kp_mero	KPN_03844	749-848	CATGGCGGCGGAAGAAGAAATTCAGTTTTGCCCACTGAGCCAGCTGCTGC CCGCTGACTTTAGCGAGCTGCCCTCAGGCAAAGTGGTTCGTGGTGAACTG	SEQ ID NO:223	R	up	
Kp_mero	KPN_03846	100-199	TGCGCCACCCTGGGGCGGCAATATGAAATTCTGTTGATCGACGATGGCAG CAGCGACGATTCCGCGCGCATGCTCACCGAAGCCGCCGAGGCGGAAGGCA	SEQ ID NO:224	R	up	
Kp_mero	KPN_03847	229-328	GAAGTCATTACGCCCGTCCCAGACCTGGGTCTCCACTCTCAATATGATCTG CCTGCTGGGCGCCACGCCGGTGATGATCGATGTCGATAACGACACAATCTGA	SEQ ID NO:225	R	up	
Kp_mero	KPN_03856	895-994	TAAGCGGATCGGCATTGACCCGGCGGTAGTTTCCGCGCCGTTTATCGCCA CGCTGATTGATGGCACCGGGCTAATTATCTATTTCAAAATCGCCCAGTAT	SEQ ID NO:226	R	up	
Kp_mero	KPN_03903	141-240	GACCAGCCAGTTCCTGCTGGCCTGTAAATACGATGCGCCAGCGACGATCG CAGCCATGCTGGATAACGGCATTGATGTGGATGGTCAGGATAAAACCGGC	SEQ ID NO:227	R	up	
Kp_mero	KPN_03934	257-356	TGCCTTATATTACCAAGCAGAATCAGGCGATTACTGCGGATCGTAACTGG CTTATTTCCAAGCAGTACGATGCTCGCTGGTCGCCGACTGAGAAGGCGCG	SEQ ID NO:228	R	up	x
Kp_mero	KPN_03993	558-657	TGGCGGCGGTCTATAACGTCCCGCTGGCCGGGGCGTTGTTCAGCCTTGAG GTCATGCTGCTGTCGTTTAGCTGGGAAAAAACGCTGGCGGCGATAATGAC	SEQ ID NO:229	R	up	
Kp_mero	KPN_04036	1361-1460	CTCGACTACCTCGACGCCTTCGGCGCGGCGATCCACGCGGCGTTTCTGAT GGCGGCCGGCATTATGGCGGTGGCGTTTGTCCTCTCATGGCTGTTAAAGG	SEQ ID NO:230	R	up	
Kp_mero	KPN_04037	309-408	GATGATGGTCGAGACGCTGGGGCATATGGCGGAGAAAAACGCCTGGTTCG CGCCGCTGTGGATGCAGGAGATCATCGGCGAGATGCCGATTCTGCGCCAG	SEQ ID NO:231	R	up	
Kp_mero	KPN_04077	10-109	ACCGTATTCTGCATTTTGCTGTTCGCCGCCCTGCTGCACGCCAGCTGGAA CGCTATCGTCAAAGCCAGCGGCGATAAAATGTACGCGGCGATCGGCGTCA	SEQ ID NO:232	R	up	
Kp_mero	KPN_04129	387-486	CGCTGGGCCGCCACACGGTGCAGATGCTGCATGACGTACTGGATGCGTTT GCGCGTATGGATCTCGACGAAGCGGTACGTATCTATCGCGAAGATAAGAA	SEQ ID NO:233	R	up	
Kp_mero	KPN_04131	431-530	GGTGGCGCAGATGCAGCACTTCTCGGGCTGGGCGGGCGTTATCGCGCTGG CGCTGCTGCAGGTGCCTATCGTTATTCGTACCACCGAAAACATGCTGAAG	SEQ ID NO:234	R	up	
Kp_mero	KPN_04132	48-147	CATGATTTTCAGTGCGCTGGTAAAACTGGCTGCGCTGATTGTGCTATTGA TGCTGGGCGGCATCATCGTTTCCCTGATCATCTCTTCCTGGCCGAGCATT	SEQ ID NO:235	R	up	

Kp_mero	KPN_04133	160-259	AATAAAGTGAACTACCAGGGTATTGGTTCCTCTGGTGGCGTTAAGCAGAT TATTGCCAACACCGTTGATTTCGGTGCTTCTGATGCTCCGCCTGGCTGATG	SEQ ID NO:236	R	up	
Kp_mero	KPN_04244	253-352	CCCGGCGGCAAGAGCGTGGAGGAGTATCGCGCCTATTATAAGAAGGGCTA CGCCACCGATGTGGAGCAGATTGGCATTGAAGATGACGTGATTGAGTTCC	SEQ ID NO:237	R	up	
Kp_cip GeneID = NC_016845	KPHS_08300 (KPN_00111 (nadC))	141-240	GCAATTATTGCCGCAGGATGCACGCTCCCATGCGGTGGTCATTACTCGTG AAGATGGCGTCTTCTGTGGCAAACGCTGGGTGGAAGAGGTCTTTATTCAG	SEQ ID NO:238	C		x
Kp_cip	KPHS_08670 (KPN_00140 (panC))	82-181	CCGACGATGGGCAACCTGCATGATGGTCATATGAAGCTGGTTGATGAAGC CAAGCCAGTGCGGACGTGGTGGTCAGTATTTTCGTCAATCCGATGC	SEQ ID NO:239	C		x
Kp_cip	KPHS_15300 (KPN_00697 (nagC))	347-446	CTGCCCGAGCGCACCCAGGAAACGCTGGAACACGCCCTGCTGAATATCAT CGCCACCTTTATCGAAACTGTCAGCGCAAAATTCGCGAGCTGATCGCTA	SEQ ID NO:240	C		x
Kp_cip	KPHS_20110 (KPN_01134 (yciD))	20-119	TGGATTATCAATTAACGCTTAACTGGCCCGACTTTATCGAACGCTACTGG CAAAACGGCCCGGTGGTATTGAAGCGCGGCTTCGCCAATTTTATCGACCC	SEQ ID NO:241	C		x
Kp_cip	KPHS_29220 (KPN_01944 (ydcG))	60-159	TGTTGCCGCCGTATGCGGAACGTCAGGAGTCGCTTCCTTATTCAGTCAGG CCGCTTTTGCCGAAGACGCGGGCATTGCCGACGGGCAAACGCGTCGTTTT	SEQ ID NO:242	C		x
Kp_cip	KPHS_33420 (KPN_02329 (yeaB))	80-179	TCAATCAGCGGCAGGCGGCGGTGCTGGTGCCGATCGTGCGCCGGCCGCAG CCCGGCCTGCTGCTGACCCAGCGTTCGCCGCTGCTGCGCAAGCACGCCGG	SEQ ID NO:243	C		x
Kp_cip	KPHS_34080 (KPN_02387 (yecM))	100-199	GCGCGACTGGGACTGGAGATCGCCGGGCTCGACGCCGACCATATCTCCCT GCGCTGTCATCAGAATACCACTGCGGAACGCTGGCGCCGCGGTCTGGAGC	SEQ ID NO:244	C		x

Kp_cip	KPHS_3703 0 (KPN_0263 7 (yojN))	2443-2542	AGATTGTATACTGAAATCGAAGCGGGCGATTTTGCTGCTCTGGCGCAAAC CGCCCACCGCCTCAAAGGGGCATTTGCTATGCTTAATCTGATACCCGGCA	SEQ ID NO:245	C		x
Kp_cip	KPHS_4292 0 (KPN_0322 9 (recB))	350-449	GAACGGCAGATGGACGAGGCGGCGGTATTCACCATCCACGGCTTTTGCCA ACGGATGCTGAGCCTTAACGCCTTCGAGTCGGGCATGCTGTTCGAGCAAC	SEQ ID NO:246	C		x
Kp_cip	KPHS_4456 0 (KPN_0338 6 (yggT))	143-242	TCGGACCGCTGCGCCGGATTATCCCGGCAATGGGGCCGATTGACAGCGCC TCGCTGCTGGTGGCATTTTATTCTCTGCGTCATCAAAGCGATCGTGCTGTT	SEQ ID NO:247	C		x
Kp_cip	KPHS_4774 0 (KPN_0363 4 (degS))	617-716	GGCGAGCTGATGGGGATTAACACCCTCTCCTTTGACAAGAGCAATGACGG CGAAACGCCGGAAGGCATTGGCTTTGCGATCCCGTTCCAGTTAGCGACCA	SEQ ID NO:248	C		x
Kp_cip	KPHS_0117 0	77-176	GAATGACCGATGCCGATTTCGGCAAACCGATTATCGCCGTCGTTAACTCC TTTACCCAGTTTGTCCCCGGGCACGTGCACCTGCGCGATCTCGGCAAACT	SEQ ID NO:249	R	dn	
Kp_cip	KPHS_0138 0	2-101	TGATCCCATTTAACGGCGCCGCCGGTGGTTGGAACCGAGCTTGATTACATG CAGTCTGCGATGAACAGCGGCAAGCTGTGCGGCGACGGCGGCTTTACGCCG	SEQ ID NO:250	R	dn	
Kp_cip	KPHS_0141 0	1140-1239	CTGCACAGTTTCTGTTTCGGCGCTATCTTCAACATGATAGTGCTGGCGCG CGAGGGGCTGGATTCGTTCGGCTCCCGCGTGGTGTGTTTTCCTCGTGATCT	SEQ ID NO:251	R	dn	
Kp_cip	KPHS_0142 0	475-574	CGACAGCGGGGCGAAAATCGTCACCGTCGCGATGGGGTCGCCGCGCCAGG AGATCTTTATGCGCGACTGCCGGCGCCTGTATCCGCACGCGCTGTATATG	SEQ ID NO:252	R	dn	
Kp_cip	KPHS_0193 0	151-250	GAAGAGGTTGCCGAGATCTATTTGCCGCTGTCGCGTTTGCTCAACTTCTA TATCAGTTCTAACCTGCGTCGCCAGGCTGTTCTCGAACAATTTCTTGGCA	SEQ ID NO:253	R	dn	
Kp_cip	KPHS_0712 0	1767-1866	CAAAAAGGCCAATACCTCTTCGCTGGATTACTATCACCAGCTGCGCCATG CGGCCAGCAGCTCGCGGCGTAAGTTCCTCTATGACACTAACGTTGGCGCG	SEQ ID NO:254	R	dn	
Kp_cip	KPHS_0756 0	587-686	CCTTGGGCGCTATCTGACCCGCCCGCTGCTGCGCTTTGTCGCCCGTTCCG GCCTGCGCGAAGTGTTCAGCGCCGTGGCCCTGTTCCTGGTCTTCGGCTTT	SEQ ID NO:255	R	dn	
Kp_cip	KPHS_1326 0	412-511	TGGGCAACCAGGCCGACACCTATGTGGAAATGAACCTCGAACATAAACAG ACCCTGGACAACGGGGCGACCACCCGTTTCAAAGTGATGGTGGCCGACGG	SEQ ID NO:256	R	dn	

Kp_cip	KPHS_1590 0	291-390	GAGATCGTCATGCGGGTCTATTTTGAAAAACCGCGCACCACCGTCGGCTG GAAAGGGCTCATCAACGATCCCCCATATGGATAACAGCTTCCGCATCAACG	SEQ ID NO:257	R	dn		
Kp_cip	KPHS_1832 0	1319-1418	GAGTGGCTGGAAACCTTCCAGGCGAAAGAGCAGGAAGCGACGGAGAAAAT GCTGTCGCTGGAACAGAAAATGAGCGTGGCGCAAACCGCGCACAGCCAGT	SEQ ID NO:258	R	dn		
Kp_cip	KPHS_1837 0	563-662	GCGACGGCTTCAGCACCGCAGCCACCTACGCGTTCGACAACGGTATCGCA CTGTCTGCAGGCTACTCCAGCTCTAACCGTAGCGTCGATCAGAAAGCTGA	SEQ ID NO:259	R	dn		
Kp_cip	KPHS_1838 0 (KPN_00956 (ompF))	39-138	CCTGCTGGTAGCCGGTGCAGCCAACGCTGCAGAAATCTATAACAAAAACG GCAACAAACTGGACTTCTATGGAAAAATGGTCGGCGAGCACGTCTGGACC	SEQ ID NO:260	R	dn	x	
Kp_cip	KPHS_1860 0	972-1071	GGAGTTCCGCGGTATCCGTCTGGGCACCGTCGGCAAAGTGCCGTTCTTTA TTCCGGGGCTGAAGCAGCGTTTGAACGATGACTATCGTATTCCAGTGGAA	SEQ ID NO:261	R	dn		
Kp_cip	KPHS_1978 0	857-956	CCGCGCTGACCTCGTTCCTGACCGGTATCACCGAGCCGATCGAGTTCTCG TTCATGTTCGTGGCGCCGATCCTGTACGTTATCCATGCCATTCTGGCGGG	SEQ ID NO:262	R	dn		
Kp_cip	KPHS_2951 0	1162-1261	GCTGCAGTCTATCGGTGAACTGATGATTTCCGGCCTCGGCCTGGCGATGG TCGCTCAGCTGGTTCCTCAGCGTCTGATGGGCTTCATCATGGGCAGCTGG	SEQ ID NO:263	R	dn		
Kp_cip	KPHS_3198 0	181-280	TACCGTGAAATGCTGATTGCTGACGGTATTGATCCGAATGAACTGCTGAG CACCATGGCTGCCGTTAAAGCCGGTACCAAAACCAAGCGTGCTGCACGTC	SEQ ID NO:264	R	dn		
Kp_cip	KPHS_3712 0	220-319	ATCGCCTATGGATTTTCGAAATTCATCATGGGATCGGTCTCTGACCGCTC GAATCCGCGCATTTTCCTGCCGGCTGGCTTGATCCTCGCCGCGCTGGTGA	SEQ ID NO:265	R	dn		
Kp_cip	KPHS_3733 0	234-333	TGGTGCTGCTGGCGAGCCTCGCGACCTGTACTTTCGCCTACCCGTGGCTT GAGGGTTACAAGGACACAACAAAGAAGAGTTCTACCTGCTGGTGCTGATCGC	SEQ ID NO:266	R	dn		
Kp_cip	KPHS_4940 0	898-997	GCTGGAGGAGATCGAACGCCAGGGGCTGTTCCTGCAGCGGATGGATGATT CCGGCGAATGGTTCCGCTATCACCCGCTGTTTGGCAGCTTCCTGCGCCAG	SEQ ID NO:267	R	dn		
Kp_cip	KPHS_0266 0	110-209	TCCGTTCCCCAAACGCGGCGGAAGAACACCTGAAAGCGCTGGCGCGTAAA GGCGCGATCGAGATCGTCTCCGGCGCTTCTCGCGGTATTCGCCTGCTGAC	SEQ ID NO:268	R	up		
Kp_cip	KPHS_0267 0	624-723	CGCGGAGTACGCCACCCTCATTATTGGCCTGCTGATGGCGAAGCGGGTGC TGACGCTGCGCGGCGTGTCGCTGGCGATGCTGAAAAACGCCTGGCGCGGG	SEQ ID NO:269	R	up		
Kp_cip	KPHS_0282 0	2299-2398	CTATAACCGCGAAACGCTGGAGATTAAGTACAAGGGTAAGACCATCCACG AAGTGCTGGATATGACCATTGAAGAGGCGCGTGAATTCTTTGATGCCGTA	SEQ ID NO:270	R	up	x	

	(KPN_04445 (uvrA))						
Kp_cip	KPHS_02830 (KPN_04446 (ssb))	114-213	CGAATCCTGGCGTGACAAGCAGACCGGCGAAATGAAAGAGCAGACCGAGT GGCACCGCGTTGTGCTGTTCGGCAAACTGGCGGAAGTCGCTGGTGAGTAT	SEQ ID NO:271	R	up	x
Kp_cip	KPHS_03430	325-424	TGTCGGTGCTGCGCCCCGCCAGCGCCCATGTCGCCGAGGCCTTTGGCATC AATGAGGGCGAGAACGTGATCCACCTGCGTACCCTGCGCCGGGTCAATGG	SEQ ID NO:272	R	up	
Kp_cip	KPHS_03440	498-597	ATTGAGATGGCCTGGCAGGAAACCTTCTGGGCCCACGGCTTCGGCAAAGT CGTCGACCGCTTTGGCGTCCCCTGGATGATCAACGTGGTCAAACAAGGCT	SEQ ID NO:273	R	up	
Kp_cip	KPHS_03450 (KPN_04502 (phnA))	145-244	AGCGACATTCTGATCGTTAAAGATGCCAATGGCAATTTACTGGCCGATGG CGACAGCGTTACCGTCGTGAAAGATCTGAAGGTTAAAGGCAGCTCTTCGA	SEQ ID NO:274	R	up	x
Kp_cip	KPHS_04910	1699-1798	ACCGACAAAGGTTACTACACCAACAGCTTCCACCTCGACGTGGAGAAGAA GGTCAACCCGTACGACAGATCGATTTCGAAGCGCCGTACCCGCCGCTGG	SEQ ID NO:275	R	up	
Kp_cip	KPHS_07720	2271-2370	CCAGCAGTCGCCGCTCGATTACGATCACTATTTAACAAAGCAGTTGCAGC CGGTGGCGGAAGGGATCCTGCCCTTCGTCAACGATGACTTTGCTACAATA	SEQ ID NO:276	R	up	
Kp_cip	KPHS_07860	913-1012	TGTTGAAGCGAACCGGCTCCGTCAACATCAGTCGAAAGTTACCAATAATT TCCGGTTTATTGCTGTCCAGCTGTATTATCGCGGCGAATTGGGTAAGCGC	SEQ ID NO:277	R	up	
Kp_cip	KPHS_09730	671-770	AGCGCTTCGGTAAATTCGGGCGTATTCTGTGGGAGCGCAGCCACGGGATT GATGAGCGGGAAATTCATAACGATCGGCAGCGTAAATCGGTGGGCGTGGA	SEQ ID NO:278	R	up	
Kp_cip	KPHS_10170	341-440	CTTGGCGCCCTGTACGACGTGGAAGCCTGGACCGATATGTTCCCGGAATT CGGCGGCGATTCCTCTGCCCAGACCGATAACTTTATGACCAAGCGCGCCA	SEQ ID NO:279	R	up	
Kp_cip	KPHS_10780	308-407	TCACCAAGCCTTTCTCTCCGAAAGAGCTGGTGGCGCGAATCAAAGCGGTG ATGCGCCGTATTTCACCGATGGCGGTGGAAGAGGTGATCGAAATGCAGGG	SEQ ID NO:280	R	up	
Kp_cip	KPHS_16320	1399-1498	GAGCACGGCGAGCGCGTGCGCTATCTGCACTCGGATATCGACACCGTCGA GCGCATGGAAATCATCCGCGACCTGCGTCTTGGCGAGTTTGACGTGCTGG	SEQ ID NO:281	R	up	
Kp_cip	KPHS_16630	125-224	GCAAGGCGCAACCACTTTAGATGGTCTGGAAGCAAAACTGGCTGCTAAAG CCGAAGCCGCTGGCGCGACCGGCTACAGCATTACTTCCGCTAACACCAAC	SEQ ID NO:282	R	up	

Kp_cip	KPHS_1993 0	157-256	CAGCTGGCGCAGAAAGCGGATGAGATGGGCGCCACTTCATACCGTATTAC TTCGGTAACCGGTCCGAATACCCTTCACGGTACCGCCGTTATCTACAAGT	SEQ ID NO:283	R	up		
Kp_cip	KPHS_2063 0	80-179	CCAAACGCATGCAGCGCATTTTCCCGGAGGCGGAAGTGCGGGTGAAGCCG ATGATGACGCTGCCGGCGATCAACACCGACGCCAGCAAGCATGAAAAAGA	SEQ ID NO:284	R	up		
Kp_cip	KPHS_2065 0	68-167	AGTGCGGCTTTCCCAGCCCGGCTCAGGACTATGTTGAGAAGCGAATCGAC CTCAACGAGCTGCTGGTGCAGCATCCCAGCGCGACCTATTTTGTCAAAGC	SEQ ID NO:285	R	up		
Kp_cip	KPHS_2066 0	276-375	GCGCTGCGAAATTTACAGTATCGATGAGGCCTTTTGCGATGTCAGCGGTG TGCGTCATTGCAGAGATCTGACCGATTTTGGCCGCGAAATCCGCGCCACG	SEQ ID NO:286	R	up		
Kp_cip	KPHS_2125 0	277-376	TGCTGGAGGCGCGGTTGATTAAAGAGCAGCAGCCGCTGTTTAACAAGCGG CTACGGCGTAACAAGCAGCTCTGCGCCTGGCTACTTGCGGACGACCGGCCC	SEQ ID NO:287	R	up		
Kp_cip	KPHS_2139 0	187-286	AGCCCGTGGCGCGGGCCTTTGGCCACCGCGGCTTCACCCACAGCCTGCTG GCCGTCTTTGGCGCGCTGACGCTGTTCTATCTGAAAGTGCCTGACAGCTG	SEQ ID NO:288	R	up		
Kp_cip	KPHS_2789 0	610-709	ACCGTCTCCCTCGACGATTTGACCAGACCGAGCTGGTGATCTCCATCGG CCATAATCCGGGCACCAACCACCCGCGGATGATGGGCACCCTGCATGAGC	SEQ ID NO:289	R	up		
Kp_cip	KPHS_3113 0	5-104	TGCGCTCTATCGCCACCGTTTCGATTTCCGGCACCCTGCCTGAGAAGCTG CACGCTATTGCGGCGGGGGTATCAGGGGGTGGAAATTTTCGAGAACGA	SEQ ID NO:290	R	up		
Kp_cip	KPHS_3163 0	182-281	TGATCGGCGTTGATATTGTGCTGGCGGTCATCTCCTCGATTATTATCGCC ATGATAATGACCTCGACCGGCCTGCCGGAAATGGGCACGATGCTGGCGAA	SEQ ID NO:291	R	up		
Kp_cip	KPHS_3381 0 (KPN_02363 (yebG))	4-103	GCGGTTGAAATTAAATATGTGGTGATCCGCGAAGGTGAGGAAAAAATGTC TTTTGCCAGCAAAAAAGAGGCCGACGCTTACGACAAAATGCTCGATCTGG	SEQ ID NO:292	R	up		x
Kp_cip	KPHS_3414 0	622-721	TCGTTAATCAACTGCAGGGAATGTCGGTAAAGTTGGCGCCGGGGAAACT CAGGCGCATTGGCGGTTGGCGGATGCCGCCGCTGTAAGGACGTGGTTGCA	SEQ ID NO:293	R	up		
Kp_cip	KPHS_3708 0 (KPN_02642 (nrdA))	2010-2109	AACAACGACGGTTATCTGCAGCTGGTGGGTATCATGCAGAAGTTTATCGA CCAGTCGATCTCTGCCAACACTAACTACGATCCGACGCGCTTCCCGTCCG	SEQ ID NO:294	R	up		x
Kp_cip	KPHS_3709 0	805-904	GCTGAACCTGCTGCGCTCCGGCAGCGACGATCCGGAAATGGCGGAAATCG CCGAAGAGTGCAAGCAGGAGTGCTATGACCTGTTCGTGCTGGCGGCGCAG	SEQ ID NO:295	R	up		x

	(KPN_02643 (nrdB))							
Kp_cip	KPHS_39770	256-355	CGTTTTGTGAAGTCAACACCGAAGCGGAACGTGAGCTTAGCGCCCGGTT TCGTATCCGCAGCATCCCGACCATTATGATGTTCAAAAATGGCGAAGTGA	SEQ ID NO:296	R	up		
Kp_cip	KPHS_40560	121-220	GCGCTGGGGCTGTGCCTCGGCGGCAGAGCGGAAGCCGACATGGTGCGTCG CGGCGCCACCCGTGCCGACCTGTGCGCGCGCTTCGCGCTGAAAGATACCC	SEQ ID NO:297	R	up		
Kp_cip	KPHS_40580	62-161	CCACTCTGGAACGAGTGGTTTACCGTCCTGACATCAACCAGGGTAACTAT CTGGCACCAAACGATGTAGCAAAAATTCGTGTCGGTATGACGCAACAGCA	SEQ ID NO:298	R	up		
Kp_cip	KPHS_41010 (KPN_03030 (recX))	380-479	ACAGCGTAAATACGGCGAACCGTTACCTTCCGCCTTTACTGAAAAGTGA AAGTTCAGCGATTCCTGCTTTACCGCGGCTACCTGATGGAAGATATCCAG	SEQ ID NO:299	R	up		x
Kp_cip	KPHS_41020 (KPN_03031 (recA))	539-638	CGGGTAACCTGAAGCAGTCCAACACGCTGCTGATCTTTATCAACCAGATC CGTATGAAAATTGGCGTGATGTTCGGTAACCCGGAAACCACTACCGGTGG	SEQ ID NO:300	R	up		x
Kp_cip	KPHS_52230	272-371	TGCTGCAGGCGGCGGAAGCGCTCAATTACCGGCCAAACATGATAGCCCAG TCGTTGCTCAGCCAGTCCACCGGCTGCATCGGCGTCATCTGCGCCCAGGA	SEQ ID NO:301	R	up		
Kp_cip	KPHS_52480	80-179	AAAGCCTTGAACAGCATTTCAATATGCTGCGCCGCCTGGCGGAAACTGG CAGAGCGGCAAAAACCGCTTTAACGCGCCGGGCGAAACGCTGCTGGGCGC	SEQ ID NO:302	R	up		
Kp_cip	KPHS_52490	10-109	ACCGTATTCTGCATTTTGCTGTTCGCCGCCCTGCTGCACGCCAGCTGGAA CGCTATCGTCAAAGCCAGCGGCGATAAAATGTACGCGGCGATCGGCGTCA	SEQ ID NO:303	R	up		
Kp_cip	KPHS_53000 (KPN_04133 (pstS))	160-259	AATAAAGTGAACTACCAGGGTATTGGTTCCTCTGGTGGCGTTAAGCAGAT TATTGCCAACACCGTTGATTTCGGTGCTTCTGATGCTCCGCTGGCTGATG	SEQ ID NO:304	R	up		x
Kp_gent GeneID = NC_01273 1	KP1_0027 (KPN_04175 (hemN))	189-288	TTGCCATAAGCTGTGTTATTTCTGCGGCTGCAATAAGATAGTCACCCGCC AGCAGCATAAGGCCGATCAATATCTCGATGTCCTTGAACAGGAGATCATC	SEQ ID NO:305	C			x

Kp_gent	KP1_0117 (KPN_04252 (yijC))	397-496	CGGAACTCGCCGACTATTTAGAACTCGAAAACCATATGCCGCGCGCCTTT ACCGAAGCGCAGGCTGAAGCTATGGTCACCATCGTTTTTTAGCGCTGGCGC	SEQ ID NO:306	C		x
Kp_gent	KP1_0163	262-361	AAGATGTGCCGGTGGAATTCCCGGAGGGCCTGGGGCTGGTGACTATCTGC GAGCGCGACGATCCGCGCGACGCGTTTGTCTCCAATCGCTATGCCTCGAT	SEQ ID NO:307	C		
Kp_gent	KP1_0191 (KPN_04329 (ubiE))	346-445	AACGTTGAGTATGTTCAGGCCAACGCGGAAGCCCTGCCTTTTGCTGATAA TACCTTTGACTGCATCACCATCTCTTTCGGTCTGCGTAACGTGACCGACA	SEQ ID NO:308	C		x
Kp_gent	KP1_0437	161-260	AGGGTAAACGTCTGGTGGCGCTGGATATCAAGCAGACCGGCGTATTGCAG GGACTACCGCTGCAGTTTAGCGGCAGCAACCTGGTGAAGAGTATTCGCGC	SEQ ID NO:309	C		
Kp_gent	KP1_0490 (KPN_04616 (ytfM))	1254-1353	GGGGCTCGGACATCAACTTCATCGTGATGCAGGCCCAGGACGTCTGGATC CGTACCCTCTATGACCGCCACCGCTTTGTGGTGCGCGGCAACCTTGGCTG	SEQ ID NO:310	C		x
Kp_gent	KP1_0974 (KPN_00146 (sfsA))	370-469	TACAGGCAGATGACCGACAAAACTGCTATATTGAAGTGAAATCGGTTACG TTGGCGGAGAAAGAATACGGTTATTTTCCCGATGCGGTGACCACGCGCGG	SEQ ID NO:311	C		x
Kp_gent	KP1_1702 (KPN_00744 (tolB))	1066-1165	GCACATTGCCAAACAAGATCTGGAAACGGGTGGTGTACAGGTTCTGTCAT CAACGTTTTTAGACGAAACGCCAAGTCTGGCACCTAACGGCACTATGGTA	SEQ ID NO:312	C		x
Kp_gent	KP1_1918	641-740	CTGTGGTATGGCGAGAAAATCCATGTCGCCGTGGCGGCCGAAGTGCCCGG CACCGGCGTGGATACCCCGGAAGATCTGGAGCGCGTCCGCGCTGAGCTGC	SEQ ID NO:313	C		
Kp_gent	KP1_4363	829-928	AGATCACCCAGAATCTGGCCGGCGGCACCGACAACACACCCTGGCCTCGGTA CTCGACTGTACGGTGACGCCGATGGGTAGCCGGATGCTCAAGCGCTGGCT	SEQ ID NO:314	C		
Kp_gent	KP1_4377 (KPN_03107 (ygbO))	317-416	CGAGGGCTGCCAGGTACTGGAATATGCTCGCCATAAGCGTAAGCTGCGTT TAGGCGCGCTGAAAGGCAACCAGTTTACCGTGATCCTGCGCGAGATTAGC	SEQ ID NO:315	C		x
Kp_gent	KP1_4445 (KPN_03164 (mltA))	512-611	TCGTTGATGGATAACTTCATCATGGACGTGCAGGGCAGCGGCTATATCGA CTTTGGCGATGGTTCGCCGCTCAACTTCTTTAGCTATGCCGGGAAAACG	SEQ ID NO:316	C		x
Kp_gent	KP1_0041	225-324	GTCATGGACGGTCATGCGCTTCTCGGAGGTGGAACAAAACGACAAGCTGG AATGGCTCATCCGCAAGGATGGCTGCATGCACTGCGCGGACCCGGGCTGC	SEQ ID NO:317	R	dn	

Kp_gent	KP1_0276	987-1086	CGACGTGGTGTTGGTAGAAGAGGGAGCCACATTCGCTATCGGTTTGCCGC CAGAACGTTGCCATTTATTCCGTGAGGATGGCACCGCGCTTGTCGTCGGCTG	SEQ ID NO:318	R	dn	
Kp_gent	KP1_0395	1-100	ATGTTAAACAACATTCGTATCGAAGAAGATCTGTTGGGCACCAGGGAAGT TCCCGCGGACGCTTACTACGGCGTTCATACTCTGCGAGCGATTGAAAACT	SEQ ID NO:319	R	dn	
Kp_gent	KP1_0425	974-1073	GAGCGTCTGCCGTTTATCTGTGAACTGGCGAAAGCCTACGTCGGCGTCGA TCCGGTGAAAGAGCCGATCCCGGTGCGCCCGACCGCGCACTACACCATGG	SEQ ID NO:320	R	dn	
Kp_gent	KP1_0908	1213-1312	GAACATTTTAACGATAAAGCCGCCGTGGTGGCTCGCCTGCGCGAGCTGCT GGCGGAGCACAAAATAATGACCATTTTAGTGAAGGGTTCACGTAGTGCCG	SEQ ID NO:321	R	dn	
Kp_gent	KP1_0909	59-158	CATATCTGACGTTTCGCGCCATCGTCAGCCTGCTGACCGCGCTGTTCATC TCGTTGTGATGGGCCCGCGCATGATCGCCCGTCTCTGCAAAAACTCGCCTT	SEQ ID NO:322	R	dn	
Kp_gent	KP1_0910	507-606	GCAGGCGGTGGCGGCAACCATCCTCAACGTGACTGAGGACCATATGGACC GCTACCCGCTGGGGCTGCAGCAGTATCGCGCGGCGAAGCTGCGGATTTAC	SEQ ID NO:323	R	dn	
Kp_gent	KP1_1258	364-463	CTGGCCTGCTGGCTGGGGGTGATGGGGTTCGTGGTTTATGTCGGCGTCTA CAGCCTGTACATGAAACGCCACTCCGTCTACGGCACGCTGATTGGCTCAC	SEQ ID NO:324	R	dn	
Kp_gent	KP1_1259	127-226	CATGCGGTTATCCTTGGCACCATTCTGGTGACCGCTGTGGTGCAGATCGT GGTACACCTCGTGTACTTCCTGCATATGAACAGCAAGTCCGATGAAGGTT	SEQ ID NO:325	R	dn	
Kp_gent	KP1_1260	467-566	CGGTGCTGATGTTCCAGGTTTCACGTCGTGGCCTGACCAGCACTAACCGC ACGCGTATCCTGTGCCTGAGCCTGTTCTGGCACTTCCTGGACGTCGTGTG	SEQ ID NO:326	R	dn	
Kp_gent	KP1_1409	690-789	GGTATCGTCTACATCGCCGCGACTCAGGTTATCGCCGGTATGTATCCTGC TTCTCAGATGGCCGCGTCCGGTGCGCCGTTCGCAATTAGCGCCTCTACCA	SEQ ID NO:327	R	dn	
Kp_gent	KP1_1410	540-639	GATATCTCCATTTCGGTTTCTGAACTGGGTTCCCTGCTGGACCACAGCGG CCCGCACAAAGAAGCGGAAGAGTATATCGCTCGCGTGTTTAACGCAGAAC	SEQ ID NO:328	R	dn	
Kp_gent	KP1_1694	256-355	TTCTATGTGGCGATGATTCTGGTGCTGGCCTCGCTGTTCTTCCGTCCGGT CGGTTTTGACTACCGTTCCAAGATCGAGGACACCCGCTGGCGCAACATGT	SEQ ID NO:329	R	dn	
Kp_gent	KP1_1902	764-863	ATTCAGTGGACCTACTTCGGTTACCTGGCTGCCGTGAAATCTCAGAACGG CGCGGCAATGTCCTTCGGTCGTACCTCCAGCTTCCTGGATATCTACATCG	SEQ ID NO:330	R	dn	
Kp_gent	KP1_1903	473-572	ATACTTTTGTGGAGGCCGTGAGCCTGGGTATCCTCGCTAACCTGATGGTT TGTCTCGCCGTATGGATGAGCTATTCCGGTCGTAGCCTGATGGATAAAGC	SEQ ID NO:331	R	dn	

Kp_gent	KP1_3311 (KPN_02199 (adhE))	1193-1292	TTCTCAGGGTGGTATCGGTGACCTGTACAACTTCAAACTCGCGCCTTCCC TGACTCTGGGTTGTGGTTCCTGGGGTGGTAACTCCATCTCTGAAAACGTT	SEQ ID NO:332	R	dn	x
Kp_gent	KP1_3327	1095-1194	TCCACCTTCCAGATGATCTCCGTGATCTTCCGTAAGCTGACTATGGACCG CGTGAAGGCCCAGGGCGGCAGCGAAGCGCAGGCGATGCGCGAGGCGGCGA	SEQ ID NO:333	R	dn	
Kp_gent	KP1_3445	45-144	TAATATTGCGAAAGAACGCCTGCAAATCATCGTCGCCGAGCGCCGCCGCG GAGACGCGGAGCCGCATTACCTGCCGCAGTTACGCAAAGATATCCTGGAA	SEQ ID NO:334	R	dn	
Kp_gent	KP1_3458	749-848	CGTATCGTCGAGGGCGGCGTGAAAATCACCAGCGTCAACATCGGCGGTAT GGCGTTCCGCCAGGGTAAAACCCAGGTTAACAACGCGATTTCAGTCGATG	SEQ ID NO:335	R	dn	
Kp_gent	KP1_3878	66-165	ATACACCACTTTTTCACAGACGAAAAACGATCAGCTGCTGGAACCCATGT TTTTTGGCCAGCCGGTTAACGTGGCCCGCTACGATCAGCAAAAATACGAC	SEQ ID NO:336	R	dn	
Kp_gent	KP1_3908	32-131	TGCTACCGCTGCTGATCGTCGGCTTGACGGTGGTTGTGATGCTCTCC ATTGCGTGGCGACGCAATCATTTTCTCAATGCCACGCTGTCGGTTCTTGG	SEQ ID NO:337	R	dn	
Kp_gent	KP1_3909	319-418	CGTGAAATCGAAAAATACCAGGGCTTCTTCCACCTCAACCTGATGTGGAT CCTGGGCGGCGTTATCGGCGTGTTCCTCGCCATCGACATGTTCCTGTTCT	SEQ ID NO:338	R	dn	
Kp_gent	KP1_3910 (KPN_02668 (nuoL))	1552-1651	TCCATCGCCAACAGTGCGCCTGGCCGCTTCTTCGGTACCTGGTGGTTCCA TGCCTGGGGCTTCGACTGGTTATACGACAAGGTGTTCGTAAAACCATTCC	SEQ ID NO:339	R	dn	x
Kp_gent	KP1_3913	315-414	GGTTATCGTTTACGCCATCCTGGGCATTAACGACCAGGGTATCGACGGTG CGGCGATTAACGCCAAAGAAGTGGGCATTGCGCTGTTTGGGCCGTACGTC	SEQ ID NO:340	R	dn	
Kp_gent	KP1_3914	14-113	TAAAAGAATTATTGGTGGGGTTCGGCACCCAGGTCCGTAGTATCTGGATG ATTGGCCTGCATGCCTTCGCCAAACGTGAAACCCGGATGTATCCGGAAGA	SEQ ID NO:341	R	dn	
Kp_gent	KP1_3915	206-305	TTAAAGAGGACTGGATCCCGCGCTTCTCCGATCGCGTGATCTTTACTCTG GCGCCGGTTATCGCCTTTACCTCGCTGCTGGCCTTCGCTATCGTGCC	SEQ ID NO:342	R	dn	
Kp_gent	KP1_3916	366-465	CATAGCTTCCGCCGCTATCGTTTCACCAAGCGTACCCACCGCAATCAGGA TCTGGGGCCGTTTATTTCGCACGAAATGAACCGCTGCATCGCCTGCTACC	SEQ ID NO:343	R	dn	
Kp_gent	KP1_3917	687-786	CCAACGGCGTCGAGTGGTACCAGAACATTTCCACCAGCAAGATGCTGGC ACCAAGCTGATGGGCTTCTCCGGCCGGGTGAAGAATCCGGGCGTCTGGGA	SEQ ID NO:344	R	dn	
Kp_gent	KP1_3919 (KPN_02675 (nuoE))	379-478	ACCCTGCTGCCGACCTGCTGCCTGGGTAACTGCGACAAGGGACCGACCAT GATGATTGATGAGGATACTCACAGCCATCTGACGCCGGAGGCAATTCCTG	SEQ ID NO:345	R	dn	x

Kp_gent	KP1_4642	714-813	CCGACCATCCTGCGCGACTCTCAGGAATATGTTTCCAAGAAACACAACCT GCCGCACAACAGCCTGAACTTCGTGTTCCACGGCGGTTCCGGTTCTTCCG	SEQ ID NO:346	R	dn		
Kp_gent	KP1_4873	89-188	ATGACACCAACGCCCCGCCACTTTGCCGGCCTTAATTTCACCGAAAAGAAA CTGCAGGAAGCCGTCAGCTTTGTGCATCAGCACCGTCGTAAGCTGCATAT	SEQ ID NO:347	R	dn		
Kp_gent	KP1_5122	390-489	ATCTGATCAATAATCCGGTGATCCATGACGCGATGCGCTTTTTCCTGCGC CATCAGCCGGAGAATATGACCCTGGTGGTCCTGTCGCGTAACCTGCCGCA	SEQ ID NO:348	R	dn		
Kp_gent	KP1_5513	63-162	CGAAAAAATCCAGGTAACGGGTAGCGAAGGTGAACTGGGTATTTACCCGG GCCACGCGCCGCTGCTCACCGCCATTAAGCCTGGTATGATTCGCATCGTT	SEQ ID NO:349	R	dn		
Kp_gent	KP1_5514	672-771	CTGACCATGGCTGAGAAATTCCGTGACGAAGGTCGTGACGTACTGCTGTT CGTCGATAACATCTATCGTTACACCCTGGCCGGTACTGAAGTATCCGCGC	SEQ ID NO:350	R	dn		
Kp_gent	KP1_5515	425-524	TAACCCATCCCTGTCCGAACTGATCGGCCCGGTAAAAGTGATGTTGCAGG CCTATGATGAAGGCCGTCTGGACAAGCTGTACGTTGTCAGCAACAAATTT	SEQ ID NO:351	R	dn		
Kp_gent	KP1_0325 (KPN_04462 (soxS))	1-100	ATGTCCCATCAGGATATTATTCAACTTTGATTGAATGGATTGATGAACA TATCGATCAACCACTTAACATTGATATAGTCGCCAGAAAGTCAGGATACT	SEQ ID NO:352	R	up	x	
Kp_gent	KP1_0533	2300-2399	CGCTGGAACCCGGCCGATCTCGGGCGCTTTATGGTCTTCTTTGGACCGAT CAGCTCGATTTTCGATATCCTCACCTTCGGCCTGATGTGGTGGGTGTTCC	SEQ ID NO:353	R	up		
Kp_gent	KP1_0837 (KPN_00016 (nhaA))	468-567	TGGCGCTGTTAGGTAGCCGGGTCCCGACGGCGCTGAAGATTTTCCTGATG GCGCTGGCGATTATTGATGACCTCGGGGCTATCGTGATTATCGCGCTGTT	SEQ ID NO:354	R	up	x	
Kp_gent	KP1_0838 (KPN_00017 (nhaR))	403-502	TGGAGCAGCTGAGCCAGCATAAGCTCGACATGATTATCTCTGACTGCCCG ATCGACTCGACGCAGCAGGAAGGGCTATTTTCGGTGAAGATCGGCGAGTG	SEQ ID NO:355	R	up	x	
Kp_gent	KP1_2104	107-206	TAGGCACCATCTCTGCTTCTGCCGGGACTAACCTGGGCTCGCTGGAAGAC CAGCTGGCGCAGAAAGCGGATGAGATGGGGCGCCACTTCATACCGTATTAC	SEQ ID NO:356	R	up		
Kp_gent	KP1_2658 (KPN_01624 (marA))	107-206	CCGGTTACTCTAAGTGGCACCTGCAACGTATGTTTAAGAAAGAGACCGGC CATTCCCTCGGCCAGTACATCCGCAGCCGCAAGCTGACGGAGATTGCGCA	SEQ ID NO:357	R	up	x	
Kp_gent	KP1_2659	65-164	ACCAGAAAAAAGATCGCCTGCTCAATGACTACCTCTCACCTATGGATATT ACCGCGACCCAGTTTCGCGTGCTCTGCTCCATTCGTTGCGAAGTATGTAT	SEQ ID NO:358	R	up		

Kp_gent	KP1_2873	406-505	GAGGCGGCGCAGCGCATTCATGCCTTGCCGGGGGCCGGTGACGAAGAGAA	SEQ ID NO:359	R	up		
Kp_gent	KP1_3472 (KPN_02345 (htpX))	1-100	ACGCTATGTCTTACGCGTCACCTGTCTGCGCGAACATGAAAATGCCGTAC ATGATGCGAATCGCGCTTTTCCTGCTGACGAACCTGGCAGTGATGGTCGT GTTCGGGCTGGTGTTAAGCCTCACGGGGATCCAATCCAGCAGCATGACCG	SEQ ID NO:360	R	up		x
Kp_gent	KP1_4962	121-220	GCTGATATTATCAACAGCGAGCAGGCCCAGGGCCGCGAGGCCATCGGCAC GGTTTCCGTCGGCGCGGTAGCATCTTCCCCGATGGATATGCATGAAATGC	SEQ ID NO:361	R	up		
Kp_gent	KP1_5196	893-992	CTTAAGCGGATCGGCATTGACCCGGCGGTAGTTTCCGCGCCGTTTATCGC CACGCTGATTGATGGCACCGGGCTAATTATCTATTTCAAAATCGCCCAGT	SEQ ID NO:362	R	up		
Kp_gent	KP1_5423	232-331	AGCGGCTCACGTGGCGTGAAGGAAGCCAGTCGTCAGGCGGTGCTGCAGGC GGCGGAAGCGCTCAATTACCGGCCAAACATGATAGCCCAGTCGTTGCTCA	SEQ ID NO:363	R	up		
Kp_gent	KP1_5452	101-200	ATATGCTGCGCCGCCTGGCGGAAACTGGCAGAGCGGCAAAAACCGCTTT AACGCGCCGGGCGAAACGCTGCTGGGCGCCTTCGTCAACCACCAGCTGGT	SEQ ID NO:364	R	up		
Kp_gent	KP1_5467 (KPN_04090 (ibpB))	180-279	TATTCAACTGGAAGGCACCCGTCTGGTGGTGAAAGGCACGCCGCAGCAGC CGGAAAAAGACCACATGGCTGCACCAGGGGTTGGTGAGCCAGGCCTTC	SEQ ID NO:365	R	up		x
Kp_gent	KP1_5468 (KPN_04091 (ibpA))	130-229	CAGAGCAACGGCGGCTACCCTCCGTATAACGTCGAGCTGGTAGACGAAAA CCACTATCGCATCGCTATCGCGGTGGCTGGCTTTGCTGAAAGCGAGCTGG	SEQ ID NO:366	R	up		x
Ec_mero	APECO78_02145 (b4235:pmbA)	51-150	ATGAGTGTGATTGCGCAGGCAGGGCGAAAGGTCGTCAGCTGCATAAATT TGGTGGCAGTAGTCTGGCTGATGTGAAGTGTTATTTGCGTGTCGCGGGCA	SEQ ID NO:367	C			x
Ec_mero	APECO78_03915	656-755	TCTGGAAGAAGCAGTTTCCACTGCGCTGGAGTTGGCCTCAGGCAAATCGG ACGGTGCGGAAGTTGCCGTCAGCAAGACCACCGGCATTAGCGTAAGCACG	SEQ ID NO:368	C			x
Ec_mero	APECO78_03915	656-755	TTGGCTCGCTTTGTAGAACTTTATCCGGTTTTACAGCAGCAGGCGCAAAC CGATGGCAAACGGATTAGCTACGTTGATTTGCGTTATGACTCTGGAGCGG	SEQ ID NO:369	C			

Ec_mero	APEC078_03920 (b0094:ftsA)	624-723	GATATCGGTGGTGGTACAATGGATATCGCCGTTTATACCGGTGGGGCATT GCGCCACACTAAGGTAATTCCTTATGCTGGCAATGTCGTGACCAGTGATA	SEQ ID NO:370	C		x
Ec_mero	APEC078_05580	362-461	GTCAGCCACGGGGCTGATGATGAGTGAAGCCGAGCAATTGAATAAAGGCTT TCTCAAGCCGATGCCGCACCGGCTTTCCTTATATTCAGTTAAAACTTGGCG	SEQ ID NO:371	C		
Ec_mero	APEC078_05715 (b0438:clpX)	935-1034	AACGTTGAATGAACTGAGCGAAGAAGCTCTGATTCAGATCCTCAAAGAGC CGAAAAACGCCCTGACCAAGCAGTATCAGGCGCTGTTTAATCTGGAAGGC	SEQ ID NO:372	C		x
Ec_mero	APEC078_09610	170-269	AGGACGGTCTGTCACTGATTCGCCGCTGGCGTAGCAATGATGTTTCACTG CCGATTCTGGTATTAACCGCCCGTGAAAGCTGGCAGGACAAAGTCGAAGT	SEQ ID NO:373	C		
Ec_mero	APEC078_13105	190-289	AACGGAAAACTGCGCATCGGCTATGTACCGCAGAAGCTGTATCTCGACAC CACGTTGCCACTGACCGTAAACCGTTTTTTTACGCTTACGCCCTGGTACAC	SEQ ID NO:374	C		
Ec_mero	APEC078_16235 (b2502:ppx)	987-1086	GAACAGGCCCGACGGGTGCTGGATACCACTATGCAAATGTACGAACAGTG GCGGGAACAGCAACCGAAGCTGGCGCATCCGCAACTGGAGGCGCTACTGC	SEQ ID NO:375	C		x
Ec_mero	APEC078_16510	1353-1452	AGGGCAGCGGTCTGGGATTAAGCATTGCCAGGGATTGTATTCGCCGTATG CAAGGGGAACTGTATCTGGTCGACGAGAGCGGGCAAGACGTTTGTTTCCG	SEQ ID NO:376	C		
Ec_mero	APEC078_17535 (b2784:relA)	289-388	GAGAGCGTCGGTAAGTCGGTCGTTAACCTTATTCACGGCGTGCGTGATAT GGCGGCGATCCGCCAGCTGAAAGCGACGCACACTGATTCTGTTTCCTCCG	SEQ ID NO:377	C		x
Ec_mero	APEC078_19825 (b3197:kdsD)	645-744	ATGCATACGGGCGATGAGATCCCGCATGTTAAGAAAACGGCCAGTCTGCG TGACGCATTGCTGGAAGTTACCCGCAAAAATCTTGGTATGACTGTCATTT	SEQ ID NO:378	C		x
Ec_mero	APEC078_19830	186-285	CGTTGTGCGCTCACCTCTGATATTGAAGTCGCTATCATTACCGGGCGAAA GGCTAAACTGGTAGAAGATCGTTGTGCCACATTGGGGATCACTCACTTGT	SEQ ID NO:379	C		
Ec_mero	APEC078_20780	1327-1426	ACAAAGCGACGGCATTGACTGAAGCAGTTAATCGCCAGCTGCACCCTAAA CCGGAAGATGAATCTCGCGTCAGTGCCTCATTACGTTCAGCAATTCAAAA	SEQ ID NO:380	C		x

	(b3398:yrfF)						
Ec_mero	APECO78_21435	1011-1110	GTCAGCAAGTGCTCACTATCATGAGCGAGCGCCTGCCGATTGAACGTATT CAACTCCGTCCGCACTGTAGCATTGGCGTGGCGATGTTCTACGGCGATCT	SEQ ID NO:381	C		
Ec_mero	APECO78_01050	279-378	TCTGCAGGATGGCGCTATCAGCGCTTATGATCTGCTTGATTTGCTGCGCG AAGCTGAACCGCAAGCCAGCCGCCAACGGTTTATCGCGCGCTGGATTTT	SEQ ID NO:382	R	dn	
Ec_mero	APECO78_08635	844-943	TGCCGCAATACCAGTTCGATTTCGATTTCGGTCTGCGTCCGTCCATCGCTTACACCA AATCTAAAGCGAAAGACGTAGAAGGTATCGGTGATGTTGATCTGGTGAAC	SEQ ID NO:383	R	dn	
Ec_mero	APECO78_12200	1-100	ATGAAAGCTACTAAACTGGTACTGGGCGCGGTAATCCTGGGTTCTACTCT GCTGGCAGGTTGCTCCAGCAACGCTAAAATCGATCAGCTGTCTTCTGACG	SEQ ID NO:384	R	dn	
Ec_mero	APECO78_16640	267-366	AAGATGCAGTTAAGCATCCGGAAAAATATCCGCAGCTGACCATCCGTGTA TCCGGTTATGCAGTTCGCTTTAACTCTCTGACTCCGGAACAGCAGCGCGA	SEQ ID NO:385	R	dn	
Ec_mero	APECO78_22630	277-376	CAGCTGCAAAAACACCAGGGAAATACCATTGAAATTCGTTACACCACGCA TGAACAATTCAAACAACACAAACCGCAGAAAGTCAGGCGGTAATTCGCAGCG	SEQ ID NO:386	R	dn	
Ec_mero	APECO78_00325 (b4484 (cpxP))	149-248	AAGTTTAACCGAACATCAGCGTCAGCAGATGCGAGATCTTATGCAACAGG CCCGGCACGAACAGCCTCCTGTTAATGTTAGCGAACTGGAGACAATGCAT	SEQ ID NO:387	R	up	
Ec_mero	APECO78_00495	133-232	ATCGATCGCCTTAGCAGCCTGAAACCGAAGTTTGTATCGGTGACCTATGG CGCGAACTCCGGCGAGCGCGACCGTACGCACACAGCATTATTATTAAAGGCATTA	SEQ ID NO:388	R	up	
Ec_mero	APECO78_00935	111-210	TGGGACAGTCTGTTCGGCACGCCAGGCGTACAGCTGACGGACGATGATAT TCAAAATATGCCCTACGCCAGCCAGTACATGCAGCTTAATGGCGGGCCGC	SEQ ID NO:389	R	up	
Ec_mero	APECO78_00940	572-671	GGACGCACGCAAAAAGCGCCGGTGGCTTACTGGAACAAGCGTCACGTAGA GCCGATGCCCGGCAGCATTATTTATGTTGGCCTCGCGGACTCCGTCTGGA	SEQ ID NO:390	R	up	
Ec_mero	APECO78_00945	1408-1507	CAACTACGACAAGTTTAACTACACCAATCCGCCGCAGGACTCGCACTTAC CGCGCGTGCGTACCCATGTGCGCGAGTATGTGCAGAACGATGTCTATGTG	SEQ ID NO:391	R	up	
Ec_mero	APECO78_03465	695-794	ATACCTGCGACCCGCGTCAGGTGCCCGATGCGAGGTTGTTGAAGTCGATG TCCTACCAGGAAGCGATGGAGCTTTCCTACTTCGGCGCTAAAGTTCTTCA	SEQ ID NO:392	R	up	
Ec_mero	APECO78_03815	578-677	GCAGGCGGCACCGGGCATGTGGTGGAGTTTTGCGGCGAAGCAATCCGTGA TTTAAGCATGGAAGGTCGTATGACCCTGTGCAATATGGCAATCGAAATGG	SEQ ID NO:393	R	up	

Ec_mero	APEC078_03820	712-811	ATCACAGTTTGACGTTCTGCTGTGCTCCAACCTGTTTGGCGACATTCTGT CTGACGAGTGCGCAATGATCACTGGCTCGATGGGGATGTTGCCTTCCGCC	SEQ ID NO:394	R	up	
Ec_mero	APEC078_03825	809-908	CACACCGCCATTAATCACCAGGAGATATGGCGCACCAGCCAGTTAGTTAG CCAGATTTGTAATATGCCGATCCCGGCAAACAAAGCCATTGTTGGCAGCG	SEQ ID NO:395	R	up	
Ec_mero	APEC078_04245 (b0161 (degP))	164-263	TTAACGTAGAAGGTAGCACAACCGTTAATACGCCGCGTATGCCGCGTAAT TTCCAGCAGTTCTTCGGTGATGATTCTCCGTTCTGCCAGGAAGGTTCTCC	SEQ ID NO:396	R	up	
Ec_mero	APEC078_04985	4-103	CCTTTACGACGGTTCTCCCCAGGACTGAAAGCCCAGTTTGCCTTCGGCAT GGTCTTTTTGTTCGTTCAGCCCGATGCCAGCGCTGCTGACATAAGTGCGC	SEQ ID NO:397	R	up	
Ec_mero	APEC078_04995	190-289	ACGCCACTCGGTAGCCTGGCGTTCCAGTATGCCGAAGGCATTAAAGGTTT TAACTCACAGAAAGGTCTATTTGACGTGGCTATCGAGGGTGACTCAACGG	SEQ ID NO:398	R	up	
Ec_mero	APEC078_05000	227-326	CCGTGATAATGAGTGGTTATCCGCGGTAAAGGGGAAACAGGTCGTATTGA TTGCGGCCAGAAAGTCAGAAGCCTTAGCAAATTATTGGTATTACAACAGC	SEQ ID NO:399	R	up	
Ec_mero	APEC078_05395 (b0379 (yaiY))	177-276	GGAAACAGGTCGCCCACGGGTGGAAATTGGTTTAGGTGTCGGCACCATTT TCGGGCTGATCCCGTTTTTAGTAGGCTGCCTCATTTTTGCAGTGGTGGCG	SEQ ID NO:400	R	up	
Ec_mero	APEC078_05500 (b0399 (phoB))	47-146	AAATGGTCTGCTTCGTGCTCGAACAAAATGGCTTTCAGCCGGTCGAAGCG GAAGATTATGACAGTGCTGTGAATCAACTGAATGAACCCTGGCCGGATTT	SEQ ID NO:401	R	up	
Ec_mero	APEC078_05505	524-623	TGGAAATTCGCGTCATGCCTTATACCCACAAACAGTTGCTGATGGTGGCG CGTGATGTCACGCAAATGCATCAACTGGAAGGGGCGCGGCGTAACTTTTT	SEQ ID NO:402	R	up	
Ec_mero	APEC078_05995	181-280	GACGGCAGCAGTGGCGAAGTGAGTCTGGTGGGACAACCGCTACATAATAT GGACGAAGAAGCGCGGGCAAAGTTGCGCGCGAAGCACGTCGGCTTTGTTT	SEQ ID NO:403	R	up	
Ec_mero	APEC078_09510 (b1110 (ycfJ))	393-492	AGCGATACTTACACGACTACGCAACAGCGTTGTAAAACGGTGTATGACAA GTCAGAAAAAATGCTCGGTTATGATGTGACCTATAAGATTGGCGATCAGC	SEQ ID NO:404	R	up	
Ec_mero	APEC078_09535	513-612	TACTGCTGAGTGTGGCGGTTAATTTCGTTCCCACGCCGTGGTGGGGAATG AACAGTGTGATCCGCAATTTGCCTTATTACAGCCTTGGCGCATGGTTTGG	SEQ ID NO:405	R	up	

Ec_mero	APEC078_09705 (b1171 (ymgD))	120-219	CCAACGAAATGGCAAAAACTGACAGCGCACAGGTTGCAGAAATTGTTGCG GTAATGGGTAATGCCAGCGTTGCCAGCCGTGATTTAAAAATTGAGCAATC	SEQ ID NO:406	R	up
Ec_mero	APEC078_09710 (b1172 (ymgG))	105-204	AGGCGTTGGTTTACTTACTGGCAATGGTGTTAATGGCGTACTGAAGGTG CAGCTGTTGGCGCTGGTGTTGGTGCAGTAACAGAAAAAGGCCGCGACGGT	SEQ ID NO:407	R	up
Ec_mero	APEC078_10895	58-157	CTCATGGCAGGGCACAAGGACATGAATTTGTGTGGGTAAAGAATGTGGA TCATCAGCCTGCGTCATGAAGCGGACAGCGATGAATTGCGTGCTGTGGCGG	SEQ ID NO:408	R	up
Ec_mero	APEC078_11400	60-159	GGTTAATCAGAAGAAAGATCGTCTGCTTAACGAGTATCTGTCTCCGCTGG ATATTACCGCGGCACAGTTTAAGGTGCTCTGCTCTATCCGCTGCGGCGG	SEQ ID NO:409	R	up
Ec_mero	APEC078_12545 (b1743 (spy))	309-408	ACCTTCGATAAAGCAAAAGCTGAAGCGCAGATCGCAAAAATGGAAGAACA GCGCAAAGCTAACATGCTGGCGCACATGGAAACCCAGAACAAAATTTACA	SEQ ID NO:410	R	up
Ec_mero	APEC078_13545	395-494	ATGCCGACGTTATCATTGAGCCGAACCGAATCGAGTATGTTGCGAATGTG GATGGCAGGTCAGGGAACCATTCAAATCTCTGACCAAATGAATATCAAAG	SEQ ID NO:411	R	up
Ec_mero	APEC078_13965	19-118	CGCGAGCGAGCGAAAACCAATGCATCGTTAATCTCTATGGTGCAACGCTT TTCAGATATCACCATCATGTTTGCCGGACTATGGCTGGTTTGCGAAGTGA	SEQ ID NO:412	R	up
Ec_mero	APEC078_13975	522-621	CCTTTGAAGTGGCGCAGTTTGTCGAAAAACCGAATCTGGAAACCGCCCAG GCCTATGTGGCAAGCGGCGAATATTACTGGAACAGCGGTATGTTCCTGTT	SEQ ID NO:413	R	up
Ec_mero	APEC078_13985	125-224	AGGGTTACTGGTTTGTGCCGGGAGGGCGCGTGCAGAAAGACGAAACGCTG GAAGCCGCATTTGAGCGGCTGACGATGGCGGAACTGGGGCTGCGTCTGCC	SEQ ID NO:414	R	up
Ec_mero	APEC078_13995	647-746	CTCGGCAATATGGATTCCCTGCGTGACTGGGGCCATGCCAAAGACTACGT AAAAATGCAGTGGATGATGCTGCAACAGGAACAGCCGGAAGATTTCGTTA	SEQ ID NO:415	R	up
Ec_mero	APEC078_14000	259-358	TATACCCTCGGTGAAATAACCATTGGCGCACATTCGGTGATATCGCAAAA AAGTTATTTATGCACCGGTAGCCACGACCATGCAAGTCAACATTTCACCA	SEQ ID NO:416	R	up
Ec_mero	APEC078_14010	523-622	CGAACCGGCATTTTTCGCTCTGGCATTAATCTCAATTTGGCTCAGCATCA AACAGTTTGGTATCAAAACGCCTAAAACCGATGCTATGATTCTCGCAGGG	SEQ ID NO:417	R	up

Ec_mero	APEC078_14025	475-574	AGGTCTTTACCTGGGCGTGGCGTTTCAAAGAGTGTTTGTTCGATACCGAA CTGAAAGCGGCACAGGATTACGACATCTTCCTGCGGATGGTGGTGGAGTA	SEQ ID NO:418	R	up		
Ec_mero	APEC078_14030	2020-2119	ATGGTGGCGCGTTATGCGGTCAACACATTGAAGAAGTGGAAACCAGTCT GAGCCGCTTTGAGCAAAACGGTATTCCGGTGAAAGGGGTGATTCTGAACT	SEQ ID NO:419	R	up		
Ec_mero	APEC078_14035	231-330	CTGATTTTGACCATGGAAAAGCGCCATATCGAACGCTTATGCGAGATGGC ACCTGAGATGCGCGGCAAGTGATGCTGTTTGGTCACTGGGATAACGAAT	SEQ ID NO:420	R	up		
Ec_mero	APEC078_14040	1035-1134	CCCGGTTTCCCGCTGGAACCGTCTGATCAATCAGTTGCTGCCAACTATTA GCGGTGTCCGTTACATGACGGATACAGCCAGCGACATTCATAACTGGTAA	SEQ ID NO:421	R	up		
Ec_mero	APEC078_14100	153-252	AGGCAGTTATAAATCCCGTTGGGTAATCGTAATCGTGGTGGTTATCGCCG CCATCGCCGCATTCTGTTCTGGCAAGGCCGCAATGACTCCCAGAGTGCA	SEQ ID NO:422	R	up		
Ec_mero	APEC078_15715	22-121	GCGGCCGCCCTGATGGCATTTACCCCGCTTGCAGCAAACGCAGGTGAAAT CACCCTACTGCCATCAATCAAATTACAAATTGGCGATCGCGATCATTACG	SEQ ID NO:423	R	up		
Ec_mero	APEC078_19610	111-210	CGAGTTCCGTAAAGCCGGACACGAAGTGATTACCATTGAAAAACAAGCGG GTAAAACGGTGAAAGGCAAAAAAGGAGAAGCCAGCGTGACCATCGATAAA	SEQ ID NO:424	R	up		
Ec_mero	APEC078_21920 (b3615 (waaH))	788-887	TTCATCAGCAAATAACTTACGAAGCATTGCGTGTTTGCCATGCGGTGCGC AAAGAGCCGGATATTCTTACCCGCCAACGGATGATTGCCGAGATATTTAC	SEQ ID NO:425	R	up		
Ec_mero	APEC078_22490	263-362	TGGTTATGGTGATCAGTAAAACCATTGCCGAGCTGGAGCGTATTGGCGAC GTGGCGGACAAAATCTGCCGTACTGCGCTGGAGAAATTCTCCCAGCAGCA	SEQ ID NO:426	R	up		
Ec_mero	APEC078_22505	5-104	CTGCAACCAAGCCTGCTTTTAACCCACCGGGTAAAAAGGGCGACATAATT TTCAGCGTGCTGGTAAAACTGGCGGCGCTGATTGTGCTATTGATGTTGGG	SEQ ID NO:427	R	up		
Ec_mero	APEC078_22510 (b3728 (pstS))	9-108	TATGCGTACCACCGTCGCAACTGTTGTCGCCGCGACCTTATCGATGAGCG CTTTCTCTGTGTTTGCAGAAGCAAGCCTGACAGGTGCAGGTGCAACCTTC	SEQ ID NO:428	R	up		
Ec_mero	APEC078_22685	525-624	AAAACGAAGTGACTTTCCCACATGCCGAAGTTGAGCAAGCGCGCCAGATG CTGGCAAAAGCGCAAAAACCGATGCTGTACGTTGGCGGTGGCGTGGGTAT	SEQ ID NO:429	R	up		
Ec_cip	b0176	432-531	GTGGTTGGTGAAATAGCAGCCAATTCGATAGCTGCGGAAGCACAAATTGC ACCAGGTACGGAACTAAAGCCGTAGATGGTATCGAAACGCCTGATTGGG	SEQ ID NO:430	C			x

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Ec_cip	b0179	374-473	TCCGGCGTTGAACTGGGCGATAACGTGATTATCGGTGCCGGTTGCTTCGT AGGTAAAAACAGCAAAATCGGTGCAGGTTCGCGTCTCTGGGCGAACGTAA	SEQ ID NO:431	C			
Ec_cip	b0761	223-322	GGCGCAGTACTGACCCGCTATGGTCAGCGACTGATTCAGCTCTATGACTT ACTGGCGCAAATCCAGCAAAAAGCCTTTGATGTGTTAAGTGACGATGACG	SEQ ID NO:432	C			x
Ec_cip	b1280	439-538	TGCTACAAATCTACCAGGCTACCAGTGAGTGGCAGAAGCAATTGATGTT GCCGAACGCCTGGTGAAGCTGGGTAAAGATAAACAGCGCGTCGAAATTGC	SEQ ID NO:433	C			x
Ec_cip	b1827	1-100	ATGGCTAACGCAGATCTGGATAAACAGCCTGATTCTGTATCTTCCGTGCT AAAAGTTTTTGGCATTTTGCAGGCGCTGGGTGAAGAGCGCGAAATAGGGA	SEQ ID NO:434	C			x
Ec_cip	b1870	142-241	ATGTTAGCCGAGCGCTTCGTTCAACCTGGTACGCAGGTTTACGATCTGGG TTGTTCTCTGGGCGCGGCGACGCTCTCGGTGCGTCGCAACATTCATCATG	SEQ ID NO:435	C			
Ec_cip	b2065	100-199	GATGTACGCCTGGGCAATAAATTTCGTACCTTCCGTGGTCACACGGCAGC GTTTATCGATCTGAGCGGTCCCAAGATGAAGTGAGCGCCGCGCTTGACC	SEQ ID NO:436	C			x
Ec_cip	b2153	167-266	CTGATGACAGTTTGATGGAAACGCCGCATCGCATCGCTAAAATGTATGTC GATGAAATTTTCTCCGGTCTGGATTACGCCAACTTCCCGAAAATCACCCT	SEQ ID NO:437	C			
Ec_cip	b2411	504-603	GAAGTGCGTGGTGAAGTGTTCCTGCCGCAGGCGGGGTTCGAAAAGATTAA CGAAGATGCGCGACGCACGGGCGGGAAAGTGTTTGCTAACCCACGTAATG	SEQ ID NO:438	C			
Ec_cip	b2515	277-376	ATTGCGCTGAAAGTAGCGGAATACGGCGTCGATTGTCTGCGTATTAACCC TGGCAATATCGGTAATGAAGAGCGTATTCGCATGGTGGTTGACTGTGCGC	SEQ ID NO:439	C			x
Ec_cip	b2516	91-190	CAGGCCGTTGCCGAGCGACTTTGCCTGAAGGTTTCCACGGTACGCGACAT TGAAGAAGATAAGGCACCCGCCGATCTTGCTTCAACATTCCTGCGCGGAT	SEQ ID NO:440	C			
Ec_cip	b2829	781-880	GGTTGATAAAGGCTCGGTGGCAGAGTGGGCGGTAAAAACGGTCATTGAAA AATTTGCCGAACAGTTTGCCGCGCTAAGCGATAACTATCTCAAAGAGCGG	SEQ ID NO:441	C			
Ec_cip	b2830	223-322	TTGCGCTACAAATTACCGAAACGTTTGGTGCGTTGGGACACGAAGCCGGT TTGTATCGGCCAAAAACACAAAAATGGTTTCTCTTGCAGCTGGTGAGCGGCG	SEQ ID NO:442	C			x
Ec_cip	b2907	605-704	TTTACGCAACATGGCCCGCTGGCGATGTTGCCGATGTCTGACGGACGCTG TTCGCTGGTCTGGTGTCATCCACTGGAACGGCGCGAAGAGGTGCTGTCGT	SEQ ID NO:443	C			
Ec_cip	b3252	1103-1202	CCACGCGTAATGCGGGATTGCAGGGCGGCAATAGCTGGGCTATTTACGAT GACTCGTTGCCTGAAAAAGGACGCGGTAATGTTCGCTGGCGTACGCTTAT	SEQ ID NO:444	C			x
Ec_cip	b3346	176-275	AGGATCTAAAATGTTCAGCCATTCGCATTGCTAACGGTGAACATACAGGC CGGAAGATTGGTTCGCCAATTACTGACCTGGCGCTACGTATGCTGCACGA	SEQ ID NO:445	C			

Ec_cip	b3803	50-149	CCGTGGACACCACGTCACAACCTGTCGCAACAGAAAAAAGAGTAAGAAC AATACCGCATTGATTCTCAGCGCGGTGGCTATCGCTATTGCTCTGGCGGC	SEQ ID NO:446	C		
Ec_cip	b4136	548-647	GAGCAGCCCACCGCGCAATTGCCCTTTTCCGCGCTCTGGGCGTTGTTGAT CGGTATTGGTATCGCCTTTACGCCATGCGTGCTGCCAATGTACCCACTGA	SEQ ID NO:447	C		
Ec_cip	b4175	175-274	ATTGAAACGGTGAAAATGCTCGACGCACGTATTCAGACCATGGACAACCA GGCCGACCGCTTTGTGACCAAAGAGAAGAAAGACCTGATCGTCGACTCTT	SEQ ID NO:448	C		
Ec_cip	b4178	208-307	CGGCGAGTGCGATACGTATTGGTGATGTGGTGCGCGAGCTGGAGCCCTTA TCGCTGGTGAATTGCAGCAGTGAGTTTTGCCACATTACACCTGCCTGTCG	SEQ ID NO:449	C		
Ec_cip	b0754	276-375	GTCTATTTTGAAAAGCCGCGTACCACGGTGGGCTGGAAAGGGCTGATTAA CGATCCGCATATGGATAACAGCTTCCAGATCAACGACGGTCTGCGTATAG	SEQ ID NO:450	R	dn	
Ec_cip	b0893	488-587	GTAATGAAAGGGCAGATTGCTCGCATGCACCGCGCACTGTCGCAGTTTAT GCTGGATCTGCATACCGAACAGCATGGCTACAGTGAGAACTATGTTCCGT	SEQ ID NO:451	R	dn	
Ec_cip	b0894	1466-1565	TCTGAAATCAACCGTACCCATGAAATCCTTCAGGATGATAAGAAGTGCGA GCTGATTGTGGTTATCGACTGCCACATGACCTCATCGGCGAAATATGCTG	SEQ ID NO:452	R	dn	
Ec_cip	b0926	311-410	CGCAAACCGGTGCAACTCATTTCCGGTTATCGTTCCATTGATACCAACAA TGAACTACGCGCCCGCAGCCGTGGAGTAGCGAAGAAAGCTATCACACTA	SEQ ID NO:453	R	dn	
Ec_cip	b0929	1-100	ATGATGAAGCGCAATATTCTGGCAGTGATCGTCCCTGCTCTGTTAGTAGC AGGTACTGCAAACGCTGCAGAAATCTATAACAAAGATGGCAACAAAGTAG	SEQ ID NO:454	R	dn	
Ec_cip	b1120	116-215	AAAAACCAAGAGTACTCGTACTGACAGGGGCAGGGATTTCTGCGGAATCA GGTATTCGTACCTTTCGCGCCGCAGATGGCCTGTGGGAAGAACATCGGGT	SEQ ID NO:455	R	dn	
Ec_cip	b1794	244-343	ACCTACCTGACCAAAGTGGATGTCGAAGCGCGCCTGCAGCATATTATGTT TGCCCGTAACAGCCAGAAAATGCACATCCCGGAGAATTTTACCGTCTCGT	SEQ ID NO:456	R	dn	
Ec_cip	b1895	28-127	GTTGCGGTTACACCGGAAAGTCAGCAACTGCTGGCAAAAGCGGTATCTAT CGCCAGGCCAGTAAAGGGACACATCAGTTTAATTACTCTCGCTTCCGACC	SEQ ID NO:457	R	dn	
Ec_cip	b2276	182-281	TGGACGTTACGCCGCTGATGCGCGTTGATGGTTTCGCCATGCTTTACACC GGGCTGGTATTGTTGGCGAGCCTCGCCACCTGTACTTTCGCCTACCCGTG	SEQ ID NO:458	R	dn	
Ec_cip	b2277	421-520	CTTCTGGGAAATGATGCTGGTGCCGATGTACTTCCTGATCGCACTGTGGG GGCATAAAGCCTCTGACGGTAAAACGCGTATCACGGCGGCAACCAAGTTC	SEQ ID NO:459	R	dn	
Ec_cip	b2281	47-146	GTATCTGGATGATCGGCCTGCACGCGTTCGCCAAACGCGAAACGCGAATG TACCCGGAAGAGCCGGTCTATCTGCCGCCCCGTTATCGTGGTCGTATCGT	SEQ ID NO:460	R	dn	
Ec_cip	b2903	1501-1600	CTCACCCATCCGGTGTTTAATCGCTACCACAGCGAAACCGAAATGATGCG CTATATGCACTCGCTGGAGCGTAAAGATCTGGCGCTGAATCAGGCGATGA	SEQ ID NO:461	R	dn	

Ec_cip	b3409	824-923	CCACTGCGGTAGATAAAATCGTGCTCAACCGTTCCTCGGTCTGCCGATT TTCCTCTTTGTGATGTACCTGATGTTCCTGCTGGCTATCAACATCGGCGG	SEQ ID NO:462	R	dn
Ec_cip	b3746	495-594	CGGAAGCAGACAGCAGTCTGGAAGCGTTATATGACCGCATGCTGATTCGT CTGTGGTTAGATAAAGTGCAGGATAAAGCGAATTTCCGCTCCATGCTGAC	SEQ ID NO:463	R	dn
Ec_cip	b3771	967-1066	AAGATGTTCACCGTGCTGGTGGTGTTATCGGTATTCTCGGCGAACTGGAT CGCGCGGGGTTACTGAACCGTGATGTGAAAAACGTACTTGGCCTGACGTT	SEQ ID NO:464	R	dn
Ec_cip	b3863	693-792	TGGCAGCGAAGCTCGAGCAAAACAAAGAAGTTGCTTATCTCTCATACCAG CTGGCGACGATTAAAACCGACGTTGAACTGGAGCTGACCTGTGAACAACT	SEQ ID NO:465	R	dn
Ec_cip	b0060	865-964	CTTCATTCTCGCTGGAAACTGTCGCTCAGGAGCTATTAGGCGAAGGAAAA TCTATCGATAACCCGTGGGATCGAATGGACGAAATTGACCGCCGTTTCGC	SEQ ID NO:466	R	up
Ec_cip	b0068	577-676	AAAACGGTCACGGTCACCAAAGGCTGGAGCGAAGCCTACGGCCTGTTTTT AAAAGGTGAAAGCGATCTGGTACTGAGTTACACCACACCTCTCCGGCTTATC	SEQ ID NO:467	R	up
Ec_cip	b0231	102-201	CCGCGAACGTCGGGGGGTGATCAGCACCGCCAATTATCCCGCGCGTAAAT TTGGCGTACGTAGCGCTATGCCGACAGGGATGGCGCTCAAATTATGCCCG	SEQ ID NO:468	R	up
Ec_cip	b0241	367-466	CGTGGAAGCCTGGACCGATATGTTCCCGGAATTTGGTGGCGACTCCTCGG CGCAGACCGACAACTTTATGACCAAACGCGCCAGCGGTCTGGCGACGTAT	SEQ ID NO:469	R	up
Ec_cip	b0313	137-236	GCGTTTCTACGGGGATCATCAGCCACTATTTCAGGGACAAAAATGGTCTG CTGGAAGCAACCATGCGCGATATCACCAGTCAGCTGCGTGACGCGGTTTT	SEQ ID NO:470	R	up
Ec_cip	b0399	46-145	GAAATGGTCTGCTTCGTGCTCGAACAAAATGGCTTTCAGCCGGTCGAAGC GGAAGATTATGACAGTGCTGTGAATCAACTGAATGAACCCTGGCCGGATT	SEQ ID NO:471	R	up
Ec_cip	b0400	334-433	GTGCTGACCACGGAAGAGGGCGGTATTTTCTGGTGTAACGGTCTGGCGCA ACAAATTCTTGGTTTGCGCTGGCCGGAAGATAACGGGCAGAACATCCTTA	SEQ ID NO:472	R	up
Ec_cip	b0458	275-374	TCGATGTCTACCCACGCTACCGCTATGAAGATATCGACGTGCTGGATTTC CGCGTTTGCTATAACGGCGAATGGTACAACACGCGCTTTGTACCTGCCGC	SEQ ID NO:473	R	up
Ec_cip	b0683	116-215	TATACAAACGTCTGATCGATATGGGTGAAGAAATTGGTCTGGCTACGGTA TATCGCGTACTGAACCAGTTTGACGACGCTGGTATCGTCACCCGCCACAA	SEQ ID NO:474	R	up
Ec_cip	b0698	1234-1333	TACGGCATGATGCTGTTTGTCCTGCTGGCGGTGTTTATTGCCGGGCTGAT GATTGGTCGTACACCGGAATATCTGGGTAAAAAATCGACGTACGCGAGA	SEQ ID NO:475	R	up
Ec_cip	b0779	881-980	GAGATGATGAACGAGCTGGGCTACTGTTCGGGGATTGAAACTACTCGCG CTTCCTCTCCGGTCGTGGACCGGGTGAGCCACCGCCGACGCTGTTTGATT	SEQ ID NO:476	R	up
Ec_cip	b0958	114-213	TGTCTATCGCGAAGATCAGCCCATGATGACGCAACTTCTACTGTTGCCAT TGTTACAGCAACTCGGTCAGCAATCGCGCTGGCAACTCTGGTTAACACCG	SEQ ID NO:477	R	up

Ec_cip	b1061	134-233	TGCGAATTGAAGTCACCATAGCGAAAACTTCTCCATTGCCAGCTGGGGCT ATTGACGCCCTGGCTGGCGAACTTTCCCGCCGTATTCAGTATGCGTTTCC	SEQ ID NO:478	R	up
Ec_cip	b1183	129-228	GTTGATCCAGCATCCCAGCGCGACTTACTTCGTCAAAGCAAGTGGTGATT CTATGATTGATGGTGGAATTAGTGACGGTGATTTACTGATTGTCGATAGC	SEQ ID NO:479	R	up
Ec_cip	b1184	453-552	CGGCAAAAAAATGGCAGCGGCAGACGGGTGGGGTGGTGGATTTATCAAAT CTGGAACGCCAGCGTAAATTAATGTCTGCTCTCCCCGTGGATGACGTCTG	SEQ ID NO:480	R	up
Ec_cip	b1207	255-354	AACGACAACCTGATGGAATTAGTCGTTATGGTTGATGCCCTGCGTCGTGC TTCCGCAGGTCGTATCACCGCTGTTATCCCCTACTTTGGCTATGCGCGCC	SEQ ID NO:481	R	up
Ec_cip	b1728	40-139	TCTATTGCTTGTGCGGTATTTGCCAAAAATGCCGAGCTGACGCCCGTGCT GGCACAGGGTGACTGGTGGCATATTGTCCCTTCCGCAATCCTGACGTGTT	SEQ ID NO:482	R	up
Ec_cip	b1848	117-216	CACCTGGCTGACAAATTCTCCAGTGCAAATGGAAGACGAGCAACGTGAAG CCCTTTCGCTATGGCTGGCAGAACAAAAAGATGTGCTGAGCACCATTCTG	SEQ ID NO:483	R	up
Ec_cip	b2231	100-199	CTGCCAGATGTCCGAGATGGCCTGAAGCCGGTACACACCGTCGCGTACTTTA CGCCATGAACGTACTAGGCAATGACTGGAACACAAAGCCTATAAAAAATCTG	SEQ ID NO:484	R	up
Ec_cip	b2234	21-120	GACAAAGCGCGACGGTAGCACAGAGCGCATCAATCTCGACACAAAATCCATC GCGTTCTGGATTGGGCGGCAGAAGGACTGCATAACGTTTCGATTTCCCAG	SEQ ID NO:485	R	up
Ec_cip	b2498	318-417	GTTGTCGGTATGTACCGTAATGAAGAAACGCTGGAGCCGGTACCGTACTT CCAGAAACTGGTTTCTAACATCGATGAGCGTATGGCGCTGATCGTTGACC	SEQ ID NO:486	R	up
Ec_cip	b2582	110-209	TGATTAATGCGACCGGTGAAACGCTCGACAAATTGCTGAAGGATGATCTA CCTGTGGTGATCGACTTCTGGGCACCGTGGTGCGGCCCCTGCCGTAATTT	SEQ ID NO:487	R	up
Ec_cip	b2616	597-696	TAATCCGCAGCCCGGAGAGTTTGAACAAATCGACGAAGAGTACAAACGTC TGGCGAACAGCGGTCAATTGCTGACCACCAGCCAGAATGCATTGGCATTA	SEQ ID NO:488	R	up
Ec_cip	b2670	153-252	GAACATCTTAATTGCATGGCCATACGGTATGTACCGCGATCTGTTTATGC GCGCGGCACGCAAAGTTAGCCCGTCGGGCTGGATAAAAAATCTGGCGGAT	SEQ ID NO:489	R	up
Ec_cip	b2698	310-409	AAGCGACAGAAAAAGCGATGCGTGAATGTGACATCGACTGGTGCGCACTG GCGCGCGATCAGGCGACGCGAAAATATGGCGAACCTTTGCCAACTGTCTT	SEQ ID NO:490	R	up
Ec_cip	b2699	40-139	AAAGCGTTGGCGGCAGCACTGGGCCAGATTGAGAAACAATTTGGTAAAGG CTCCATCATGCGCCTGGGTGAAGACCGTTCCATGGATGTGGAAACCATCT	SEQ ID NO:491	R	up
Ec_cip	b2700	274-373	TGAAAGCGGCTCGTGCTGATTATGCCGTGTCTATTAGTGGTATCGCCGGG CCGGATGGCGGCAGTGAAGAGAAGCCTGTCGGCACCGTCTGGTTTGCTTT	SEQ ID NO:492	R	up
Ec_cip	b2980	427-526	GATAACCCGCTGTTATGAAAAAATGCTCGCCGCCAGTGAGAACAACAAAG AGATTTCGCTGATCGAACATGCGCAGTTGGATCACGCTTTCCATCTCGCC	SEQ ID NO:493	R	up

Ec_cip	b3065	56-155	TCAAGCGTTCCTGCGAAAAGCAGGTGTTCTGGCGGAAGTTCGTCGTCGT GAGTTCTATGAAAAACCGACTACCGAACGTAAGCGCGCTAAAGCTTCTGC	SEQ ID NO:494	R	up
Ec_cip	b3173	625-724	AGAGCATCAAAGATTACTCTCAATTGCAAACACGGTGCCGTATTTTCAAT TATCAGTCAGGGATACAGGTATTGATACCTACGTGTTGATTGTGGGGAG	SEQ ID NO:495	R	up
Ec_cip	b3348	41-140	AGAGCCGACTGGCTTTTCAGGAAATCACCATTGAAGAACTGAACGTCACG GTGACCGCTCATGAAATGGAGATGGCGAAACTGCGCGATCATCTGCGTCT	SEQ ID NO:496	R	up
Ec_cip	b3434	64-163	CCTATTTTCATGTCCGTACTGAAACATACTGAACCGAAAAGACGGCGGGC AATCATGGTGCGAGAGTTGCTTATTGCTCTCCTGGTGATGCTGGTGTTCC	SEQ ID NO:497	R	up
Ec_cip	b3452	487-586	TTGCCTCAGTATGGAAGCAAATCAGCTACAACTTCCTGTTCTTCTATGCC GCGCTGCAATCCATTCCCCGTTCGTTGATCGAAGCCGCAGCCATCGACGG	SEQ ID NO:498	R	up
Ec_cip	b3453	100-199	AAGGGGAACTGGGTAAAGAGGTGGATTCTCTGGCCCAACGTTTTAACGCC GAAAACCCGGATTACAAAATTGTACCGACCTATAAAGGCAACTACGAACA	SEQ ID NO:499	R	up
Ec_cip	b3645	256-355	TTCATCTCTCCCGCTATGCCTGTTACCTGGTAGTACAAAACGGCGACCCT GCGAACCGGTTATTGCGGCAGGGCAAACTTATTTTGCTATCCAGACCCG	SEQ ID NO:500	R	up
Ec_cip	b3666	700-799	AAGAGGACAAAGAGACAGAATCTACCGATATGACCAAGTGGCAGATCTTT GTTGAGTATGTGCTGAAAACAAAGTGATCTGGCTGCTGTGCTTCGCCAA	SEQ ID NO:501	R	up
Ec_cip	b3700	817-916	GCTTAAGCTGTTGATGTGCGCCTTACGTCTGGCGCAAGGAGAGTTCCTCA CCCGTGAAAGCGGGCGGCGGTGTCTCTACCTGATAGATGATTTTGCCTCT	SEQ ID NO:502	R	up
Ec_cip	b3701	37-136	CCGCTACAACAGGTGAGCGGTCCGTTAGGTGGTCGTCCTACGCTACCGAT TCTCGGTAATCTGCTGTTACAGGTTGCTGACGGTACGTTGTCGCTGACCG	SEQ ID NO:503	R	up
Ec_cip	b3702	370-469	TCCCGGCCCCGGCAGAACCGACCTATCGTTCTAACGTAAACGTCAAACAC ACGTTTGATAACTTCGTTGAAGGTAAATCTAACCAACTGGCGCGCCGGGC	SEQ ID NO:504	R	up
Ec_cip	b3727	5-104	CTGCAACCAAGCCTGCTTTTTAACCCACCGGGTAAAAAGGGCGACATAATT TTCAGCGTGCTGGTAAAACTGGCGGCGCTGATTGTGTCTATTGATGTTGGG	SEQ ID NO:505	R	up
Ec_cip	b3728	8-107	TTATGCGTACCACCGTCGCAACTGTTGTCGCCGCGACCTTATCGATGAGC GCTTTCTCTGTGTTTGCAGAAGCAAGCCTGACAGGTGCAGGTGCAACCTT	SEQ ID NO:506	R	up
Ec_cip	b3820	241-340	GTGTGCGTGGGAAGTACCTTAACCCGCCACGAAACCATCAGTGAAGATGA ACTACGCCAGCGCTATCGCGGATGGGGACCATTGATCTTCGCGTTGATT	SEQ ID NO:507	R	up
Ec_cip	b3832	833-932	CGCTACAGGAACATATCGCGTCGGTGCGTAACCATATCCGTTTGCTGGGA CGCAAAGATTATCAACAGCTGCCGGGGCTGCGAACTCTGGATTACGTGCT	SEQ ID NO:508	R	up
Ec_cip	b3846	168-267	AGATGGCATTGCCGAACTGGTATTTGATGCCCCAGGTTCAGTTAATAAAC TCGACACTGCGACCGTCGCCAGCCTCGGCGAGGCCATCGGCGTGCTGGAA	SEQ ID NO:509	R	up

Ec_cip	b4043	11-110	TAACGGCCAGGCAACAAGAGGTGTTTGATCTCATCCGTGATCACATCAGC CAGACAGGTATGCCGCCGACGCGTGCGGAAATCGCGCCAGCGTTTGGGGTT	SEQ ID NO:510	R	up		
Ec_cip	b4044	509-608	TACTCGGCGTGCAATATGCCCGTGCGCCAGTAATTTTGTTAGTGGTCGGC AATATCCTCAACATTGTGCTGGATGTCTGGTGATGGGGCTGCATAT	SEQ ID NO:511	R	up		
Ec_cip	b4058	64-163	CCCCGCGACAAGCTCATTGTCGTGACCGGGCTTTCGGGTTCTGGCAAATC CTCGCTCGCTTTCGACACCTTATATGCCGAAGGGCAGCGCCGTTACGTTG	SEQ ID NO:512	R	up		
Ec_cip	b4060	100-199	ATGGCTACCCTCACCACTGGCGTGGTTCTTCTTCGCTGGCAACTTCTTAG TGCCGTAATGATGTTTCTGGCCAGCACACTCAACATCCGTTTTCGTCGGT	SEQ ID NO:513	R	up		
Ec_cip	b4062	171-270	CGCCTGTTACTGGCGCCGCGTTGAGTTGCGCACCACCGAGCGTCCGATTTT TGATATCGCAATGGACCTGGGTTATGTCTCGCAGCAGACCTTCTCCCGCG	SEQ ID NO:514	R	up		
Ec_cip	b4105	374-473	AACAAAGATAGTCCGATCAACAACCTGAACGATCTGCTGGCGAAGCGGAA AGATCTCACCTTCGGCAATGGCGATCCTAACTCCACCTCNNNNNNNNNNN	SEQ ID NO:515	R	up		
Ec_cip	b4106	610-709	ACCGTGGTCGTCACGCTGCATCAGGTGGATTACGCCCTGCGCTACTGCGA ACGCATCGTCGCCCTGCGCCAGGGGCACGTCTTCTACGACGGCAGCAGCC	SEQ ID NO:516	R	up		
Ec_cip	b4142	24-123	TTGCATGATCGCGTGATCGTCAAGCGTAAAGAAGTTGAAACTAAATCTGC TGGCGGCATCGTTCTGACCGGCTCTGCAGCGGCTAAATCCACCCGCGGCG	SEQ ID NO:517	R	up		
Ec_cip	b4143	490-589	AGCGATGGACAAAGTCGGTAAAGAAGGCGTTATCACCGTTGAAGACGGTA CCGGTCTGCAGGACGAACTGGACGTGGTTGAAGGTATGCAGTTCGACCGT	SEQ ID NO:518	R	up		
Ec_cip	b4166	397-496	AAACTCGGCTATGTTAGCCGTTATGCGCTGGGCCGTGACTATCACAAACT TCTGCGCAACCGACTCAAAAAGCTGGGCGAGATGATTCAGCAACATTGTG	SEQ ID NO:519	R	up		
Ec_cip	b4242	808-907	CGTGTTAGTGAGCAGGAAGCGAGCCGAATGCCTTTCAGCAAGGGATCAG CCGCGTCAGTATGCTGCTGATTCGCTTTATGCTGGTGATGGCTCCGGTGG	SEQ ID NO:520	R	up		
Ec_gent GeneID = NC_000913	b1272	523-622	GCTGCCAGCGGCGGTTACATGATGGCCTGTGTGGCGGACAAAATTGTTTC CGCACCGTTTGCTATTGTGGGTTCCATTGGGGTGGTGGCGCAAATGCCCA	SEQ ID NO:521	C		x	
Ec_gent	b1719	481-580	ACGAAAACATCGCCCCATGATGACAAGCCAGGTCTGTACTTCCATGAAGAA TATGTCGATATGTGCCCGCGGTCCGCACGTACCGAACATGCGTTTCTGCCA	SEQ ID NO:522	C		x	
Ec_gent	b1914	392-491	ACAAATGGCGTTAAGCCAGATCGAACCAGAAAAACAGAAAGCCCATTTG CCAGTTTGTCTGAACGTGAATTGCAGATTATGCTGATGATCACCAAGGGC	SEQ ID NO:523	C			
Ec_gent	b2821	743-842	CGGACACCTTTGGTCGCGTGCCGAACAAAGAGAGCAAAAAACCGGAAATC ACCGTGCCGGTAGTCACCGACGCGCAAAAGGGCATTATCATTCATTACGT	SEQ ID NO:524	C		x	

Ec_gent	b2830	223-322	TTGCGCTACAAATTACCGAAACGTTTGGTGCGTTGGGACACGAAGCCGGT TTGTATCGGCCAAAAACAAAAATGGTTTCTCTTGCAGCTGGTGAGCGGCG	SEQ ID NO:525	C		x
Ec_gent	b2910	23-122	TCCAAATTTTTGGCCGTTCACTGCGTGTGAACTGCCCGCCTGACCAAAGG GATGCGTTGAATCAGGCAGCGGACGATCTGAACCAACGGTTGCAAGATCT	SEQ ID NO:526	C		x
Ec_gent	b3040	300-399	CATGCGCATCCGCAGGATTTAATGCAAAAATCGGTGCAGCCGTTGCCAAA ATCGATCAAGCGCACAGCCATTCTGCTCACTCTCGGCATCAGTCTGCATA	SEQ ID NO:527	C		x
Ec_gent	b3389	102-201	CGAGCAGGTCATGTTGGTCACCAACGAAACCCTGGCTCCTCTGTATCTCG ATAAGGTCCGCGGCGTACTTGAACAGGCGGGTGTTAACGTCGATAGCGTT	SEQ ID NO:528	C		
Ec_gent	b3929	443-542	GGTTGGTGCCGCTGGCGAAGGCATTGGCGAAAGCGATGTCCGCGTCAATT TTGGCGGTGTCACCTTCTTCTCCGGCGACCATCTTNNNTATGCCGACAAT	SEQ ID NO:529	C		
Ec_gent	b4041	1507-1606	ACTGGCGTGAATCTATCGATCCCATCGAAGCGGTGCGTCCGGCCTGGTTA ACGCCGACGGTCAATAATATTGCTGCCGATCTGATGGTACGCATTAACAA	SEQ ID NO:530	C		x
Ec_gent	b4059	171-270	CGTTGTGCTGTTCGGCAAACTGGCAGAAGTGGCCAGCGAATATCTGCGTA AAGGTTCTCAGGTTTATATCGAAGGTCAGCTGCGTACCCGTAAATGGACC	SEQ ID NO:531	C		
Ec_gent	b4169	448-547	GCCTGCGGTTGTCGCACCGCGCGTCAGCGAACCGGCGCGCAATCCGTTTA AAACGGAAAGTAACCGCACTACGGGTGTTATCAGCAGTAATACGGTAACG	SEQ ID NO:532	C		
Ec_gent	b4174	729-828	GAAGAAGTAAAAGCGGCGTTTGACGATGCGATTGCCGCGCGTGAAAACGA ACAGCAATACATTCGTGAAGCAGAAGCGTATACCAACGAAGTTCAGCCGC	SEQ ID NO:533	C		
Ec_gent	b4175	175-274	ATTGAAACGGTGAAAATGCTCGACGCACGTATTCAGACCATGGACAACCA GGCCGACCGCTTTGTGACCAAAGAGAAGAAAGACCTGATCGTCGACTCTT	SEQ ID NO:534	C		x
Ec_gent	b4220	495-594	CGCAGCTGGGCATTGCGCTCGGCCTGCATAAAGCCTTCTGGGATATTGAT TATAACAGTGGCGAACGTTACCGCTTTGGCATGTGACCTTTGAAGGATC	SEQ ID NO:535	C		x
Ec_gent	b4255	100-199	ACACCATCGAACACCATCTTTCCGCAGACGATCTGGAAACCCTGGAAAAA GCAGCAGTTGAAGCGTTTAAACTCGGTTACGAAGTGACCGATCCAGAAGA	SEQ ID NO:536	C		x
Ec_gent	b0085	379-478	TGGCGCAGTGGAGCCAACTGCTTGGCGAAACCAGCGCGGTAATGGGCACC GTTGGTAACGGCCTGCTGGGGAAAGTGATCCCGACAGAAATACCACCGG	SEQ ID NO:537	R	dn	
Ec_gent	b0086	362-461	TTTTAAGCCAGTGCGGCAACACGCTTTATACGGCAGGCAATCTCAACAAC GACATCGGTGTACCGATGACGCTGTTGCGCTTAACGCCGGAATACGATTA	SEQ ID NO:538	R	dn	
Ec_gent	b0087	860-959	CCTGCTGGTGATTATGGGGGCGTGTTCGTGGTAGAAACGCTTTCTGTCA TCCTGCAGGTCGGCTCCTTTAAACTGCGCGGACAACGTATTTTTCCGCATG	SEQ ID NO:539	R	dn	
Ec_gent	b0428	254-353	GGACGAAGAATCGGGTGCTGGTTAAAGGCCTGATCTCTCCTGCTGTCTCG CTGGTGTACGCCACCTTGCTGGGTATTGCTGGCTTTATGCTGCTGTGGTT	SEQ ID NO:540	R	dn	

Ec_gent	b0429	156-255	GATCATTCTGACGGTGATTCCGTTCTGGATGGTGATGACAGGGGCTGCCT CTCCGGCCGTAATTCTGGGAACAATCCTGGCAATGGCAGTGGTACAGGTT	SEQ ID NO:541	R	dn	
Ec_gent	b0430	163-262	GCAGGCGGCCCGACAGGTAAGGACATTTTCGAACTGCCGTTCGTTCTGGT TGAAACTTTCTTGCTGTTGTTCAGCTCCATCACCTACGGCATGGCGGCTA	SEQ ID NO:542	R	dn	
Ec_gent	b0733	1104-1203	TCTCCCGCTATGCGCCGGATATGAATCATGTCACAGCCGCACAGTACCAG GCGGCGATGCGTGGCGCGATACCTCAGGTTGCGCCGGTATTCTGGAGTTT	SEQ ID NO:543	R	dn	
Ec_gent	b0734	291-390	TCTTCCGTCCGGTCGGTTTTGACTACCGCTCCAAGATTGAAGAACCCGC TGGCGTAACATGTGGGACTGGGGCATCTTCATTGGTAGCTTCGTTCCGCC	SEQ ID NO:544	R	dn	
Ec_gent	b0735	95-194	TGTTTTGGGACCCATCTCGTTTTTGCCGCGAAGACCAGTGAACTGGAAATC TGGCATGGTTTATTGCTGATGTGGGCCGTCTGTGCTGGTGTGATTCACGG	SEQ ID NO:545	R	dn	
Ec_gent	b0794	563-662	TGGCGGGCGAAGGGATGTTAATCCTCTGGAGTACCTCGTATCTCGACGAA GCCGAGCAGTGCCGTGACGTGTTACTGATGAACGAAGGCGAGTTGCTGTA	SEQ ID NO:546	R	dn	
Ec_gent	b1049	748-847	CCGGAGCATCGCACGGCGTTGATCATGCCTATCTGTAACGAAGACGTGAA CCGTGTTTTTGCTGGCCTGCGTGCAACGTGGGAATCAGTAAAAGCCACCG	SEQ ID NO:547	R	dn	
Ec_gent	b1244	397-496	GCTGGCAATGACCGGGGTTGTTATCCCCAGTTTTGTGGTTGCGCCATTAT TAGTCATGATATTTGCGATCATTTTGCATTGGCTGCCGGGCGGTGGCTGG	SEQ ID NO:548	R	dn	
Ec_gent	b1378	1056-1155	GAAACTCTGCCCCGTGTCATTGGTGGGCGCTATGGTCTTTCATCCAAAGA ATTTGGCCCGGACTGTGTACTGGCGGTATTTGCCGAGCTCAACGCGGCTA	SEQ ID NO:549	R	dn	
Ec_gent	b2255	944-1043	CCGGGTACTCATCCTCGGGGTGAATGGCTTTATTGGCAACCATCTGACAG AACGCCTGCTGCGCGAAGATCATTATGAAGTTTACGGTCTGGATATTGGC	SEQ ID NO:550	R	dn	
Ec_gent	b2276	182-281	TGGACGTTTACGCCGCTGATGCGGCGTTGATGGTTTCGCCATGCTTTACACC GGGCTGGTATTTGTTGGCGAGCCTCGCCACCTGTACTTTCGCCTACCCGTG	SEQ ID NO:551	R	dn	
Ec_gent	b2277	421-520	CTTCTGGGAAATGATGCTGGTGCCGATGTACTTCCTGATCGCACTGTGGG GGCATAAAGCCTCTGACGGTAAAACGCGTATCACGGCGGCAACCAAGTTC	SEQ ID NO:552	R	dn	
Ec_gent	b2278	904-1003	GACATCAAACGTGTTCTCGCTTACTCTACCATGAGCCAGATTGGCTACAT GTTCCTCGCGCTTGGCGTGCAGGCATGGGATGCGGCGATTTTCCACTTGA	SEQ ID NO:553	R	dn	
Ec_gent	b2279	178-277	GTGATGTACATTCTCGCCATCAGCCTCGCGGCGGCAGAAGCGAGTATCGG CCTTGCGCTGCTGCTGCAACTTCACCGTCGTCGCCAGAACCTGAACATCG	SEQ ID NO:554	R	dn	
Ec_gent	b2280	311-410	TGGTGGTGATTGTTTACGCCATCCTCGGTGTTAACGATCAGGGTATCGAC GGTACGCCAATCAGTGCTAAAGCAGTGGGTATTACGCTGTTCGGGCCTTA	SEQ ID NO:555	R	dn	
Ec_gent	b2281	47-146	GTATCTGGATGATCGGCCTGCACGCGTTCGCCAAACGCGAAACGCGAATG TACCCGGAAGAGCCGGTCTATCTGCCGCCCCGTTATCGTGGTCGTATCGT	SEQ ID NO:556	R	dn	

Ec_gent	b2282	723-822	ATCGGGATTGTGACCATCTCTGCATTGATGGTGACGCTGTTCTTCGGTGG CTGGCAAGGCCCGTTGTTACCGCCATTCATCTGGTTCGCGCTGAAAACCG	SEQ ID NO:557	R	dn
Ec_gent	b2283	160-259	CAATACCAAAACGCGGAAGACACGCGTGGTCGCCTGGTGATGTCCTGTAT GACACCGGCTTCCGATGGCACCTTTATTTCCATTGACGACGAAGAAGCGA	SEQ ID NO:558	R	dn
Ec_gent	b2284	655-754	GAAACCCTGTGTAACGTTCCGGCGATCCTCTCGCTAACGGCGTGGAGTGGTA TCAGAACATCTCGAAAAGTAAAGATGCTGGCACCAAGCTGATGGGCTTCT	SEQ ID NO:559	R	dn
Ec_gent	b2285	32-131	CTTTTGAGCTGAGTGCGGCAGAGCGTGAAGCGATTGAGCACGAGATGCAC CACTACGAAGACCCGCGTGCGGCGTCCATTGAAGCGCTGAAAATCGTTCA	SEQ ID NO:560	R	dn
Ec_gent	b2286	192-291	AAAGAAACTGCCGAAACCTTACGTCATGCTGTTTGACTTACACGGCATGG ACGAACGTCTGCGCACACACCGCGAAGGGTTACCTGCCGCGGATTTTTCC	SEQ ID NO:561	R	dn
Ec_gent	b2726	31-130	TGCCAACGGGCACTGGAATTGATCGAACAGGCAGGCCGCAAAACACGGCGC AAAACGCGTAACTGGGGTCTGGCTCAAAATTGGCGCATTTTCTTGTGTCG	SEQ ID NO:562	R	dn
Ec_gent	b2727	1-100	ATGTGTACAACATGCGGTTGCGGTGAAGGCAACCTGTATATCGAGGGTGA TGAACATAACCCTCATTCCGCGTTTCGTAGCGCGCCATTTGCCCCGGCGG	SEQ ID NO:563	R	dn
Ec_gent	b2729	725-824	AAATAGCGGCCCACAGCAAGGTAGAGAATCAGTATCGTCGGGTGGTACCG GATGCCGGTAACCTGCTGGCGCAACAGGCGATTGCCGATGTGTTCTGTGT	SEQ ID NO:564	R	dn
Ec_gent	b2957	72-171	CAATATCACCATTTTAGCAACCGGCGGGACCATTGCCGGTGGTGGTGACT CCGCAACCAAATCTAACTACACAGCGGGTAAAGTTGGCGTAGAAAATCTG	SEQ ID NO:565	R	dn
Ec_gent	b2996	917-1016	GGTTCTGGTACTGACGGGTGTGCCTTATGAAAATCTCGACCTGCCGAAAC TGGACGATCTTTCTACCGGTGCGCGTTCCGAANNNNNNNNNNNNNNNNNN	SEQ ID NO:566	R	dn
Ec_gent	b3118	187-286	TAACACCTGCCGGTCAATTGTTACTCTCCCGTTCCGAATCCATTACCCGT GAAATGAAAAATATGGTTAATGAGATAAGCGGTATGTCTTCTGAGGCGGT	SEQ ID NO:567	R	dn
Ec_gent	b3745	435-534	CAGCTATTAGAAGAAGAACGCGAACAACTGTTGAGTGAAGTTCAGGAACG CATGACGCTGAGCGGACAACTTGAACCGATTCTCGCAGATAACAATACCG	SEQ ID NO:568	R	dn
Ec_gent	b3891	371-470	CAGTGATTGAGAATCTGGAGAAGGCATCGACTCAGGAGCTGGAAGATATG GCCAGCGCACTGTTTGCCTCTGATTTCTCGTCCGTCAGCAGCGATAAAGC	SEQ ID NO:569	R	dn
Ec_gent	b3892	287-386	TCGTCAACGAGGAAGTAGGTGACACCGGGCGTTATAACTTCGGTCAGAAA TGCGTTTTCTGGGCGGCGATTATTTCCTGGTTCTGCTGGTGAGCGG	SEQ ID NO:570	R	dn
Ec_gent	b4139	503-602	TGGGTCACCAGAAAGGTGAATATCAGTACCTGAACCCGAACGACCATGTT AACAAATGTCAGTCCACTAACGACGCCTACCCGACCGGTTTCCGTATCGC	SEQ ID NO:571	R	dn
Ec_gent	b4152	140-239	TGTTTGCCCTGAAAAATGGCCCGGAAGCCTGGGCGGGATTCGTCGACTTT TTACAAAACCCGGTTATCGTGATCATTAACCTGATCACTCTGGCGGCAGC	SEQ ID NO:572	R	dn

Ec_gent	b4153	169-268	TCCTGCCGTATGGCGATTTGTGTTCCTGCGGCATGATGGTTAACAACGT GCCAAACTGGCATGTAAAACCTTCCTGCGTGATTACACCGACGGTATGA	SEQ ID NO:573	R	dn	
Ec_gent	b4154	959-1058	GCGAGAAAAACTGCATGAACGTCTGCCGTTCATCTGCGAACTGGCGAAA GCGTACGTTTGGCGTCGATCCGGTTAAAGAACCGATTCCGGTACGTCCGAC	SEQ ID NO:574	R	dn	
Ec_gent	b0014	208-307	ACGCCTGATTGGCCGCCGCTTCCAGGACGAAGAAGTACAGCGTGATGTTT CCATCATGCCGTTCAAAATTATTGCTGCTGATAACGGCGACGCATGGGTC	SEQ ID NO:575	R	up	
Ec_gent	b0015	289-388	TTTCGGCGATATTTTTGGCGGCGGACGTGGTCGTCAACGTGCGGCGCGCG GTGCTGATTTACGCTATAACATGGAGCTCACCCTCGAAGAAGCTGTACGT	SEQ ID NO:576	R	up	
Ec_gent	b0019	464-563	TTGATGGCTCTGGCTATTATCGACGATCTTGGGGCCATCATTATCATCGC ATTGTTCTACACTAATGACTTATCGATGGCCTCTCTTGGCGTCGCGGCTG	SEQ ID NO:577	R	up	
Ec_gent	b0161	769-868	CGGCGGCAACATCGGTATCGGTTTTGCTATCCCGAGCAACATGGTGAAAA ACCTGACCTCGCAGATGGTGGAATACGGCCAGGTGAAACGCGGTGAGCTG	SEQ ID NO:578	R	up	
Ec_gent	b0199	787-886	CTGACTGCGTGCCGATGCTGCGTCTGGAGTTTACCGGTCAATCGGTCGAT GCCCCACTGCTTTCTGAAACCGCGCGTCGTTTCAACGTCAACAACAACAT	SEQ ID NO:579	R	up	
Ec_gent	b0313	137-236	GCGTTTCTACGGGGATCATCAGCCACTATTTCAGGGACAAAAATGGTCTG CTGGAAGCAACCATGCGCGATATCACCAGTCAGCTGCGTGACGCGGTTTT	SEQ ID NO:580	R	up	
Ec_gent	b0460	298-397	TGCCAGACAATTGACACGCTGGAGCGTGTTATCGAGAAAAATAAATACGA ATTATCAGATAATGAACTGGCGGTATTTTACTCAGCCGCAGATCACCGCC	SEQ ID NO:581	R	up	
Ec_gent	b0631	67-166	GCGTTACCTGAGCTGGTTGATCAGGTGGTTGAAGTGGTACAGCGCCATGC GCCAGGTGACTACACCCCAACGGTAAAACCAAGCAGCAAAGGCAACTACC	SEQ ID NO:582	R	up	
Ec_gent	b0841	233-332	TCCGCACGACCGACCCTTTGTCGAAAATATCGGCTATAACTTCCTGCATC ATGCGGCGGATGACTCATTCCCAAGCGATCACGGTACGGTGATTTTCACC	SEQ ID NO:583	R	up	
Ec_gent	b1113	737-836	GTCTGGCGGCCTATGGCGGCGTTTATTTGCTTCACGGTACGAACGCCGAT TTCGGCATTGGCATGCGGGTAAGTTCTGGCTGTATTCGTCTGCGGGATGA	SEQ ID NO:584	R	up	
Ec_gent	b1304	368-467	CGAGCTGGAAAACAAATTGAGCGAACACGCGCTCGCCAGCAGGCATTGA TGTTACGCCATCAGGCGGCAAACTCGTCGCGCGATGTGCGTCGTCAGCTG	SEQ ID NO:585	R	up	
Ec_gent	b1305	72-171	GCATTACAGCAATCGTTCTGGTCGCAGTGAATTGTCGCAAAGTGAGCAGC AGCGATTAGCGCAACTGGCTGATGAAGCAAAACGGATGCGCGCGAACGTATT	SEQ ID NO:586	R	up	
Ec_gent	b1306	91-190	GATGTACCGGTAAAACTGGTGCGTATCCTGGTGGTGCTGTCGATTTCTT CGGTCTGGCGCTGTTTACCCTGGTTGCTTACATCATTTTGTCATTTGCGC	SEQ ID NO:587	R	up	
Ec_gent	b1436	58-157	CTCATGGCAGGGCACAAAGGACATGAATTTGTGTGGGTAAAGAATGTGGA TCATCAGCTGCGTCATGAAGCGGACAGCGATGAATTGCGTGCTGTGGCGG	SEQ ID NO:588	R	up	

Ec_gent	b1530	73-172	AAAGATCGTCTGCTTAACGAGTATCTGTCTCCGCTGGATATTACCGCGGC ACAGTTTAAGGTGCTCTGCTCTATCCGCTGCGCGGCGTGTATTACTCCGG	SEQ ID NO:589	R	up
Ec_gent	b1531	112-211	GGTTACTCCAAATGGCACCTGCAACGGATGTTTAAAAAAGAAACCGGTCA TTCATTAGGCCAATACATCCGCAGCCGTAAGATGACGGAAATCGCGCAAA	SEQ ID NO:590	R	up
Ec_gent	b1599	127-226	CGGCGGTGCTGGCTGCCTTTAGTGCGCTTTCTCAGGCCGTTAAAGGATC GACTTGTCTGTCGCTTATGCATTGTGGGCGGGTTTGGTATTGCCGCCAC	SEQ ID NO:591	R	up
Ec_gent	b1728	40-139	TCTATTGCTTGTGCGGTATTTGCCAAAAATGCCGAGCTGACGCCCGTGCT GGCACAGGGTGACTGGTGGCATATTGTCCCTTCCGCAATCCTGACGTGTT	SEQ ID NO:592	R	up
Ec_gent	b1829	27-126	AACGAACCTGGCCGTAATGGTCGTTTTCGGGCTGGTACTGAGCCTGACAG GGATACAGTCGAGCAGCGTTCAGGGGCTGATGATCATGGCCTTGCTGTTC	SEQ ID NO:593	R	up
Ec_gent	b2106	505-604	AGGATGCCCATGCACGAGCCCATGCCAATGACATTAAACGACGCTTTGAT GGTAGAGAGGTCACCAACTGGCAAATTTTGCTATTTGGCTTAACCGGTGG	SEQ ID NO:594	R	up
Ec_gent	b2119	114-213	ATACGCCGATGAACTGGCAAAATTAAAACAAAATGATAACGCACCTTGCC CGCCCGGTTGGCAGTTAAGTTTGCCTGCGGCCCGTGCTTTTATCCTTGGC	SEQ ID NO:595	R	up
Ec_gent	b2181	108-207	CGGTGACAACAGCCTGGTGGCGCTTAAATTGCTTAGCCCGGATGGTGATA ATGCATGGTCGGTGATGTATAAACTAAGCCAGGCGTTAAGCGACATCGAA	SEQ ID NO:596	R	up
Ec_gent	b2392	669-768	ATGGCGGTTCGCGTCAACAACGTTATTCCGCCACCAAATGGGATGTGGCT ATCGCCATGACGATTGCCGGTTTTGTCAATCTGGCGATGATGGCTACAGC	SEQ ID NO:597	R	up
Ec_gent	b2531	137-236	TTTCCCGTCTGCGTAAAAATGGTCTGGTTTCCAGCGTACGTGGACCAGGC GGTGGTTATCTGTTAGGCAAAGATGCCAGCAGCATCGCCGTTGGCGAAGT	SEQ ID NO:598	R	up
Ec_gent	b2582	110-209	TGATTAATGCGACCGGTGAAACGCTCGACAAATTGCTGAAGGATGATCTA CCTGTGGTGATCGACTTCTGGGCACCGTGGTGCGGCCCCTGCCGTAATTT	SEQ ID NO:599	R	up
Ec_gent	b2667	113-212	GCACCAGCGCGGGAGAGCTGACGCGCATTACCGGACTGAGTGCCTCTGCG ACATCACAGCATCTCGCTCGTATGCGGGACGAAGGGCTTATCGACAGCCA	SEQ ID NO:600	R	up
Ec_gent	b2980	427-526	GATAACCCGCTGTTATGAAAAAATGCTCGCCGCCAGTGAGAACAACAAAG AGATTTCGCTGATCGAACATGCGCAGTTGGATCACGCTTTCCATCTCGCC	SEQ ID NO:601	R	up
Ec_gent	b3184	20-119	TTGGCATTCTTTTGGCGCTCACCACAGCAATTTGCTGGGGGGCGTTGCCA ATCGCAATGAAGCAGGTGCTGGAGGTGATGGAACCTCCGACACAATCGTGTT	SEQ ID NO:602	R	up
Ec_gent	b3343	1-100	ATGCTGCACACATTACATCGTTCACCCTGGCTGACGGATTTTGCTGCGCT GCTGCGTCTGCTCAGTGAAGGAGACGAACTGCTATTATTGCAAGATGGCG	SEQ ID NO:603	R	up
Ec_gent	b3399	178-277	GTTACGCCACAGGAAGCGATGGAATATATGCGCCAGCAATATCACGACGT ACAGCATACGCTAAACTGGTACTGTCTTGATTACTGGAGTGAGCAACTGG	SEQ ID NO:604	R	up

Ec_gent	b3400	147-246	GAGCTGAATGCCACCGCTCACTCTGCGCCAGGGAAATGACGAACGCACGGT GATTGTAAAGGCGATTACTGAACAGCGTCGCCCCGCCAGCGAGGCAGCCT	SEQ ID NO:605	R	up
Ec_gent	b3401	390-489	GTTGGTCTGGAAGGTGATACCCTGGCGGCCTGCCTGGAAGATTACTTTAT GCGTTCTGAACAGCTGCCGACGCGCCTGTTTATTCGCACCGGCGACGTAG	SEQ ID NO:606	R	up
Ec_gent	b3461	130-229	CATGGCGATCTGGAAGCAGCTAAAACGCTGATCCTGTCTCACCTGCGTT TGTTGTTCATATTGCTCGTAATTATGCGGGCTATGGCCTGCCACAGGCGG	SEQ ID NO:607	R	up
Ec_gent	b3635	113-212	CAGAAGAGATCTACCGTTTAAGCGACCAACCAGTGCTTAGCGTGCAGCGG CGGGCTAAATATCTGCTGGAGGCTGCCTGAGGGCTGGATTATCATTCA	SEQ ID NO:608	R	up
Ec_gent	b3686	100-199	TTCCCGCCGTACAACATTGAGAAAAGCGACGATAACCACTACCGCATTAC CCTTGCGCTGGCAGGTTTCCGTCAGGAAGATTTAGAGATTCAACTGGAAG	SEQ ID NO:609	R	up
Ec_gent	b3687	101-200	GCGGCTACCCTCCGTATAACGTTGAACTGGTAGACGAAAACCATTACCGC ATTGCTATCGCTGTGGCTGGTTTTGCTGAGAGCGAACTGGAAATTACCGC	SEQ ID NO:610	R	up
Ec_gent	b3743	149-248	GGATCATTACCGGGGCGCGTATTGATGTCAGCCCGAAGCAGCTCGGTTAT GACGTAGGCTGCTTTATCGGCATTATATTAAAGAGCGCCAAAGACTACCC	SEQ ID NO:611	R	up
Ec_gent	b3820	241-340	GTGTGCGTGGGAAGTACCTTAACCCGCCACGAAACCATCAGTGAAGATGA ACTACGCCAGCGGCTATCGCGGATGGGGACCATTGATCTTCGCGTTGATT	SEQ ID NO:612	R	up
Ec_gent	b3828	62-161	CCGCTGCGGCGACGTTGCATCAGACGCAATCCGCCCTGTCTCACCAGTTT AGCGATCTGGAACAACGCCTTGGCTTCCGGCTATTTGTGCGTAAGAGCCA	SEQ ID NO:613	R	up
Ec_gent	b3932	133-232	GCGGGCTTTGCGGGCGGTACTGCGGATGCTTTTACGCTGTTCGAACTGTT TGAACGTAAACTGGAAATGCATCAGGGCCATCTGGTCAAAGCCGCCGTTG	SEQ ID NO:614	R	up
Ec_gent	b3941	125-224	GGAACTCCATCGATCGCCTTAGCAGCCTGAAACCGAAGTTTGTATCGGTG ACCTATGGCGCGAACTCCGGCGAGCGCGACCGTACGCACAGCATTATTAA	SEQ ID NO:615	R	up
Ec_gent	b4060	100-199	ATGGCTACCCTCACCACTGGCGTGGTTCTTCTTCGCTGGCAACTTCTTAG TGCCGTAATGATGTTTCTGGCCAGCACACTCAACATCCGTTTTCGTCGGT	SEQ ID NO:616	R	up
Ec_gent	b4062	171-270	CGCCTGTTACTGGCCGCCGTTGAGTTGCGCACCACCGAGCGTCCGATTTT TGATATCGCAATGGACCTGGGTTATGTCTCGCAGCAGACCTTCTCCCGCG	SEQ ID NO:617	R	up
Ec_gent	b4242	808-907	CGTGTTAGTGAGCAGGAAGCGAGCCGAATGCCTTTCAGCAAGGGATCAG CCGCGTCAGTATGCTGCTGATTCGCTTTATGCTGGTGATGGCTCCGGTGG	SEQ ID NO:618	R	up
Ec_gent	b4321	100-199	GCGGCGCTGTCCGTCGGGATGCTGGCGGGCATGGATTTGATGTCGCTGCT GCACACCATGAAAGCGGGCTTCGGCAACACGCTGGGGGAACTGGCTATCA	SEQ ID NO:619	R	up
Ec_gent	b4322	867-966	GGTCCGCGTATTTACTTCACCCATCTGCGCTCCACCATGCGTGAAGATAA CCCGAAAACCTTCCACGAAGCGGCGCACCTGAACGGTGACGTTGATATGT	SEQ ID NO:620	R	up

Ec_gent	b4484	128-227	GAGCCATATGTTCGACGGCATAAGTTTAACCGAACATCAGCGTCAGCAGA TGCGAGATCTTATGCAACAGGCCCGGCACGAACAGCCTCCTGTTATAGTT	SEQ ID NO:621	R	up		
Ec_gent	b4550	6-105	CCGATATCAGCATACTAAAGGGCAGATAAAGGATAATGCGATAGAAGCAT TACTACATGATCCCTTATTCCGACAGCGCGTAGAGAAAAATAAGAGGGG	SEQ ID NO:622	R	up		
Ab_mero GeneID = NC_021726 (alt GeneID = NC_017847, used for FIG. 6 heatmap)	BJAB07104_00229 (ABTJ_03609)	1591-1690	GGACCAATATTTAAGTCATGCTGTCGGGAAAACCAATCAGCGAGTTTACT TCCTTGATGAAACAGGGCGCAGCTATGCCTTGCCAATTAGTAACTTACCT	SEQ ID NO:623	C			x
Ab_mero	BJAB07104_00412 (ABTJ_03419)	877-976	GATTTTTGCACTATAACCCTTCGCAAGAATATTGGGCCGATAGTGTCGACC CACTCTGGAAACAGCGCTATGACTTAGGGGTAAAAGAGCGTTTTATAGCG	SEQ ID NO:624	C			x
Ab_mero	BJAB07104_00560 (ABTJ_03270)	163-262	ACGAATAAGGCAGATCCATTACGTTTACAACTTGATGCTAGCGAAGGTGT TGTTTTTACCCTTGATCCTAAAGGTGAAGTTGCTGCATACCGTGGTAAAC	SEQ ID NO:625	C			x
Ab_mero	BJAB07104_01090 (ABTJ_02819)	326-425	TCCTGACACGGTTACTTGATGAAGTGCATCAACAATTACCGAAGATTCAG TTGCATTTACATGAAGCTCAAAGTGAGAAGATTGTAGAGCGCCTAGAACA	SEQ ID NO:626	C			x
Ab_mero	BJAB07104_01651	58-157	GCTAATGCAGCTGGTTATGGGGTAATTGATCTAGCTAAAGTTGTTGAAAG TAGTACTTATTTGAAACAGCAAAATGCAAGCTTAAACCAGTCAGTGAAAC	SEQ ID NO:627	C			
Ab_mero	BJAB07104_01716 (ABTJ_01686)	419-518	TAAGCAAGCTCAAGTCATTGGTAATCCGGGTTGTTACCCAACGACTGTTC AACTGGGCTTGGCTCCACTTTTAAAATCAGCACAAGCATTGATTGAAACA	SEQ ID NO:628	C			x
Ab_mero	BJAB07104_02033	221-320	CAGCTGCGGTGAATGATGCTGTGCGTCAAGCTGAAGTAGTTTCTGAAGAA AAAATGCAAAAAGCTAACTCTGGTATGGGTTTACCTCCTGGTTTAGCAGG	SEQ ID NO:629	C			

Ab_mero	BJAB07104_02399	139-238	GTAGATGTTAATGAAGTGGCTGCGGAAAGCCAGCGAAAAGCAGCATTAAG TGAACATGACAACTTAGAACCGGGGTCAAATTTATGGATTGCTCGTCAGG	SEQ ID NO:630	C			
Ab_mero	BJAB07104_03654 (ABTJ_00121)	896-995	TACCACGTAATCTTTAAACTTTCGGCTGAAGATGTTTGGGATGGCGTGAAC TATATTTTATCGCTTAAGTTCCAAGAACCACAGTTCTCTGGTCAAACCAA	SEQ ID NO:631	C			x
Ab_mero	BJAB07104_03685 (ABTJ_00092)	148-247	GACCAGTCAACTCGTTGCAGACAGCTTATCTGAGCTTGAACCTGCCAATA CGGTCTCTTTAGCTCTGATTGCCAATCGCTATGCGACCAATCCAAGTGTG	SEQ ID NO:632	C			x
Ab_mero	BJAB07104_03755 (ABTJ_00027)	466-565	TTGTGTCTGGCGGACCAATGGAAGCAGGTAAGGTTAAATTCCGCGGTGAT GAAAAGCAATTGACCTTGTAGATGCTATGGTTGTTGCAGCTGATGACAG	SEQ ID NO:633	C			x
Ab_mero	BJAB07104_00185	361-460	CTCATGAACTTAATGGACTTGATCCCAGTTGACTGGATTCCTCAAGTTGC TGCATTTGTGGGTGCTAACGTATTTGGTATGGACCCTCACCACGTTTACT	SEQ ID NO:634	R	dn		
Ab_mero	BJAB07104_00186 (ABTJ_03655)	105-204	AGAAGCTGTTGCTCGTCAACCAGAATTAGCTCCACAACTTCAAACTCGTA TGTTCTTAATCGCGGGTCTTCTTGATGCTGTGCCTATGATCGGTGTTGGT	SEQ ID NO:635	R	dn		x
Ab_mero	BJAB07104_00187	227-326	TCGAACAAGCGAACCGTCGTGCAGCGCAATTGATCGAAGAAGCTCGTACT CAAGCTGCGGCTGAAGGTGAGCGTATTCGTCAACAGGCTAAAGAAGCTGT	SEQ ID NO:636	R	dn		
Ab_mero	BJAB07104_00188 (ABTJ_03653)	404-503	CAGCACAGTAACTGTTTCAGTTGAAGTTAAACCTGAGCTTATTGCAGGTG TTGTAATTCGTGCAGGCGATCAAGTGATAGATGATTCTGCGCTTAACAAG	SEQ ID NO:637	R	dn		x
Ab_mero	BJAB07104_00189	410-509	AAGTAGCACCAGGTGTAATTTGGCGTCAATCTGTAGACCAACCTGTTCAA ACTGGTTATAAATCAGTTGATACCATGATTCCTGTGGGTCGTGGTCAGCG	SEQ ID NO:638	R	dn		
Ab_mero	BJAB07104_00190 (ABTJ_03651)	730-829	CACGTATGGTCGCAATGAAAGCAGCGACAGATAACGCAGGTCAGCTTATC AAAGACTTACAACTCATCTATAACAAGCTGCGTCAAGCCGCGATTACTCA	SEQ ID NO:639	R	dn		x

Ab_mero	BJAB07104_00191 (ABTJ_03650)	868-967	ACTAAATCTGGTTCGATCACTTCGATCCAAGCAGTATATGTACCTGCCGA TGACTTAACAGACCCATCGCCTGCAACTACATTTGCTCACTTAGACGCAA	SEQ ID NO:640	R	dn	x
Ab_mero	BJAB07104_00192 (ABTJ_03649)	215-314	AACCTCATGTTGTGACGGTTCTTGCAGATACTGCAATCCGTGCTGACAAT TTGGATGAAGCTGCAATTTTAGAAGCACGTAAAAATGCTGAACAATTGCT	SEQ ID NO:641	R	dn	x
Ab_mero	BJAB07104_00485	1153-1252	AGCATTTATTGCTGGTGTTGACCGTATCATGGATATGGCTCGTACTGCGT TGAACGTTGTAGGTAACGCGCTTGCTGTACTTGTAATCAGTAAATGGGAA	SEQ ID NO:642	R	dn	
Ab_mero	BJAB07104_00893	336-435	TAACCATATTCAACATGATGATGCCGATTATGTGGGGGCAGTAAAGAAA ATATGATGGGGATTATTAGAGAAAAGAAAAGAAGAAAGGAAAGAACTGG	SEQ ID NO:643	R	dn	
Ab_mero	BJAB07104_01701	93-192	TTTACTGGTGCATCCTTCCCTCATGTTAGATGCAAACGGACACTACAATC ATAGCCAGCTTATGCTGGTGATGGTGGGTATTTCCGGAGGCTTCATTTAT	SEQ ID NO:644	R	dn	
Ab_mero	BJAB07104_01703	381-480	CAACATCTAGGAGTAACTTGGTTAGTTGCCCTAGGTTCTAACATGTCAGC GCTCTGGATTTTAGTTGCGAATGGCTGGATGCAAAACCCTGTAGGTGCAG	SEQ ID NO:645	R	dn	
Ab_mero	BJAB07104_03045	361-460	AGCCGTTTCTTCAATGGTTTCCGTCGTGATGCTCACCCTATGGCAATCAT GGTTGGTGTAGTAGGCGCATTATCTGCTTTCTATCACAACACCTTGACA	SEQ ID NO:646	R	dn	
Ab_mero	BJAB07104_03047	673-772	TTTAGAAGAAACTCCTCCTGATGAAGCCTTTGGGAAGGTGAATGTTTCG TATTTGATGGACGTACTGCTGTAACTCATGGTGTTGAAGAAGGTGCAAAC	SEQ ID NO:647	R	dn	
Ab_mero	BJAB07104_03111	62-161	TCAATAGCTGCTATATGTTGAATGACCAAGGTAAAGAAGTACCAATCACA ACTGCAATGATTCGTTCAGTATGTCATCAGTTACTTAACCAGTGCCGCGC	SEQ ID NO:648	R	dn	
Ab_mero	BJAB07104_00049	107-206	ATCATGATGACGATCGTTATGACCGTAACGATGGACGTCGATATAGTGAG TGGGAACGCAAACGTTGGGAAGAGCGTAAAAGATTATATGAACAACAACG	SEQ ID NO:649	R	up	
Ab_mero	BJAB07104_00069 (ABTJ_03781)	132-231	TATGGCAAGCTTTGCTGATCCTCCTTTGACCGAGGACATGGCCCGAAAG GTCCTAAAGGCGGACCTCGTGGTGAATGGAATGATCGTGTGGGCATAAATTT	SEQ ID NO:650	R	up	x
Ab_mero	BJAB07104_00138	260-359	AAGACTTGATCCGTGCCAACATGAAAGAAATCGCACAAGTATTGACGGCT GAACAAGGTAAAACTTTGGCAGATGCCGAAGGTGATATTCAACGTGGTCT	SEQ ID NO:651	R	up	

Ab_mero	BJAB07104_00139	518-617	ATAACCTGATTTAGGAATTTCAATGGCTGCGGTGGCCGAAGGCATGGCA CTCGGTGTGAAGCTAGGCATCGACCCACAAGCATTGGCAGGTGTAATTAA	SEQ ID NO:652	R	up		
Ab_mero	BJAB07104_00140	1011-1110	GGGCAAACTGAAGTAGGCATGGTGGTGTGTAATCATCATGGTTTAAAACA TGAAATTCATGCTGGTTCAGCAGGTTTTCCAAGTCCGGGCTATCGTGTTG	SEQ ID NO:653	R	up		
Ab_mero	BJAB07104_00444	132-231	TGTGACTCTTGATATTTCAAGTGCATCACACCCGTTCTACACAGGTGAAG TACGTCAAGCAAGTAATGAAGGGCGTGTTGCAAGCTTTAACAAACGCTTC	SEQ ID NO:654	R	up		
Ab_mero	BJAB07104_00589	373-472	GCTGATTTAACCGCGAATAAACAAGGCTTACGGACCAACTCTAGTGTTTC TACAGGACATTCTTTCGACTTAAATTCGGGAGATGACAGCGCGAAAGGTT	SEQ ID NO:655	R	up		
Ab_mero	BJAB07104_00590	1663-1762	GAATATTATGCTGGTTTCGGTGACTGAACGTACGCAAGAAATTGGTGTGC GTATGGCTGTGGGTGCTCGACAAAGTGATATTTTGCAGCAGTTCCTGATT	SEQ ID NO:656	R	up		
Ab_mero	BJAB07104_00591 (ABTJ_03239)	1104-1203	TGAACAAAAACAACTTATTGAACAAGGCAAAGCAACACTAAGTGTAGTTC GCGTTTTACAAGCAGATGGTACGACTAAACCAACACACAATTTTGGTAGGT	SEQ ID NO:657	R	up		x
Ab_mero	BJAB07104_00622	436-535	TGATTAATGGCACACAGATATGCCACGCTTTTTGGTACAGAACACATTGCCCAA GCCCAAGAAATGCTAGAAGCAGTCAATCACCCTGCCTTAAAAATGCAATA	SEQ ID NO:658	R	up		
Ab_mero	BJAB07104_01132	328-427	CGTTCTAAGTTGAAAAAAATTATCGATGAAGATAGTTATTTGACTGCCGA ACATGAATTAAGTCCAATGACGATTAATGTAGATAAGGCAACGCAAGAAA	SEQ ID NO:659	R	up		
Ab_mero	BJAB07104_01335	1390-1489	CTGGTAGAAGGCACTAAACAAGCTCAGGTTGAACTTGATAAAGCACGTAT TGCTTTTGAAAAAGCTCAGCGCGAAGGCGATTTGGCAGAAGCAGCACGTT	SEQ ID NO:660	R	up		
Ab_mero	BJAB07104_01499	775-874	ACAGGCCAAAAACTACGTAACCACCCTCACCTCAATAAATATTCGATTCC ATTTAGTATGGAAGCCGACTCGGTAAACAGTGCAATTTTAAGCCCTGAGG	SEQ ID NO:661	R	up		
Ab_mero	BJAB07104_01500	798-897	TAAAGTTCAATGAAGAAACAGGCCACTATGAGTTTGGCGAGATTGACTGG CACGAATTTAATGAAGTGATTGCCGGACGTGGACCATGTAATCACGAGCG	SEQ ID NO:662	R	up		
Ab_mero	BJAB07104_01502	227-326	AGAACGTGAGTTTTTAAACCTCTTGTTGTGCGAACAACCCAATGGTGACT TTGCACAAACGATTGTACGCCAATGGTTGATGGACCATTACCATCTTCAT	SEQ ID NO:663	R	up		
Ab_mero	BJAB07104_01504	472-571	GCCGAGCAAATTATGGATTTGAAAGATCAGTTCAAAGAACGCTTTCAACT TATCAATATTTTTTCTCGTGAGTTCAACGATAGTGAACTAATGAACGGTC	SEQ ID NO:664	R	up		
Ab_mero	BJAB07104_01505	525-624	TGCAGTCAAGTGGTTCCGACCGAATTAACCGTTGAATATGCGGTTCAACT TGCAGCCAAAATTGCCAAACAAGCGCCTTTAGCGATTCGCGTGATTAAAC	SEQ ID NO:665	R	up		

Ab_mero	BJAB07104_01508	927-1026	CAGGTTTAACGCTAGATCAGATGGATGTGATTGAGCTGAATGAAGCATTC GCAGCCCAATCTTTGGCTTGTATGCGTGAACTTGGTCTAAAAGATGACGA	SEQ ID NO:666	R	up
Ab_mero	BJAB07104_01509	228-327	AGACAACTATCCGTTTGGTATGTTTGCCGTACCGCAAGAGCAAATTGTGC GTTTACATGCATCATCTGGTACAACGGGTAAACCGACTGTGGTGGGTTAT	SEQ ID NO:667	R	up
Ab_mero	BJAB07104_01629	567-666	GAGTATGTAGCACAGCTCCCTAAAAATATTGTACCGCTTGCCATGCAAGT TGCAGCGATGCAACGTGATTTAATTGAGTTACAGGATCAGTCTTCTACCG	SEQ ID NO:668	R	up
Ab_mero	BJAB07104_01630	1236-1335	ATTGGTTATGAAAACTCTGCAAAAGTGGCGAAAACTGCTTATAAAGAGAA TAAAACTTTAAAACAAGTTGCTGTAGAGCTAGGACTTGTTACAGCAGAGC	SEQ ID NO:669	R	up
Ab_mero	BJAB07104_01739	705-804	AATTGCAAGTGTGCTTGGCATGATTGTCGGGAATACGGGCAAGATGGCAC GGGATTGGTCACTCATGATGCAAACTGAAATTGCAGAGTTGTTTGAGCCA	SEQ ID NO:670	R	up
Ab_mero	BJAB07104_01740	425-524	TTTAGCCGAGCTAGTTAAAACTACCCATACCCGCTGGTTCAGTGAAAAAT TTGACTATCAGCATAATGTGGTTGCACAGACAACGATTCAAAGTCTCGCA	SEQ ID NO:671	R	up
Ab_mero	BJAB07104_01741	792-891	CCAAAGGTACGGTTTTTGCTTTGGGTGACTTACTTCATGGGACTCGTGGTT GTTTACTTGCTAACAAGTTGGTTACCAACACTTATGCGTGAAACAGGTGC	SEQ ID NO:672	R	up
Ab_mero	BJAB07104_01742	268-367	ACTAAAGAAGATTTAAAGAGCTGATCTTACACAGTTCACTCTATGCGGG TTTACCTGCTGCAAACGCTGCAATGCATATGGCTGAAGAAGTCTTTAAAG	SEQ ID NO:673	R	up
Ab_mero	BJAB07104_01743	291-390	TCTAGAAGTATGGCAAGCCAATGCTTCTGGTCGTTACCGCCATCCAAACG ATAAGTTTATTGGTGCAATGGACCCTAACTTTGGTGGGTGTGGTCGTACC	SEQ ID NO:674	R	up
Ab_mero	BJAB07104_01744	459-558	TTTGAAGATGAAGCAGAGGCAAATGCTAACGATCCAATTCTAAATAGCAT TGAATGGGCACCACGTCGCCAAACACTTATTGCGAAACGTTTTGAAGAAA	SEQ ID NO:675	R	up
Ab_mero	BJAB07104_01747	393-492	TCGCGGGAAAATTTGGCGTTTATCCCAAGCATGGGTGAAGAAGGGCTTTG TTGATAATACTGTACAGGTCAAATTTGGTCGTATGGGAATGTCAGAGGAC	SEQ ID NO:676	R	up
Ab_mero	BJAB07104_01949	63-162	ATTAGGAACAGGTATTGCGATTGGCATGTGTATGTACAAGAAAAAGCAAA AGAACAGTAAGAGCTTCTCTACTGATAGTGATACCGACTCATTGATTAGT	SEQ ID NO:677	R	up
Ab_mero	BJAB07104_01991	713-812	TATTAGTGGTTGGATACACTTCTGCTGGTTCATTAACGTTTTATGTAGAG ACCGTTTATTCAAAAACCTATTTAACCAACTTAGGGATGGACGGAAAAAC	SEQ ID NO:678	R	up
Ab_mero	BJAB07104_02013	837-936	GGACTAGAACGTTTAGGTGTAGAACTCAATCCACAAGGTTTTGTGGCAAT TGATGACTATTGTAAAACCAACGTAGCAGGGCTTTATGCCATTGGTGATG	SEQ ID NO:679	R	up
Ab_mero	BJAB07104_02014	1274-1373	GGTGGTAGCTTTAGCATTTCAAATTTAGGAATGTTAGGCATTAAACAGTT CGATGCCATTATTAACCCACCGCAAGGTGCAATTATGGCATTAGGTGCTT	SEQ ID NO:680	R	up

Ab_mero	BJAB07104_02015	459-558	TCCGTTATATGTTTGGCGGAAAAGCAAAAGCACCAATGGTTGTACGTGGC ATGATTGGCGCAGGTTTCTCTGCGGCAGCTCAGCATTCTCAGTCACCATA	SEQ ID NO:681	R	up		
Ab_mero	BJAB07104_02016	305-404	TTGCCGATTTAGATAAGGTATGCTCGGTGCCAACGGGATTGTGGTGGT GGGCCTCCTTTAGCAATTGGTGCAGCGTTGACAGCGAAAACCTTAAGAC	SEQ ID NO:682	R	up		
Ab_mero	BJAB07104_02018	727-826	CTATGCCTTATATGGCGATCGACCAGTGAGTACCACTACACTAAAAGCTG AGCTCTCACAGCTTCGAAACCTGATTCCCGATGTGATCGAGTCACGACCA	SEQ ID NO:683	R	up		
Ab_mero	BJAB07104_02356	1747-1846	GTGACTGATGAAATCAAACTGTTAAATGAAGAAGACGGTATTGCGCCAGG TGTAGAAATTCGCCACCGTAATGAACTTGACGCAGTTCAACGTGAGCTGC	SEQ ID NO:684	R	up		
Ab_mero	BJAB07104_02449	155-254	ATGACGCCTTAGGTAAAGTGAAATTACCAAATAAAAAAGTGCAGGCACTG ATCAATGCCAAAAAACTTGGACAAAATGATGAGACCTTGCCGTGCCCTGT	SEQ ID NO:685	R	up		
Ab_mero	BJAB07104_02515 (ABTJ_01386)	227-326	ATCTGCAATTGGCGGTGGTTTAGGTGGCGGTGCAGGTTATACTGTTGGTA AAAGCATGGGTGGTACAAACGGTGGTTACATCGGTGCTGCTTTAGGTGCA	SEQ ID NO:686	R	up		x
Ab_mero	BJAB07104_02516 (ABTJ_01385)	229-328	GCGACCGTCGTAACCGTACAGAAGCGGCTATTGGTGGTGCTTTAGGCGGT GGCGCGGGTTACACCGTTGGTAAAAACATGGGCGGTACAAATGGCGGATA	SEQ ID NO:687	R	up		x
Ab_mero	BJAB07104_02813	410-509	CGGCATTAACTTGGTAAATGTCCGCTTTTTTGGGGAATCGGAGTTCTTAT TTTCCTGCATTAAAATTGTTGCGATTTTAAGTATGATTGGCTTCGGTGCT	SEQ ID NO:688	R	up		
Ab_mero	BJAB07104_02814	398-497	TTGCCCAAACTCGTTTAACTCCTGCAAATGCAGCTTCTGAAATTGACCGC GTATTGCGTCAGTGTTTCCTTGAACGCCGTCCTGTACACATCCAACTACC	SEQ ID NO:689	R	up		
Ab_mero	BJAB07104_02816	606-705	TGTGGTTGGTGCTGGTGAGATTGGTGAAGCATTATCTTCTCATCCAGATG TGCAAAAAGTCGTGTTTACGGGATCAACTCGAACACAGGGCAGCACATTATG	SEQ ID NO:690	R	up		
Ab_mero	BJAB07104_02819	240-339	AATACCCACAAGTGAAAGTGGAAACTGGTGCCCAAAGCACTTATCCAATT TATGACAATGACAGTAATAAATTAAAGAATGGCGTGGCCGCGCGGAAAT	SEQ ID NO:691	R	up		
Ab_mero	BJAB07104_02995	847-946	GGCTATCCTGCCGCAGGTTTGGGTATTTCTTTATCTTCGGGTGCAAATGC AATTCAGACCTCTAAGCTCATCCACCAAACTCTAGATCAGCTTACAACGA	SEQ ID NO:692	R	up		
Ab_mero	BJAB07104_03220	980-1079	TTACATCAGCATGAAGAATCACGACGTCAATGGGTTGCAGATACCTCTCA TGAATTGAAAACTCCATTGGCTGTTTTGCAAGCGCAGATTGAAGCGATGC	SEQ ID NO:693	R	up		

Ab_mero	BJAB07104_03221	183-282	TGGGAACAACACCGTGCAGAGCGTAAAGCTCGTTTTGAGCAAATTCAAAA AGCATGTGAAGGTAAAGCTGTTGGACAAACTGTCAATGTTCAAGTTGGAG	SEQ ID NO:694	R	up		
Ab_mero	BJAB07104_03416	84-183	ACTTGCTTCTGCCTCTATTTTTGCACAAAGTGCGGGCGTTAATGCAGGTG CATCTGCTCAAGTCAACGTACAACCAGGTGGTCTTGTTAGTGGCGTAGCC	SEQ ID NO:695	R	up		
Ab_mero	BJAB07104_03517	916-1015	GGTTTAATTGGCGGAATGCCAGTGACCTCAGTGATTGTCCGTAGTTCTGT AAATGCCAATACAGGTGCACGTAGTAAATGCTCAACCATTATTCACGGTG	SEQ ID NO:696	R	up		
Ab_mero	BJAB07104_03543	158-257	AAAGCTTATCTAAAGTAAAGTGACTACAACCGTCAACGGCCAACCAGGT TCTATTAGCGATTTGGTCAATAGCGGACAAGTACAGCAAGTTTCTGCTGC	SEQ ID NO:697	R	up		
Ab_mero	BJAB07104_03610 (ABTJ_00167)	255-354	CGGCACAAAAGACACTCAATATGGCGTAGGCGTTGAGTACTTCGTTCCTA ACTCTGACTTTTACCTTAGCGGTGATGTAGGCAGAAACGAACGTGAAATC	SEQ ID NO:698	R	up	x	
Ab_mero	BJAB07104_03637	67-166	CTAAACGGAACGGTATGGAAAACGATTGATGACCAAACCAATAAGCCCAA AGCCGTAGTAAAATTTACGGAACAGAAGGATGGAACCTTAACTGCAACCA	SEQ ID NO:699	R	up		
Ab_cip GeneID = NC_017847	ABTJ_00146	382-481	TCAGTGATTGCTGAATTGGGGTTGCCTGTCATTATCAAGCCTGTACATGA AGGTTCAAGTGTAGGCATGAGTAAAGTTGAGAAAGCTGAAGATTTTGCGG	SEQ ID NO:700	C			
Ab_cip	ABTJ_00148	617-716	ATGGTGTCTGTCTTGTCGATATTGGTGCAGGTATTACCAATCTGGCAGTT TATTTAGATGGCCGTTTGGCTTTAGCACGCACCTTACAGCGTGGAGGTGA	SEQ ID NO:701	C			
Ab_cip	ABTJ_00291	614-713	ATTGGTTTGACCAATAGTGAAGGTCAAGGTATCGAAGGCTTGGAAATGCA GTTGAATAAGCAACTGTCAGGTGTAGACGGTGAGCAAAAAATTATTCGCG	SEQ ID NO:702	C			
Ab_cip	ABTJ_00304	588-687	TTTGGCTTGAAGAAAATATGGATGGCCTAGTTGCAAGAGATGCTGACCTT TTAGCAGAGGCTGTTTATCGTTCATGTGCTCACAAAGCCCGCATTGTTGC	SEQ ID NO:703	C		x	
Ab_cip	ABTJ_00727	257-356	TATTTGCTGAAGGAAGCTATGTTCGTGAAGGTCAGGCGCTTTATGAGCTC GACTCTAGAACGAACCGTGCAACGTTAGAAAATGCAAAAGCATCACTCCT	SEQ ID NO:704	C		x	
Ab_cip	ABTJ_00860	314-413	TGACAGGAGTTGCACCTTTACCCAATTGCAAGGTATGTTAACTGCTCAA GGGCAAGTGGCAGGTATTATGGTGACGGGTATTGACCCTAAATATGAAAA	SEQ ID NO:705	C		x	
Ab_cip	ABTJ_01079	1236-1335	TCATTGGCTTAGTAAAATCTGGAAAACCGCTTGATATGGTGGATGTCCAA ATTGGGAATAACCATTATAAAGTGAAGCCAGATGAAGTGGGGTATTGGAA	SEQ ID NO:706	C		x	

Ab_cip	ABTJ_0205 6	1002-1101	CCAGTTTCCACGAATGCTTGTAAGCGCAGAAACTATTGAAGAAAAAGCTG GTGCACTTAATCTTAAAACTGAACAACCACCCAAGTTGCCAGTCGATCCG	SEQ ID NO:707	C		x
Ab_cip	ABTJ_0209 3	213-312	TGTGAAAGTCGTTATATTAGGGCAAGATCCATATCATGGTCCAAATCAGG CAAATGGCTTAAGTTTCTCGGTTCAAAGAGGGGTTGCATTACCACCATCT	SEQ ID NO:708	C		x
Ab_cip	ABTJ_0211 4	722-821	CTGGGCGCGGTGTTACGCGCGGAACAAAACTATATGTAAAAGATGTTCCA GTTCTAGCAGTTCCCTACTTTAACTTCCCGATCGATGACCGCCGTACTAC	SEQ ID NO:709	C		x
Ab_cip	ABTJ_0247 7	288-387	CGTGAAATTCAAACGATCACTGCTAAAGGTAGACCGTCTAAGTTTCAGCA ACAAATAAGTGCTGATAAAGGTATTGCACGCGGTGAAGGACAAACGATTG	SEQ ID NO:710	C		x
Ab_cip	ABTJ_0264 0	997-1096	GCACATGAACAAACCTTAATGCGTTATGAACACCGCCGTAAAGGACAAAA TGATGCGATGATGCATAGTATGTCGGCAATTGGTTGGCTAGAAAGCAGTG	SEQ ID NO:711	C		x
Ab_cip	ABTJ_0281 7	536-635	AGCGCCTCAACCATTAGGCCGTTTATTACCTTCACACATTGCTTCAGCAT TCCAGCAGAATCTTGAAGAAGCGGGTGTTAAATTTGCCTTAGGCACAACC	SEQ ID NO:712	C		x
Ab_cip	ABTJ_0282 1	1195-1294	TGGTAAAGAAGTGACGGCGGTAATTGAATTACGTGCCCGTTTCGATGAAG AGTCGAATATCGAAGTGGCTAACGTTTTACAAGAAGCAGGGGCAGTCGTT	SEQ ID NO:713	C		
Ab_cip	ABTJ_0292 0	831-930	TGTGCAGTTGGCTAGAGAACAACTTGCTCAGCGTCAGCTTATGCCTGTTT TACAATGGGTGATTATTGTTGTAGCAATTGCAGTTTGGGCTGTGCCGGAA	SEQ ID NO:714	C		
Ab_cip	ABTJ_0320 2	1860-1959	ATTGATGGTTTAGACAATGTTGAGCTACATATTGCGCAGTGTTGCCAACC AGTTCATGGTGAATCAATTGCCGGTTATATCACGTTGAACCGTGGGGTAA	SEQ ID NO:715	C		
Ab_cip	ABTJ_0330 2	360-459	TATGGTCCAGATTTCCCGTTAGTAACGGTCCGTGACTGGGTCAAAACTCA AGCCATGCTTTCTGACCGCTTAGGAATAAGTGTCTGGTATGCGGTGGTCG	SEQ ID NO:716	C		
Ab_cip	ABTJ_0333 0	249-348	TGAAGAGCATATGGCGGCAAAAGGACAAGTTTCTCCGGAAGTTTCTGTTT TGCAGCAATTGGCAAAAGATGGCTTCGTTGCAGAATTAAACGTGCTTAC	SEQ ID NO:717	C		x
Ab_cip	ABTJ_0342 5	576-675	CAAGACTACCGCCAAATCATTTTAAATGAGCTGGACTTGAGTATTGAGGC AGATAACACCCGTCGTATGCGCCATTACTTCACTGGTTCAACCATGATGT	SEQ ID NO:718	C		x
Ab_cip	ABTJ_0350 3	352-451	GATTTAAGCGATCAAGGTATGCCAAGTATTGCGGAGCGTGCAGCAGAAAC TGAAGTGAGTCGTGATGGAATGCCTCAGCGAGTTTCTGTGCCAAAACCAG	SEQ ID NO:719	C		x
Ab_cip	ABTJ_0354 4	97-196	AAATACTTTGGTGTGGCGGCACAGGGGCGACTAGATGCCAGTATCTTGTT TAGCATCATTGGATATCGTTTACCTGAATTTCTAACCCTCATTTTACCAC	SEQ ID NO:720	C		
Ab_cip	ABTJ_0379 3	1243-1342	ACACTGCTGGCGTCATAAGACTCCGATATTTTCCGTGCTACACCACAAT GGTTTATCAGCATGGATCAAAAAGGTTTACGTGACGGTGCGCTTAATGCC	SEQ ID NO:721	C		x

Ab_cip	ABTJ_0018 5	132-231	CATGTTAGTGCTTTATGTGGGCTTTATGCTACTTGTGGGCTACAACACAAAG AATTTTTGATGAGTTCCTTTAGTGGTGGTGTAACGACATGGGGGATCCCG	SEQ ID NO:722	R	dn
Ab_cip	ABTJ_0018 6	798-897	TGCTGCAAAAATTATGGGACCAGGTAAACTTGCCGCAAACCCGATTGATG CCTTATCTCTTGGCTTAGCACTCATGTTTGGTACAGCAGGTCTTCCACAC	SEQ ID NO:723	R	dn
Ab_cip	ABTJ_0020 4	60-159	TAAATCACGCCACTTAACCATGATCTCGATTGCAGGGTTATTGGTGGCT CTCTCTTTGTTGGCTCAGGCAGTATTATCTACAACACCGGCCCTGTAGTT	SEQ ID NO:724	R	dn
Ab_cip	ABTJ_0051 0	339-438	GCGAACCTCTTCTTGACTCACGGTTTTAAAAAGGAAAATATTTACGTTAT TGGACGTGGTTCAACTCAACCGTATGTACCGAATACAACCAATGAAAATC	SEQ ID NO:725	R	dn
Ab_cip	ABTJ_0053 6	182-281	TTTCAGCTGAGCTTAACTATGCTCAGCCAGCAAATCAGGCAGAAGTTATT CAGGCTCTCGACAAAGCTGGTTTTAAAGATGCTGTAGTACAAACTTTAGG	SEQ ID NO:726	R	dn
Ab_cip	ABTJ_0068 9	390-489	TGACCAAAAGCGTGAGTCGGTTAAAGCACTACATGGTTTGAATTTCCGTG TGATTGCAGCAGGTGATTCATATAATGATACAACGATGCTTGGTGAAGCC	SEQ ID NO:727	R	dn
Ab_cip	ABTJ_0070 0	68-167	GTGGAGCAATTGGTACCGGATTATTTTTAGGCTCGGCGCAAGTGATTCAA TCTGCGGGACCATCCATTATTTTAGGATATGCCATTGGTGGCTTAATTGC	SEQ ID NO:728	R	dn
Ab_cip	ABTJ_0114 8	1608-1707	GGCAGGTACAAACTTATGTCCAAGCGGGTTCAAATTTAGATAAAGGCTGG CGTGTGGGAGTAGGGCCGACATTAGGATGTATGAATCAGTGGCTTGAAAA	SEQ ID NO:729	R	dn
Ab_cip	ABTJ_0119 9	313-412	AAGTTTAGCCAAACTGGCATGGCATCGTGGTATGGTCGTCAATTTCATGG CCGTAAAACTGCAAGTGGTGAAACATTCGATATGAATGCACTTACTGCTG	SEQ ID NO:730	R	dn
Ab_cip	ABTJ_0140 3	122-221	TGATGGCAATTGTATGGCTTGGAACAGTGGTTACAGGCATTAGTACAATC TTAGGTTACACCACGCTGATATTTGGTTTAGTGGTTACAGCAATTCTGTT	SEQ ID NO:731	R	dn
Ab_cip	ABTJ_0144 2	391-490	TGTATTCGTGCTCAAGAAGGCGGCATCTCTGAAATTGATGAAGATACCAT TGCCTACCATTTCCATGAACCACTAGGTGTGGTTGGTCAAATCATTCCAT	SEQ ID NO:732	R	dn
Ab_cip	ABTJ_0144 5	306-405	TGTCCACAACGGTGTGAATGCCTATAACGAAATGGCTGTGACTTTATTG TGTCGTTAGGCGGTGGCTCATCTCATGACTGTGCAAAAGGGATTGGCTTA	SEQ ID NO:733	R	dn
Ab_cip	ABTJ_0166 9	93-192	TTTACTGGTGCATCCTTCCCTCATGTTAGATGCAAACGGACACTACAATC ATAGCCAGCTTATGCTGGTGATGGTGGGTATTTCCGGAGGCTTCATTTAT	SEQ ID NO:734	R	dn
Ab_cip	ABTJ_0167 1	518-617	TTGTCAGCCTTTCTATGTTGTGCTCATGGCGGCGCTTGGCTTATGCTA CGCACAGACGGTGCCTTGAAACAACGCTCTGCTAAAGCAACTCAAATTAT	SEQ ID NO:735	R	dn
Ab_cip	ABTJ_0167 2	381-480	CAACATCTAGGAGTAACTTGGTTAGTTGCCCTAGGTTCTAACATGTCAGC GCTCTGGATTTTAGTTGCGAATGGCTGGATGCAAAAACCCTGTAGGTGCAG	SEQ ID NO:736	R	dn

Ab_cip	ABTJ_0194 6	1188-1287	ACGGCGAACCCTGAACACTGTAAAGCTTTGGTTGAAAATTCAATTGGTAT TGTGACTGCACTTAACCCATACCTAGGTTATGAAACTACAACTCGTATTG	SEQ ID NO:737	R	dn	
Ab_cip	ABTJ_0213 4	1959-2058	AAACGCGCAGCTGACCTCATGGAAAGCCGTATTCAAGAGTTGATGGTATT ACTTTGCCGTGAAAGTGGTAAAACTTATGCCAATGCGATTGCAGAAGTTC	SEQ ID NO:738	R	dn	
Ab_cip	ABTJ_0220 4	280-379	GTCTCACTTGCCATCGGTATGGGTTTAGCAAACTTTTTCCAACCTGGCGC GGCGCTAGACCTAGCATTACCAACAGCTCAACACAACTTAGTAGTTCTTCTC	SEQ ID NO:739	R	dn	
Ab_cip	ABTJ_0280 6	402-501	GGCAGCCATGCTCCCTCTTTATCAACGCCTCGGTATGAATACACTGATCA TGACAGCACTTATGTTGTTATGTAGTGGTGTAATGAATCTGACCCCATGG	SEQ ID NO:740	R	dn	
Ab_cip	ABTJ_0305 1	1030-1129	GCAGTAGCGTTAATGTCTAGCCCATATAACAACGTAGATGAAGCGCAAAG CCTTGCAGACTACCGTGGTTTGTTCTGGCGCCGTCCAGTACTTACAGCAA	SEQ ID NO:741	R	dn	
Ab_cip	ABTJ_0305 2	710-809	TTGCAGTGAAGTTACCAGTTTTCCCATTGCATGGCTGGTTACCGGATGCC CATGCTCAAGCACCTACAGCGGGTTCTGTAGACTTGGCGGGTATCTTGAT	SEQ ID NO:742	R	dn	
Ab_cip	ABTJ_0339 0	176-275	AGGTGAAGACCTTGTCAAAAAATTTGCTGTGAATGGTGTGTACCGTTGGT TTTGTAGCGAATGTGGTTCACCGCTTATTAGCTCGCGTGATGCTCAGCCT	SEQ ID NO:743	R	dn	
Ab_cip	ABTJ_0343 1	100-199	GGCTTAGCAGTGCTGGGCTATGCGGTTAACTTATTTTTGTTTGCGATGGG TCGTTTGCAAGTCAGCTCACCAGCCATCCTCTAACCGAAACCACCACAATTA	SEQ ID NO:744	R	dn	
Ab_cip	ABTJ_0343 2	1131-1230	TTAAAGATTGCACCGAGAATTAAACAAGAAAAAGCAGCCATGCTGACTTA TTTCCTGATTGCCATGATGCTCGCAGGCTTACCACCTTTTAGTGGCTTCT	SEQ ID NO:745	R	dn	
Ab_cip	ABTJ_0343 3	394-493	GAGCGTGGTGATATTTTGGTCCACTCTCTTAGCACAGAAAATACTGAAAG TGATGTGCAAGACATCAAACAACGCTATGAGGCTCCACTCATGGAAATTT	SEQ ID NO:746	R	dn	
Ab_cip	ABTJ_0350 6	544-643	CAGAACGGACAGCTACAAGTGGACATCCGTGATCAGCGTAATCAAAAAAT GGCCAATCTTTTACTAGATGCCAATATGATGCTGGATGTTCAGCTCACAC	SEQ ID NO:747	R	dn	
Ab_cip	ABTJ_0350 7	1-100	ATGAAACCGGATATTAGTGAATTATCTGTTGAAGAGTTAAAACGCTTACA AGAAGAAGCAGAAGCTTTAATTGCAAGCAAAAAGATCAAGCAATCGAAG	SEQ ID NO:748	R	dn	
Ab_cip	ABTJ_0373 4	909-1008	TGTTCTACATCGACCAAAACACAATCGACTACTTACGCCTAACAGGCCGT GAAGATGCTCAAGTGGCATTGGTTGAACAGTACGCAAAAGAAATTGGCCT	SEQ ID NO:749	R	dn	
Ab_cip	ABTJ_0373 5	126-225	TGTACCGTAGGACGTAGCGGTAACGACTTGCACTATCGTGGCTATGACAT TCTTGACCTTGCGGCAGGTAGCGAGTTTGAAGAAGTTGCTCACTTGCTCG	SEQ ID NO:750	R	dn	
Ab_cip	ABTJ_0373 6	885-984	TTACCACTGAAGAGTTAGCATCTGCCGATGTAAGCCTTGCGCTTTATCCG CTTTCTGCTTTCCGTGCCATGAACAAGGCAGCCGAAACTGTGTATGAAAC	SEQ ID NO:751	R	dn	

Ab_cip	ABTJ_0000 4	1055-1154	GTATCAAGTGAGGTAAAACCAGCGGTAGAGCAAGCAATGAACAAAGAGTT CTCTGCTTACTTACTTGAGAATCCACACAAGCTGCAAAATCAATTGCAGGCA	SEQ ID NO:752	R	up	
Ab_cip	ABTJ_0009 4	125-224	GGCTTGGTTTTATGCTTGCAGGGATGTTTTTTTTGGGGGCTATTGGAAGTG GTCCGTTTTTGGAGTTCAAGTCACTTTTGAAATGCCAGTCACACATATAGTTA	SEQ ID NO:753	R	up	x
Ab_cip	ABTJ_0012 0	100-199	TTGCCAGATTTAAATAGATCTCCGGAACAGGTAGTAGCACAGGTTTCAGA GCTGATTGAGTCTTTACAAGAGGTGGCTTTAGTCGGCAGTAGTCTTGGTG	SEQ ID NO:754	R	up	
Ab_cip	ABTJ_0012 1	880-979	GAGTTACGTAATTTATTACCACGTAATCTTAAACTTTCGGCTGAAGATGT TTGGGATGGCGTGAACTATATTTTATCGCTTAAGTTCCAAGAACCACAGT	SEQ ID NO:755	R	up	x
Ab_cip	ABTJ_0019 2	1893-1992	AACCATCCCACTTGGCATTATGACTTGTGTCACGGGTGTTTCAGGTTCAG GTAAATCAACACTGATTAACCGTACGTTACTCCCACTGGCTGCCAACACAG	SEQ ID NO:756	R	up	x
Ab_cip	ABTJ_0035 7	160-259	GACGACGGTTCAATCCAGCACTTTGAAGGCTACCGTGTACAACACAACTT GTCTCGTGGTCCTGGTAAAGGTGGTGTTCGTTACCATCCAAATGTTGACT	SEQ ID NO:757	R	up	x
Ab_cip	ABTJ_0037 5	427-526	CTAAAAACAATTCCGGGTGCATCGCCTGAACTGATCCATGAAGCAGGTTT ATATGCTGACCGGATGAGTATTAATTTAGAGATGCCGACTGAGATTGGGT	SEQ ID NO:758	R	up	x
Ab_cip	ABTJ_0037 6	440-539	AGTCTGGTTCGTCCTGATTTTAATGTCTTACCACTCATTCAGCCGCATTT TAAACGGCGTTATCAAGATCAGCGTTGGCTCATTTATGATGAGCAACGTA	SEQ ID NO:759	R	up	
Ab_cip	ABTJ_0088 6	398-497	CTTTGGCACAAGGAACTTCTAGCGCTGCGGCCCTGCCTCAGATTCAATTT GTTTCGAACTCACCTGTTGCAGAAGCAGAAGCAGCCTTACAGTCACTAGG	SEQ ID NO:760	R	up	
Ab_cip	ABTJ_0088 7	874-973	ACATGGCAACAAAAAAATTTCGGCATTGCGTGGCCGTGTTATGAAGCGTCT GGTTGATGAAGTCACTACAGCTTTTGCCAAACATCATTATGAAATTATTA	SEQ ID NO:761	R	up	
Ab_cip	ABTJ_0093 0	31-130	GCTTTGGTGAAATTGCCATTTCCAATGCCGAATGAAAGTAACCAAGCAGG CGATGCTGTACACAACCAAGTACGTCCGAAACCTGAACAATATGCAGATA	SEQ ID NO:762	R	up	
Ab_cip	ABTJ_0145 0	1020-1119	ATATTTGTACAACCTGTATGGAAGCATGGCGAAAAATCGAACCTCGTTT AAACTTTTACTCGGTTAAACGTTGTATGTACTGTGGTTCAAATGATCTAA	SEQ ID NO:763	R	up	
Ab_cip	ABTJ_0157 6	525-624	CATCACCTTAGATCCATTAATTATGGAAGACCTCATGCAACAGACATCAG TCAAAGAGGTATGGGAATCGGCTATCAATTAGTCAAACAGCTACAAAGT	SEQ ID NO:764	R	up	
Ab_cip	ABTJ_0162 5	25-124	TCTCAGCAGCGCCCTCCTCTTACTGGCCAACGTTTACGCTCATATGCTTT TGCTTTACTCACTCGCCGAGATTACTCTAAAGCAGAGCTTATCGAGAAAT	SEQ ID NO:765	R	up	
Ab_cip	ABTJ_0162 6	446-545	CTAAAGCAGAAATCGAAGGTGAGATGGGTGACTCTCTCATATGGGTCTACAA GCACGTCTTATGAGCCAGGCACTTCGTAAAATTACGGGTAATGCTAAACG	SEQ ID NO:766	R	up	x

Ab_cip	ABTJ_0206 6	269-368	AAAACATACTTATAACGCCCGTCATGAAACAATTTTCCAAAAACCGAGTT TTCAAGAAGCTGCTCTTAAATGTAAGTTCGGTGTAATACCCGTGACGGAG	SEQ ID NO:767	R	up		x
Ab_cip	ABTJ_0228 0	200-299	ACAACGATAAAATTTACCACATTCCTTTGGCGACAGAACGTGTTGCTGCG GGTTTCCCATCACCAGCGCAAGACGATATTGAGCAAGCACTCGATTTAAA	SEQ ID NO:768	R	up		
Ab_cip	ABTJ_0263 2	77-176	GGGTCGCCAGTAATTATCATTCACGCCGTGGAGAGGTCGATCTGATTGTA AAACGCGGTAACGAATTGATTTTTGTTGAGGTAAAAGCGCGAGGGCAGGG	SEQ ID NO:769	R	up		
Ab_cip	ABTJ_0290 6	812-911	ACATGAAATCGCGCTTGATATTCAAGAAGGCGCCGACATGGTGATTGTAA AACCGGGCATGCCATATCTGGATGTGGTACGTGAAGTGAAAGATACCTTT	SEQ ID NO:770	R	up		
Ab_cip	ABTJ_0306 8	1045-1144	TTATGACATTTATGGTGCAATGCGTGACAACGCGATGCTCTCTAAATGGG CAGGTGGTTTAGGTAATGACTGGACACCTGTACGTGCCTTGAACTCTTAT	SEQ ID NO:771	R	up		x
Ab_cip	ABTJ_0307 0	377-476	TTAAATATGAGTGGGCTTGGCAAAAATATCTAGATGGTTGTGCAAACCAC TGGATGCCTCAAGAAGTGAACATGAACCACGATATCGCACTTTGGAAGTC	SEQ ID NO:772	R	up		x
Ab_cip	ABTJ_0334 0	1-100	ATGACTAAACCACCATATCATGATGATCAAGCGTCATTTTCCGCACCCAT TGAAGATTTGCAAGTGCGAATTGCATTTTTAGATGATTTAGTTGAGGAAT	SEQ ID NO:773	R	up		
Ab_cip	ABTJ_0360 9	1577-1676	AACTACCGTGCTGGGGACCAATATTTAAGTCATGCTGTCGGGAAAACCAA TCAGCGAGTTTACTTCCTTGATGAAACAGGGCGCAGCTATGCCTTGCCAA	SEQ ID NO:774	R	up		x
Ab_cip	ABTJ_0378 4	72-171	GCTAGGTGGTTGTGCCAAAAAAGAGGAGCACACCACAACACTTTAAATA TCGGCTATCAGAAATATGGCATCCTTCCTATTCTAAAAGCACGTGGTGAC	SEQ ID NO:775	R	up		
Ab_cip	ABTJ_0378 5	197-296	AATTTCCAAATGCCAAAATCACTTGGAATGAGTTCCCCGCTGGCCCTCAA ATTTTAGAAGCCTTAGCTGTTGGCTCACTCGATGTTGGCGTTACTGGAGA	SEQ ID NO:776	R	up		
Ab_cip	ABTJ_0380 8	298-397	CAGTATTTCCCGAATGTACAGATCATTGCTACGCCGGAAACAGTAAAGCA TATTCAGGATACTCAAGCGCTTAAAGTTAAATATTGGGGGCCACAAATGG	SEQ ID NO:777	R	up		
Ab_cip	ABTJ_0382 7	339-438	CCCAACTGAAATCCAGTTTCAAGACAAAACATATGCAAGCGAAATTGCCC AGTTCTTTGTTCAGGAACTCTTAAAACACGGTACAACCACGGCCCTCGTT	SEQ ID NO:778	R	up		
Ab_cip	ABTJ_0382 9	144-243	CATGGCAGACTTATGCCGTACGATTACCAAACCACATGAACTCGACTTTA TGACAGTGTCTAGCTATGGCGGCGGTACCACTTCAAGTCGAGACGTTAAA	SEQ ID NO:779	R	up		
Ab_gent GeneID = NC_01784 7	ABTJ_0011 3	325-424	TGTATGCTAGATGACAATGAAGAACGTATTCGTCTAGCTCAATATGGCAC TTCTAATATTGGCCGTTTCAAGACGCTTTATCGCCGTGGTTTAGGTATTC	SEQ ID NO:780	C			x

Ab_gent	ABTJ_0013 4	254-353	GCCTAAAGCAGTTTCTCAATATGATGAGAACTATGGCCAAAGCCAAGTTT ATTACCATCAAGTCAACTTCCAGATTAAAACCAAGCCTTCAGAGCACTAC	SEQ ID NO:781	C		x
Ab_gent	ABTJ_0065 5	351-450	TATATCTATATTCATGGTACACCTGATAAAGAACCGATGGGGGTTCCAAT GTCACATGGGTGTATTCGAATGCGTAATGAAGAAATCATTGAATTGTTTG	SEQ ID NO:782	C		x
Ab_gent	ABTJ_0066 6	964-1063	AGGAATTGGTTTAACTGGACCAAATGCTATGGCTCTAGCCATGTCAAAGC AAGGTGCTCGTGCAGGAACAGCCAGTGCAATTATGGGCAGTATGCAATTT	SEQ ID NO:783	C		x
Ab_gent	ABTJ_0073 5	95-194	GGGCATCTTTAGAGACTCGCCGTAAAGACTTGCAATCAAAAACTGAAAAG TTACAGGCAGAGCGAAATGCCGGTGCTAAACAAGTGGGTCAGATTAAAAA	SEQ ID NO:784	C		x
Ab_gent	ABTJ_0086 0	314-413	TGACAGGAGTTGCACCTTTTACCCAATTGCAAGGTATGTTAACTGCTCAA GGGCAAGTGGCAGGTATTATGGTGACGGGTATTGACCCTAAATATGAAAA	SEQ ID NO:785	C		x
Ab_gent	ABTJ_0088 5	565-664	TCGTGTCACGATCTGCAAACCTCATGGATGTACCCATTACAGTTGAGGGT GCAGAAGAAGTTGCACGCCGTTCACGCGGAACACCGCGTATTGCCAATCG	SEQ ID NO:786	C		
Ab_gent	ABTJ_0088 6	398-497	CTTTGGCACAAGGAACTTCTAGCGCTGCGGCCCTGCCTCAGATTCAATTT GTTTCGAACTCACCTGTTGCAGAAGCAGAAGCAGCCTTACAGTCACTAGG	SEQ ID NO:787	C		
Ab_gent	ABTJ_0125 4	645-744	GTAGAAAATGAGGATTGGGAAGAACAAAGTACATCTGCTTTGCATGACGC AATGAACCAGCTAGATGACCGTTCACGTAATATTTTGCAGCGCCGTTGGT	SEQ ID NO:788	C		
Ab_gent	ABTJ_0247 9	378-477	TTACTGTTCCAAACGGACATGAGGAAGTGCGCCGTCGTGCGGATTTGGTA ACACAGGCGATGGGTGGCCGTGGAGCTGTGCGTGAAGTTTGTGATATGTT	SEQ ID NO:789	C		
Ab_gent	ABTJ_0281 9	326-425	TCCTGACACGGTTACTTGATGAAGTGCATCAACAATTACCGAAGATTCAG TTGCATTTACATGAAGCTCAAAGTGAGAAGATTGTAGAGCGCCTAGAACA	SEQ ID NO:790	C		x
Ab_gent	ABTJ_0313 1	621-720	TGCTTTTTATGCACACAAAGTAAATTACTTCATGATGCTTTAGAGCAAGTTC AATATGGTGAGTTAGCTAAAGTCATTGGTATTTTCTTGGGTGTTGCAGGC	SEQ ID NO:791	C		
Ab_gent	ABTJ_0339 9	562-661	AAACTGGTGACATGGGTATTGGTAAAGATGGCGAGCCTACACATAACTTT ACTCCGGGTTATGAACTTCACGCTAAATACACTCTCTTTGCTGAAGGCTG	SEQ ID NO:792	C		x
Ab_gent	ABTJ_0021 1	1097-1196	AAGTGACCTTAACGCGTGCAGTTGTAGACTCGCAAACTATTGCTTTAAAC AAAGAGCTACAACAACGTCACTTAGAACCAAACCGTAAAGTATTCTACTG	SEQ ID NO:793	R	dn	
Ab_gent	ABTJ_0052 6	25-124	GAATTAGAGTTATTTGAAGTTAATCACGCTGTACAAAAACACCCAAAAAGA GATTGCAACACGTTTTGACTTCCGTGGTCATGATGTTTCTATCGAATTAA	SEQ ID NO:794	R	dn	
Ab_gent	ABTJ_0053 7	519-618	GATCACTGTTCAGTTTGCTGACAATGCGGATCGTGATGCAGCAATGGATT TTTACGCCGTAATGGTAATGAATATACCCAACAGGCATTAGCGAGCACG	SEQ ID NO:795	R	dn	

Ab_gent	ABTJ_0066 9	139-238	TTCTTGCAAAGTATTCGTGTTATGAAAAGCAGCCGTACAGAAGGCGAAGA TGAGCATGGCCTTACACCTTTCCAAGCGTTTGTAACTGGTCTTGCGAGCCC	SEQ ID NO:796	R	dn	
Ab_gent	ABTJ_0070 9	85-184	AATGCGGCAACTTCTGATAAAGAGGAAATTCGAAAGCTTCGTCAAGAAGT TGAAGCATTAAAAGCATTAGTTCAAGAACAACGTCAAGTACAGCAACAAC	SEQ ID NO:797	R	dn	
Ab_gent	ABTJ_0075 9	769-868	AAGGTAACATCGGTTGTATGGTTAACGGTGCTGGTCTTGCAATGGCAACT ATGGACATCATTAAACTTTATGGTGGTCAGCCTGCAAACTTCCTTGACGT	SEQ ID NO:798	R	dn	x
Ab_gent	ABTJ_0081 6	116-215	CAGATGCTTCTGGAAATACCGAATTAGCGTTAGATGGGGGTAAAATCCAA AAAGGTTTGTCTTCAAATGCCAAAACTACATTAAACATGGATGCTGAAAC	SEQ ID NO:799	R	dn	
Ab_gent	ABTJ_0107 2	647-746	AACGGTATCAAACAAGGTAACCGTAATGCTTTACTTTACACTGACCCAAG TGTTGATGGCTTAAAAACAGGCCATACTGATGAAGCTGGTTACTGCTTAA	SEQ ID NO:800	R	dn	
Ab_gent	ABTJ_0167 2	381-480	CAACATCTAGGAGTAACTTGGTTAGTTGCCCTAGGTTCTAACATGTCAGC GCTCTGGATTTTAGTTGCGAATGGCTGGATGCAAAACCCTGTAGGTGCAG	SEQ ID NO:801	R	dn	
Ab_gent	ABTJ_0205 8	423-522	GGCGTGCGATTATTGGCTTTGTAGATGGAACAGAAAATCCTGAACCTGTA ATTGCTGCACAATGGGCATTAGTGGGTAACGAAGATCCTGACTTTATTGG	SEQ ID NO:802	R	dn	
Ab_gent	ABTJ_0261 0	667-766	TGAAAGACGCAATCTTCCGTGAGCCAATCGATCAGTCTACTAAGCTTTAT GTCAACTTATTGGGTGTTGCTGAAGCGAACAAAAATGACCCGATCTATAC	SEQ ID NO:803	R	dn	
Ab_gent	ABTJ_0280 9	620-719	AAATGGCGATAACGTTGTAAATCCATCAGCTCATACTCCTTGGTACAAGG GGCAAACCTTAATGAGTATTCTTGAGTCTGTGGAAATCAACCGCGAGTCA	SEQ ID NO:804	R	dn	x
Ab_gent	ABTJ_0281 0	411-510	GCGCCGTGACGAAGAAAAATCACGTGCGAAAGAGCGTGTGTATTCATTCC GTGATAGTAAACATCGTTGGGATCCTAAAAACCAACGTCCTGAACTTTGG	SEQ ID NO:805	R	dn	
Ab_gent	ABTJ_0292 1	338-437	ACCATATTCAACATGATGATGCCGATTATGTGGGGGCAGTAAAAGAAAAT ATGATGGGGATTATTAGAGAAAAAGAAAAGAAGGAAAGAACTGGTT	SEQ ID NO:806	R	dn	
Ab_gent	ABTJ_0305 1	1024-1123	TTTGGTGCAGTAGCGTTAATGTCTAGCCCATATAACAACGTAGATGAAGC GCAAAGCCTTGCAGACTACCGTGGTTTGTTCTGGCGCCGTCCAGTACTTA	SEQ ID NO:807	R	dn	
Ab_gent	ABTJ_0305 2	717-816	GAAGTTACCAGTTTTCCCATTGCATGGCTGGTTACCGGATGCCCATGCTC AAGCACCTACAGCGGGTTCTGTAGACTTGGCGGGTATCTTGATTAAAACA	SEQ ID NO:808	R	dn	
Ab_gent	ABTJ_0305 3	683-782	TAAATCTGCACAAATTCCATTGCAAACATGGTTAGCAGATGCGATGGCAG GTCCTACACCTGTTTCTGCATTAATCCACGCAGCAACAATGGTAACAGCT	SEQ ID NO:809	R	dn	
Ab_gent	ABTJ_0305 4	128-227	CTGCAGCGTTAGCATTCGTTCTTGCGGGTAGCGTATGGGCACAACCAGAT GGACAAGTCATGTTCATTCTGATTTTAACCCTTGCTGCGGCAGAGGCGTG	SEQ ID NO:810	R	dn	x

Ab_gent	ABTJ_0305 6	168-267	GGAAGAGCGTTGTGTGGCATGTAACCTTTGTGCGGTTGCATGTCCGGTTG GCTGTATTTCACTGCAAAAAGCTGAAAAAGAAGACGGACGGTTGGTATCCG	SEQ ID NO:811	R	dn	
Ab_gent	ABTJ_0305 7	341-440	TGGGTGTTGCGGACATGAGCATCGGTTTGTTGTTCTTTATGGCAATGGCT GGTATTGCGGTTTATGCAGTGTTATTCGGTGGTTGGTCATCAAATACACAA	SEQ ID NO:812	R	dn	x
Ab_gent	ABTJ_0305 8	1755-1854	GTGAAACTGAAACTGTGAAACAGGCTGATATTGTACTTTCAGCAGCAAGC TTTGCCGAAGGTGATGGTACTGTCGTAAGCCAAGAAGGTCGTGCACAACG	SEQ ID NO:813	R	dn	
Ab_gent	ABTJ_0324 2	220-319	TTTGCTGAGCAATTCGGTTCTAAGCTTGTGTTTCCATGTGATGTTGCCGT TGATGCTGAAATTGATAATGCATTTGCGGAACTTGCAAACACATTGGGACG	SEQ ID NO:814	R	dn	
Ab_gent	ABTJ_0024 9	526-625	TGCTGGAAAGGTAAATTTGCGTCGCGTCACCATTATTCAACTTGGTGTCG CCTCTCTACTTTCTTTTACCATTATGCCTATAGTAGGTGAACATACAATT	SEQ ID NO:815	R	up	
Ab_gent	ABTJ_0034 6	530-629	GCAATTGCTTTACTTGCACTGCTGAGTTGGGTTGGCTTAAAGAAACAAAT GCCTAGTCATAAGGTGAGTGTAACCAAACAGCCTTTTAGTTATCTTTTTG	SEQ ID NO:816	R	up	x
Ab_gent	ABTJ_0061 8	443-542	TAAAAGCATCCGGGTCTTGTCCGAATGCTTCGTCAGTTTGAGGCAACAT GGCAAAAACAGTTGGGCACTTTAGGCGGCGGTAATCACTTTATAGAGTTA	SEQ ID NO:817	R	up	
Ab_gent	ABTJ_0073 8	190-289	TTAGAGAGACGGTTTTATCGAACGAAAAATTCAGGATACTTCCCCTAT TCGTGTCGATTATTCCCTCACGCCACTTGGGCAAAATGTAGCTGCTATGG	SEQ ID NO:818	R	up	
Ab_gent	ABTJ_0074 4	34-133	ATGTTAGACCGCACTCCATCTCGCGAACTCCGTGAAGACCTTTGGGTATT TCCAATGGACTATCCAATTAAACTCATTGGCGATGCGGGTGAAGAATTAC	SEQ ID NO:819	R	up	x
Ab_gent	ABTJ_0074 5	647-746	AGGTGATGATGATTCTGAAGGTGATTCAGGTCCAGACCCTGAAGTTGCAA AAGTTCGTTTTGCTGAATTAGAAGCTGCATGGGCTCAAACTAAAGCTGTC	SEQ ID NO:820	R	up	
Ab_gent	ABTJ_0103 4	324-423	GCTTAATGAATGTATGCAGCAACATCCGAATCTGCCGCTTGAACTTCAAA CTCACCCGACAGGATATTTGTTAAATGCTGTGCAACAAGGAGAAGTCGAT	SEQ ID NO:821	R	up	
Ab_gent	ABTJ_0138 4	484-583	GTGGACATCAGGAAACAGAAGATCAGTTCCGAGAGATGTTGTAGAAATC TTGCAATATTTCAAAGCACCTCAAGTGGGCCAAAAGATTATTGCGACACC	SEQ ID NO:822	R	up	
Ab_gent	ABTJ_0138 5	224-323	AGCAAGCGACCGTCGTAACCGTACAGAAGCGGCTATTGGTGGTGCTTTAG GCGGTGGCGCGGGTTACACCGTTGGTAAAAACATGGGCGGTACAAATGGC	SEQ ID NO:823	R	up	x
Ab_gent	ABTJ_0140 3	122-221	TGATGGCAATTGTATGGCTTGGAACAGTGGTTACAGGCATTAGTACAATC TTAGGTTACACCACGCTGATATTTGGTTTAGTGGTTACAGCAATTCTGTT	SEQ ID NO:824	R	up	
Ab_gent	ABTJ_0148 6	329-428	GGGAAAGAACGATCTCTGTGCGGATTTTACATGCGATTGGTTTTGAGGGT GGTTTGCTGATTGCGACTGTTCCAATGATTGCATATATATGATGCAGATGAC	SEQ ID NO:825	R	up	

Ab_gent	ABTJ_0149 2	127-226	AGTGCAGCATTGAATTTAACTGCCAATCAGCTTTTATGGATTATTGATAT TTATTCGCTGATTATGGCGGGTTTGATTTTACCGATGGGTGCACTCGGTG	SEQ ID NO:826	R	up		
Ab_gent	ABTJ_0159 2	443-542	GCATCGGCGATTTATACATGCTTATTGCAATTATTTTGTGTGGATTTGGC TATGCAGAAGGCGGAGTACTTTCGAAAAAAATAGGTGGATGGCAGGTGAT	SEQ ID NO:827	R	up		
Ab_gent	ABTJ_0170 9	705-804	AATTGCAAGTGTGCTTGGCATGATTGTCGGGAATACGGGCAAGATGGCAC GGGATTGGTCACTCATGATGCAAACTGAAATTGCAGAGTTGTTTGAGCCA	SEQ ID NO:828	R	up		
Ab_gent	ABTJ_0171 0	425-524	TTTAGCCGAGCTAGTTAAAACTACCCATACCCGCTGGTTCAGTGAAAAAT TTGACTATCAGCATAATGTGGTTGCACAGACAACGATTCAAAGTCTCGCA	SEQ ID NO:829	R	up		
Ab_gent	ABTJ_0171 1	792-891	CCAAAGGTACGGTTTTGCTTTGGGTGACTTACTTCATGGGACTCGTGGTT GTTTACTTGCTAACAAGTTGGTTACCAACACTTATGCGTGAAACAGGTGC	SEQ ID NO:830	R	up		
Ab_gent	ABTJ_0178 7	465-564	AGGTGCGCTTGCCGAAGTTACACTTAATTTTATTGCCCAAGACCCTTCTC AAGCCGAGCGTTACCGCAAATCTGGTTTTGAAGCATTTTGGCATGCAGTT	SEQ ID NO:831	R	up		
Ab_gent	ABTJ_0180 7	39-138	AATGGGGCTATCGGTCGAAGCTGGGCTTTTAGGGCCGTTAGGAAGGAAG TAGGTGAGTTGTGGGCCACTTTTAGTATTTTTTGGTGTGGGTGCAGCACTT	SEQ ID NO:832	R	up		
Ab_gent	ABTJ_0192 4	178-277	ACTATGCACCATGTTAAAACAGGCGCATTGTCTATTAGCCGCTTGGAATA TGGCGCAGATGTTATTATTGAACCAGATCATCTTGATAACTTTTACTTAA	SEQ ID NO:833	R	up		
Ab_gent	ABTJ_0204 7	380-479	AAATCACTCTTGCCAACCTCATTAGCCGAGACAACGTTCAAACTGTTGCA TTACGCCAAAATGTAACTGGCACAGATTCAGCTCTTTTATCGGGTACAGG	SEQ ID NO:834	R	up		
Ab_gent	ABTJ_0205 0	125-224	AATTTGTAGATGATATCGATGAACATGATCAAATTTTCGAACAATTCGGC GTTAAGGTTTTTGTAGATCCTAAAAGCTTAGTTTACTTAGACGGCTTAGA	SEQ ID NO:835	R	up	x	
Ab_gent	ABTJ_0205 1	219-318	AGCTCTTAAAAAGCAAGATCATCATCTTGATCAATCTATTAGTGATTTCG AATTTCTACAATCCGCTTTAGAACTTCGTGAACACAACTTGATGAAGCGACA	SEQ ID NO:836	R	up		
Ab_gent	ABTJ_0205 2	1358-1457	TACTTCATGGCATTCCACCAATGACTGCAGGCCAAGCTCGTATTGAAGTC ACTTTCCAAGTTGATGCAGATGGCTTACTCACCGTTTCTGCTCGTGAAGC	SEQ ID NO:837	R	up		
Ab_gent	ABTJ_0221 5	737-836	AGCTTACCTTTAGATGTATTACGTATTGCGATTCCACTCACGATTTACTT TGTAGTGATGTTCTTTATTAGTTTCTTTATGAGTAAACGGATGAGGAATA	SEQ ID NO:838	R	up		
Ab_gent	ABTJ_0231 5	151-250	GACGGGGCCGACTTAGGTTTTTTGGCATTAAGCCTCACTAGTCTTAAAGC AGAGTTTCATTTAACTGGTGTGCAAGCCGGAACATTAGGAAGCTTGACAC	SEQ ID NO:839	R	up		
Ab_gent	ABTJ_0231 7	229-328	GCAGGTGCAGATCTAAAAGAAATGGCAACCGCAACTTCCACAGAAATGTT ATTGCGTCATACAGAACGTTATTGGAACGCGATTGCCCAGTGCCCTAAAC	SEQ ID NO:840	R	up		

Ab_gent	ABTJ_0231 8	367-466	TTAAAGCAAGCACAGGCAGGCGTGATTATAAATATGTCATCTATTGCCGG ACGCTTAGGCTATCCATATCGATTGGCCTATTCCACTTCAAAATGGGGAC	SEQ ID NO:841	R	up		
Ab_gent	ABTJ_0232 4	591-690	GTGGTTGAAGATGTGGCAATTAAACTTGCTCACAAACCAAGCCAAGCCTT ACAGCTCAGTAAAAAGTTACTAAGAGATATGCCAATTGATGATCTACTCA	SEQ ID NO:842	R	up		
Ab_gent	ABTJ_0232 5	220-319	CAGATGACAGGTTTGCCAAAACCAACCATTACTCGCCTCACACATACCTT GTCGCGTTTGGGTTATATCAAACAAGTACCTAACTCAAGCAAATTTCAGC	SEQ ID NO:843	R	up		
Ab_gent	ABTJ_0232 7	148-247	TTCGGTCTTACAATTCCCGAAGAATATGGTGGCTTAGGCATCACTATGGA AGAGGAAGTCAGAGTTGCATTTGAACTTGGACAAACTTCACCGGCTTTTC	SEQ ID NO:844	R	up		
Ab_gent	ABTJ_0244 5	190-289	GGTCAAACCCTTAAAAAAGATTATGCTTCTGTTGCATCAAAATTTAAGTT TTCTGAAAAGCAATTAGGTAATGCTTCTGAAGGTTCAAATTGTAGTCAGT	SEQ ID NO:845	R	up		
Ab_gent	ABTJ_0250 7	111-210	CAATGCCAATGGTTCAGTTTTGTATATTGTTAAAGAGGAAAGTAAGATTC CACTGGATGTAGAAAAGTTTAAAACTGACCGACCTAAAATCTATGATGCG	SEQ ID NO:846	R	up		
Ab_gent	ABTJ_0280 8	2-101	TGAATACTAAAATCACCTATACTGCTTTCACTGGAAGCACGCTTATTGCG AGTGACTCCCTTGTTGAACTTGCAAAGAAACTAAAAGCTCTTCCTAAAAC	SEQ ID NO:847	R	up		
Ab_gent	ABTJ_0284 7	1054-1153	GCAGGTTTAATGTTTGGCCTTATGTTTGGGTAAGTGGTATTGCCGCAGC GGGCTAGGGCATTTAGCGGATATTAACGGCATTGAATGGGTATTTGGTT	SEQ ID NO:848	R	up	x	
Ab_gent	ABTJ_0286 1	756-855	CTGGTACGTCAACTCACCATTGGGTGGTGCATTTGAATATTACACCAACG ATGATTATTTGACCGAAGAATGGCAGCCACGTGTAGAAGAACATCGTCTA	SEQ ID NO:849	R	up		
Ab_gent	ABTJ_0286 2	623-722	TTGAAGCAACCGAGTATGTGCCACAGGAACGTCATGATTTATATGTCAAC GGAAGAGCGATTCAACGCCAGCAACTTCCACACAAGATTTAAATGGAACAGC	SEQ ID NO:850	R	up		
Ab_gent	ABTJ_0286 3	315-414	AATGACTGGAACCAAGTGTTTAAAGAGCTATCCGGTCATTGAACAGCATG GTGCAATCTTCATCTGGTTTGGTATCGATGCAAATGAACAACCCGCACCG	SEQ ID NO:851	R	up		
Ab_gent	ABTJ_0305 5	151-250	GCCGGCGCCCTCGAAATCATTGTTTATGCTGGTGCGATTATGGTCTTGTT CGTATTCGTTGTGATGATGCTTAACTTAGGGCAACACACAGTTGAACAAG	SEQ ID NO:852	R	up		
Ab_gent	ABTJ_0345 6	118-217	CCGTGGACACGTGATGGTCGAGTTCGTGGTGACGTTATTCAGGTCTCTTC AGATGTAGCAGGACTTGTAACGGAAGTATTGGTTCAAGATAACCAGACTG	SEQ ID NO:853	R	up		
Ab_gent	ABTJ_0345 7	67-166	CCTGCTTTGCTCGTCCAAGCCATTTTTGCATATATATGTTTTCGCTGGTT AAGTCCCTTAACCAACAAATGGATTGCACACAAGGCTGGATTGCATTACCCA	SEQ ID NO:854	R	up		
Ab_gent	ABTJ_0345 8	851-950	GAACAAAAAGATCAGATGACTGATGAAAATATTCTCGCAGTTACCTGACGA GTTTGAAAATGATTTCTTGAACTTAAATGATTCGGCTTCTGAACATCAGC	SEQ ID NO:855	R	up		

Ab_gent	ABTJ_0371 5	235-334	GGCGATGTATTTGATCAGGTGGCTAGAGACTTAGTTGAGATTCCTGAAGT ACTCGAATGTCACCTCATTTCAGGTGAATTTGACTACTACCTTGTAAAAGCGC	SEQ ID NO:856	R	up	
Ab_gent	ABTJ_0377 4	235-334	TACCAACAACGTAGCTATTCGATTATTGAAGTAACCACTCACTCAAGGTGAAAT CGCTTTAGGTATTAAAGTACAAGGCTTGGTGTCTCGTGCAGCTCAACTAT	SEQ ID NO:857	R	up	x
Pa_cip GeneID = NC_00846 3	PA14_0439 0	12-111	CGATGGTTTTCGCCCGAATGTCGGCATCATTCTCGCCAACGAGGCGGGGC AGGTGCTGTGGGCGCGGCGTATCAATCAGGAAGCCTGGCAGTTCCCGCAG	SEQ ID NO:858	C		x
Pa_cip	PA14_0463 0	1118-1217	CCTTCTTCAAGGCCGGTCCGGCGGGCATCCCGACCCAGACCGCGTTCAGC CAGAACACCCGCTGGCCGAGCCTGGACGACGACCGCGCCGAGGGCTGCAT	SEQ ID NO:859	C		x
Pa_cip	PA14_0548 0	542-641	AGCGTATCCGTTCGCGCTACGACGAACCGTCGCGCCTGTCGCTGCTCTAC CTCGCCCAGCAGGCCGCGCCTACCGTGGCGTCGACGACCGCGACCTGCG	SEQ ID NO:860	C		
Pa_cip	PA14_0556 0	714-813	TGCTGGCGCCACCTGGTAACCGTCGGCGCCTGGGAACAGGTGCTGGTCTTC ACCCGTACCAAGCACGGCGCCAACCGTCTCGCCGAGTACCTGACCAAGCA	SEQ ID NO:861	C		x
Pa_cip	PA14_0592 0	764-863	ACGAGCGCGCCAGTTCCTCGCACTACCCGTACAACCGGCTGGCCGAGGCG TTCTTCCACAGCGACGTGCTGTTCCGCTGCCAGCGCCTGCTCAACCAGCA	SEQ ID NO:862	C		x
Pa_cip	PA14_0770 0	157-256	TATGCCATGCGCGAGTCGGTGGTCAGCGTCCTGGGCAACCACGACCTGCA CCTGCTGGCGGTGGCGCACAAGTCCGAGCGCCTGAAGAAGTCCGACACGC	SEQ ID NO:863	C		x
Pa_cip	PA14_1004 0	711-810	TCGCCGACGATCCCGATACCCGCGGCGACCTCTGGCGCATGCAGCCCTGG GTGCCGATCCCCAAGGCCTCCGAGGTACGCCCGGCGAGCTACCCGGCCCT	SEQ ID NO:864	C		x
Pa_cip	PA14_1490 0	290-389	GTTCGTGGCCAAGGTCGCGGTCGACAGCGGCAAGCTGGATGACGCCGTTG CCGAGCTGAAGGCGGTCATGGACAAGCCGGCCGACGCCACCCTCGGCGAA	SEQ ID NO:865	C		x
Pa_cip	PA14_2500 0	743-842	CGCGGCAGGACCCGGAAAAGGCCCTTAGCCTGCTCGACTACTACAGCTCG GCGCTACCCTTCTCCAGCGACGAGAAGGTCGCCATCGCCCGCGAGATCGG	SEQ ID NO:866	C		
Pa_cip	PA14_2588 0	335-434	CGAGATCGTCGAAGTGGTCAGCCCCGACACCTTCAAGCGTCCGATCTACG CCGGTAACGCCATCGCTACCGTGCAGTCCTCGGCTGCGGTCAAGGTGATC	SEQ ID NO:867	C		x
Pa_cip	PA14_3023 0	281-380	GTGCAGAGTTCCGGCAAGCGCGAAGTGACCGGGGCCAATGTCCTGGTGGC GATCTTCAGCGAACAGGAAAGCCAGGCGGTGTTCCTGCTCAAGCAGCAGA	SEQ ID NO:868	C		x
Pa_cip	PA14_0252 0	120-219	ATGGGCTGCGGCAACGGCGCCAGCCGCACCCAGCATCCCAGCGAACTGTT CGGCGAGGACTGGGCCGGTGAATGGGAAGTCGAAGGAACGGAGGACGCCA	SEQ ID NO:869	R	dn	

Pa_cip	PA14_1686 0	2184-2283	GACCGCCGAGGAACTGGAGAACCTCTGCACCGTGATGGCCCAGCGCCTGT CGATCCTGCATGGCCTGAACGCCCCGGAGTTCTTCGACAAGAGCCTGTTC	SEQ ID NO:870	R	dn	
Pa_cip	PA14_1755 0	383-482	CATGGCCGCCGCCCACGAAGGCGCCGGGCTGGAGAACAGCCTGGGCTTCA ACATCACCCTGCCCTTCGAGCAGCACGCCAACCATACGGTGGACGGCAGC	SEQ ID NO:871	R	dn	
Pa_cip	PA14_2513 0	211-310	GCTCCTCGCGTGGATGCATTGCTGAATGCCGAAGTGCTGGCGGCCGCGCC CAGCCCCGAGCTGGCTGAACTGGTGGAGTTGGCGTCGCAGCCGGAAACCT	SEQ ID NO:872	R	dn	
Pa_cip	PA14_2959 0	70-169	CTGAAAAGCGACAGCAGCCTGAAGCAGGAACTGGAATTCAAGGACAAGTT GCAGGCGTTGATGGACAAGTACGGCATGACCCTGCACAACATCATCGCCA	SEQ ID NO:873	R	dn	x
Pa_cip	PA14_0081 0	616-715	GCCCTCGGCGCCGACTGCGGGCGATCCGCCACGCTCAGCGGCAACGGCATCC CGGTGGGCGTGCTCTGCTCGCCGATGATCCCGATGGTCAACGACATGGAG	SEQ ID NO:874	R	up	
Pa_cip	PA14_0431 0	471-570	CGGTCTACCGCGAAGGCGTGCTGACCGACAACGGCAATATCATCCTCGAC GTGCCACAACCTGCGCATCGACAGCCCGGTGGAACTGGAAGAGAAGATCAA	SEQ ID NO:875	R	up	
Pa_cip	PA14_0562 0	409-508	TGGACGACGGCGGTGACCTGACCGAGATCCTGCACAAGAAATACCGCAG ATGCTCGAGCGCATCCACGGCATCACCGAAGACCACCACCGGGGTCCA	SEQ ID NO:876	R	up	
Pa_cip	PA14_0777 0	62-161	TGGCTCTGCAGCCGGTCGCAGCATTGACTGTACAGGCCGCCGATCAGTTC GACTGCAAGGTATCGGCCACCGGCGCTGGGATTGCTCCCCGCTGCAGAA	SEQ ID NO:877	R	up	
Pa_cip	PA14_0796 0	2-101	TGGACAAGAGCACCCAGATCCCGCCCGACAGCTTCGCCGCTCGCCTCAAG CAGGCCATGGCGATGCGCAACCTGAAGCAGGAAACCCTCGCCGAAGCGGC	SEQ ID NO:878	R	up	x
Pa_cip	PA14_0797 0	4-103	GCTGACCTTGCCGATCACGCCAACGAACTGGTCCTGGCTCGCCTCGACGG CCTCCTGGCGGCGCCGCCGGCGCTGGCCATCCGCGAGTCCGCGGAAGACT	SEQ ID NO:879	R	up	
Pa_cip	PA14_0798 0	130-229	CGCGGCCACCGTGGCAGCCGGGTGATCCTCGACCGTGTGGCGGAGGTCGA TCGCCTGGTAAATCGCCTACCCGAGGAACTGAAGGAACGTGGTGGTGGAGC	SEQ ID NO:880	R	up	x
Pa_cip	PA14_0799 0	108-207	CCGCAGACACTGACGGAAATGCCGCTCTGGGTACTGATCCTGCTCGCCGC GCTGGGCGGCGTCAGCGGCGAGATGTGGCGTGCCGACAAGGCCGGTCTCG	SEQ ID NO:881	R	up	
Pa_cip	PA14_0818 0	13-112	GCTCTGCTCCTGCCGGCCGTGTTGCTGGTCCTGCTGGGCGGCGCCTTGCT CGGCGGCGGCCTGGTTGCCCGCCACTATCGTCCGCAACTGGAGGAGGCCC	SEQ ID NO:882	R	up	
Pa_cip	PA14_1201 0	131-230	CCGCCCGCGCGGAGTTGTCCCACGCCAACGAGCAGGACCTCGCCGCCGGC CGCGCCAATGGCCTGGAGCCGGCGATGCTGGACCGCCTGGCGCTGACCCC	SEQ ID NO:883	R	up	
Pa_cip	PA14_1255 0	291-390	GATGGCGGTCGCCGAGCACGACCGCGACTGCGACGCCGAGACCCGCGACG CCTGGCGCGACGTGATGGGTCGCGGCATCGCCGTGATCAAGTCGTACTAC	SEQ ID NO:884	R	up	

Pa_cip	PA14_1303 0	536-635	CGTTCCCCTACCGCCTGCTGCACATGTCGGTCGCCGCGCGTTCCTCGCCACC GCCTTCTTCGTCGGCGCCTCGGCCGCCTGGCACCTGCTGCGCCGGGCGCGA	SEQ ID NO:885	R	up		
Pa_cip	PA14_1352 0	363-462	CACCGCTGGCCGGACGACTATTTCTACGGCCCCGGCGACCTGGCGCGGAC CACTTCCTGGAACAACTCCACCGAGATCGGCCTGAACTACAAGCTCGATC	SEQ ID NO:886	R	up		
Pa_cip	PA14_1353 0	1282-1381	GCCCCACGGCGGCACCTTCGCCCTCACCGCGGTACTGATCTCGGCGCTCT CCTCGACCTCGCCGAATCCCGGCCGGTTGTCGCTGCAACTCACCCTCGGG	SEQ ID NO:887	R	up		
Pa_cip	PA14_1450 0	313-412	CGGCGCTGCTGGTGGCGATCCTGGTGGCCTGGCTGAGCCTGTTCCTGGCG CCCCAGGGCATCAACCAGTTCGCCCTGCTGTTGAACAAGCAGGATACCCT	SEQ ID NO:888	R	up		
Pa_cip	PA14_1460 0	645-744	GTCGGTGGGCGAGCCGAAGGAAGATGATCCGCGTGCTCGATTTCCTGC CGCCGCAGATGCCGGCCGACAAGCCGCGCTACCTGATGGGCGTGGGCAAG	SEQ ID NO:889	R	up		
Pa_cip	PA14_1461 0	197-296	TCACTTCCGGCGGTATCGCCGGCAAGGTGACCAAGGTCGCCGACGATTTC GTCGTCGTCGAGGTTTCCGACAACGTCGAGCTGAAGTTCCAGAAGGCCGC	SEQ ID NO:890	R	up		
Pa_cip	PA14_1468 0	299-398	ACTTCGCCGTGAGCATCGCCTGCAAGTACAAGGGCGCCGCCTGGAGCACGCC GTGGTCCTCGACCCGGTACGCCAGGAAGAATTCACCGCCAGCCGCGGTCG	SEQ ID NO:891	R	up		x
Pa_cip	PA14_1531 0	33-132	CGACGACGTCCTTCTGATCCCCGGTTATTCCGAAGTCCTGCCCAAGGACG TGAGTTTGAAAACTCGCCTGACCCGCGGCATCGAACTGAACATCCCGCTG	SEQ ID NO:892	R	up		
Pa_cip	PA14_1574 0	1382-1481	CGACTTCGCCTCGGTGCAGCGCGACAACCCGGAAATGGAGCGACGTTGCC AGGAAGTGATCGACCGCTGCTGGCAGCTCGGCGAGCGCAACCCGATCAGC	SEQ ID NO:893	R	up		
Pa_cip	PA14_1596 0	62-161	AGCTGACCGAGGACAACATCAAGGACACTCTGCGCGAAGTGCGCATGGCC CTGCTCGAGGCCGACGTGGCCCTGCCGGTGGTCAAGGACTTCGTCAACAA	SEQ ID NO:894	R	up		
Pa_cip	PA14_1597 0	60-159	CGTGACCAACAGCCGCAATGCGCGCGATGGTCGCTTCGTCGAGCGCATCG GTTTCTTCAACCCGGTTGCGACTGGTGGCGAAGTGCGTCTGTCCGTCGAC	SEQ ID NO:895	R	up		
Pa_cip	PA14_1598 0	241-340	GCCCGCACCTTCACCGGTTACGAGATCTGCATCCCGCGTAGCGAGTTGCC CTCTTCTCGAGGAAGGTGAGTACTACTGGCACCAGCTGGAAGGCCTGAAGG	SEQ ID NO:896	R	up		
Pa_cip	PA14_1599 0	417-516	CGATTATGTCCTGTCCGGCGGTGAGTTGCCGGCCATGGTGCTGGTCGATG CAGTGACGCGGTTGCTGCCCGGTGCATTGGGTCATGCAGATTCCGCCGAG	SEQ ID NO:897	R	up		
Pa_cip	PA14_1601 0	21-120	AATCCTGCGTCGCACCGAGCTTTCCGAAACCCGTGTGACCAAGGCGGTAT TCCCGCCCACCACCAATCACCACACCCTGTTCGGCGGGACTGCGCTG	SEQ ID NO:898	R	up		
Pa_cip	PA14_1753 0	347-446	CAGCCGGACACCGGCGAGCAGGCCCTGGAAATCACCGACATGCTGGTGCG CTCCAACGCGGTCGACGTGATCATCGTCGACTCCGTGGCCGCGCTGGTAC	SEQ ID NO:899	R	up		

Pa_cip	PA14_1754 0	141-240	CGACCGCCTGGCCGAGGAAGGTCTGCTCGACGAATCCCGCTATCTCGAAA GCTTCATCGCCAGTCGCGCCCGTAGCGGCCATGGGCCGTTGCGCATCCGT	SEQ ID NO:900	R	up	x
Pa_cip	PA14_1869 0	197-296	AGGCGCGCAACGTCGAGGTGATCGGCGTTTCCATCGACTCCCACTTCACC CACAACGCCTGGCGCAACACCCCGGTGGACAAGGGCGGCATCGGCGCCGT	SEQ ID NO:901	R	up	
Pa_cip	PA14_1875 0	271-370	CCAGGCCTGCGACGACATCCGCAACAACGGCGGCCAGGTCACCCGCGAAG CCGGGCCGATGAAGCACGGTACCACCGTGATCGCCTTCGTGACCGACCCG	SEQ ID NO:902	R	up	
Pa_cip	PA14_1994 0	417-516	CAGCCGCTACCGCGTGGCCGGCACCGAGGTCTATCGCCTGCGCGGCAGCC AGGCCGGCAAGCCCTACCACGCGCTCTACCTGCTCGACGGTCCCCAGGTG	SEQ ID NO:903	R	up	
Pa_cip	PA14_1995 0	44-143	GTTTGTTCATGGACAAGGCTGAAGCCGATCGTTACCGACACAAGATGCTGGAG CTGGCGGAAACGCCTGGCCGAGGTGCTGCAGAAGGCCGGTGCCGTCGCTGAA	SEQ ID NO:904	R	up	x
Pa_cip	PA14_2325 0	51-150	GGACGGTACGCTGCGGTTGCTGGATCAGCGCCTGCTGCCCCAGGAGGAGGG TCTGGCTCGAACACGAGTCGGCGGCCGAGGTGGCCAAGGCCATTCGCGAT	SEQ ID NO:905	R	up	
Pa_cip	PA14_2390 0	52-151	ATCGTCGTTTCCAGCCTGATCAGTCTGAGTCGCGGCTTCGTCAAGGAAGC CTTGTCCCTGCTTACCTGGATAGTCGCCGGCGCGGTGGCCTGGATGTTCG	SEQ ID NO:906	R	up	
Pa_cip	PA14_2392 0	457-556	TTCGCCGCGGTTTCCTGCGTGCACGACCGTTGCGTCGGCGGCTACGCGGT GGTGGCGATGATCACCGGCCATGGCATCGTCGGTTTCCGCGACCCCAATG	SEQ ID NO:907	R	up	
Pa_cip	PA14_2516 0	298-397	TCGAGGAATCCTGCCGTATCAATCCCGCCTTCTTCAATCCTCGCGCCGAC TACCTGTTGCGCGTGCGGCATGAGCATGAAGGACATCGGCATCCTCGA	SEQ ID NO:908	R	up	x
Pa_cip	PA14_2562 0	404-503	CCATGACCCCGAAGTATGTCAGCACCCGGCTGGATTCGTCGTCGAAGACG AGCCGGAGTCGAGCGAAGTCGAGGACAAGCGTCCTAATCCGTTCAGCGTA	SEQ ID NO:909	R	up	
Pa_cip	PA14_2563 0	40-139	GACATGCGTCGTTCCCACGATGCGCTCGAGTCCAATGCTCTGTCCGTGGA AAAGAGCACCGGTGAAGTCCACCTGCGCCACCACGTATCCCCGGACGGCT	SEQ ID NO:910	R	up	
Pa_cip	PA14_2705 0	695-794	CTGCGCGTCGACCGCCACCTGGTGCTGGACAATCGCGCCGACATGGCCTG GTACGTGCGCCGCGATGCCAGCACCCTGCGCGCGACCATCGACCGCTTCC	SEQ ID NO:911	R	up	
Pa_cip	PA14_2737 0	659-758	GCCGCCAAGACCCAGACCGTGGCGCGCATCGAGCAGGTCCACCTGATGGT CCATGCCGACCAGAAGGCCGGTTCGATCCAGCGTCTGCTGGAAGTCGAGC	SEQ ID NO:912	R	up	x
Pa_cip	PA14_2798 0	536-635	CGCCATCCTCGAAGGGCTCTCGCCCAAGGAAAACCGCGAGGTGCCGCCGC TGCGCTACGAGGTCGGCGCAATTGAAGAAGGACTTCCCGGACCTGGAG	SEQ ID NO:913	R	up	
Pa_cip	PA14_2845 0	8-107	CACTACTGATCGCCGCCGGCGTTGCCGCTCTTTCCAGCACCGCCATGGCC GCCAAACTGGATGAAAAGGTTCCCTACCCGAANNNNNNNNNNNNNNNNNN	SEQ ID NO:914	R	up	

Pa_cip	PA14_28650	1644-1743	CCGATTTCGCCGCCGAGGTGGTGCGGATCCTCGGGGAAAGCGGATTCCGT GCCAAGTCCGACTTGAGAAACGAGAAGATCGGCTTTAAAATCCGCGAGCA	SEQ ID NO:915	R	up		
Pa_cip	PA14_28660	246-345	GAAGCAGGCTGCGGTCGCCAAGAAGAACCAGAAGCAGGCGCAGGTCAAAG AAATCAAGTTTCGTCCAGGGACGGAAGAAGGGGATTACCAGGTAAAACTA	SEQ ID NO:916	R	up		
Pa_cip	PA14_30180	761-860	AGGCGACCATGATGAAGATTTCCCACCCGATCGTCTTCGGACATGCGGTG AGCGTCTACTACAAGGACGTCTTCGACAAGTGGGGCCAACTCTTCGAAGA	SEQ ID NO:917	R	up		x
Pa_cip	PA14_30190	348-447	AACGTGGCCCTGCGCCAGCAACTCGATCTCTACGTCTGCCAGCGCCCGGT ACGCTGGTTCGAAGGCGTGCCCAGCCCCGGTGAAGAAGCCCGGCGACGTGG	SEQ ID NO:918	R	up		
Pa_cip	PA14_30240	55-154	AACACCATGTTCCGTGTGGAGTTGGAAAATGGGCACGTCGTCACCGCGCA CATCTCCGGCAAAATGCGCAAGAACTACATCCGCATCCTCACCGGCGACA	SEQ ID NO:919	R	up		
Pa_cip	PA14_52480	260-359	ACTTCACTGCAAGGCGCTTCCGAAACGGTGGACGTGCAAACGGGATTCCA CCTGTATCGCGGTCTGTTCATCACGCGCGTTGTTGCCCGGCGAACCGCAG	SEQ ID NO:920	R	up		
Pa_cip	PA14_52510	85-184	AACGCCTTGCTGGGAGGCTTCGGCGGCGCCATCTTCTTTGTCGTGTTCGC CCGTGACTACAACGCCCCTGACCCGCCTCGGCTACCTGCTGGTGTCCTGGG	SEQ ID NO:921	R	up		x
Sa_levo GeneID = NC_002745	SA0013	1180-1279	AAAAGCCAGAGTTAAGAGAGCGATTTATTACATCAGATGATGCTTGGGA TATGATGACATCTAAGACAACCGTAGTGATTGTTGATACGCATAAACCGG	SEQ ID NO:922	C			x
Sa_levo	SA0441	183-282	CAAACGTGTGGTAATAGAGAACAGTTGGTTTCACCTATTACACCTATGGG AGGCAGTGCGGATTCGTACATTCCATATCCAGTTGAAGTTGAAGTTGGCG	SEQ ID NO:923	C			x
Sa_levo	SA0448	1526-1625	ATGGTTACTGGGCAACCTAAACCTATTTTCCCAAGATTGGATAGCGAAGC GGAAATTGCATATATCAAAGAATCAATGCAACCGCCTGCTACTGAAGAGG	SEQ ID NO:924	C			x
Sa_levo	SA0490	501-600	TGGCTTTTGGGTAGCTGGCACTGAAGCTAATAATGCAACAGATTATAGAA ATCTAGAAGCGGACATGTCATTGGCTATTGTAATTGGTAGCGAAGGACAG	SEQ ID NO:925	C			x
Sa_levo	SA0491	302-401	TACAGTTGTAACAAGTGATATGAGTGAGCAACATGCTATCTTTGGATCAG GTGCATATAGAATATCATCTCGCGAAATGTGGAGAGATTTAAAAGAAAAT	SEQ ID NO:926	C			
Sa_levo	SA0811	226-325	TATGAAGCGAACGTAAAAAGCTATGTTGATCCTATCCCGCAAGCACTTAT TTTAACAGCAATCGTTATCGCCTTTGCGACAACAGCCTTTTTCTTAGTAT	SEQ ID NO:927	C			x
Sa_levo	SA0869	572-671	TCCAATCCGTACATTAAGTGCAAAAGGTGTGGGTGGTTTCAATACAATTC TTAAAGAAATCGAAGAGCGTGCACCTTTAAAACGTAACGTTGATCAAGTA	SEQ ID NO:928	C			

Sa_levo	SA1055	1574-1673	CATAAAACGACAGACTTATTAAAATGTCACTATTGTGGTTACCAAGAGAC GCCACCGAATCAATGTCCAAATTGTGAGAGTGAACACACATTCGACAAGTAG	SEQ ID NO:929	C		
Sa_levo	SA1077	1584-1683	TTGATGTGCCATCTAAATTAACTCAGGCAATTGAAACAGCATTAGGTGCT TCATTACAACATGTCATTGTAGATTCAGAAAAAGATGGACGCCAGGCTAT	SEQ ID NO:930	C		x
Sa_levo	SA1135	147-246	GCATCAAAAACAAGCAGTAAACTTTCAAAATTACGGGAAACAAAATGCGC TAGAACAGTCGGAACATACCATTCAAGTATAGAAGCAGAAATAAATACA	SEQ ID NO:931	C		x
Sa_levo	SA1288	754-853	GACCGCAACAATTATATTTAGCGGAAACTATATTAGATCAGCTCATGCAT AGTGAAAAAGCAATGATTGAAGCATCACTAGGCAGTGGTAAATCATTAGC	SEQ ID NO:932	C		x
Sa_levo	SA1296	540-639	GTAACTATAGTGATGCGATTCGCTTATACGATGAAATTAATGAAGATGAA ATGACTTCAGAAGATTATCTCAAAAAAGCCATTTCTTACGATAAAAATGA	SEQ ID NO:933	C		
Sa_levo	SA1394	596-695	AAATTGGTAAATCATTCCGTAATGAAATCACTCCAGGTAACTTCATTTTC AGAACAAGAGAATTTGAACAAATGGAACTTGAATTCTTCTGTAAACCTGG	SEQ ID NO:934	C		
Sa_levo	SA1445	90-189	TTATCGAACATTAGATGAACGAGGATATAATGCCGTAAACCAAATTGTAG GTTATTTATTATCAGGTGACCCTGCGTATATTCCACGCCAAAATGAAGCA	SEQ ID NO:935	C		x
Sa_levo	SA1525	1358-1457	ACACATGCGGCAGGAATTATTATTAATGACCATCCATTATATGAATATGC CCCTTTAACGAAAGGGGATACAGGATTATTAACGCAATGGACAATGACTG	SEQ ID NO:936	C		x
Sa_levo	SA1526	870-969	GATATTGCGCAAGATTTTGGTGGCGGTGGTCATCCGAATGCGTCAGGAGT TTCAGTGAACAGCTGGGATGAATTTGAGCAACTTGCTACAGCTTTACGCA	SEQ ID NO:937	C		
Sa_levo	SA1579	1311-1410	ACAATGACAACTGTTCCTGAAGAAGAGCTACCATTGTTGTTACCTGAAAC AGATGAAATCAAGCCATCAGGGACTGGTGAGTCTCCACTAGCTAATATTG	SEQ ID NO:938	C		x
Sa_levo	SA1654	427-526	TTTGGAGTCAGTGCATTAATTTTTCCATATGTTGGTTTACGCTTAAGATG GCAATGGTATCAATCGGGACTTAAAACATGGCAAGTTAATTTAATATCAT	SEQ ID NO:939	C		
Sa_levo	SA1682	685-784	ACTATAGCGAAGAACGTCCTATTACAAAAAAACATATTCACCAACAGAAT AGAAAGAAAATACTTTTCAGAGAAGTAGTTCAGACGACTAGACAAGCTTA	SEQ ID NO:940	C		
Sa_levo	SA1687	282-381	TTTAATATTTCCGCAGCGACGCCAGTAGTTATTATGTCTATTTTAAGTTT TATTATGCTAGTCATTTGACGATGATTAGTGCATTGGTTAAACCAGTAA	SEQ ID NO:941	C		x
Sa_levo	SA1886	282-381	CAATTGGCACAAGCTTACTTGAGACATGTAAACCCTAAAGTAATTGCCGT CACAGGGTCTAATGGTAAAACAACGACTAAAGATATGATTGATTGAAAGTGTAT	SEQ ID NO:942	C		x
Sa_levo	SA2055	211-310	TTCCAAAAGAGAATTGGTGGGTATTTATCGTCTTATTACTCTTAGTCGGT AATGTCGAAGTGACAGGATTTAAAATGCTTAAAAAAAGATCTAAAAAGGCGT	SEQ ID NO:943	C		

Sa_levo	SA0269	688-787	ATTAAGGTTAATGGTGAAAGTACAAAGTTAGACCTGTCACGTTAACACT TAGCAGAGCTGACACTAAAAAAATTACATTAGCTGTATTATTAGAAGAAGCTA	SEQ ID NO:944	R	dn		
Sa_levo	SA0682	100-199	TTCTGGGAAAGGTTTAGTTATTATGGCATGCGTGCCCTACTCATTTTCTA CATGTACTTTGCCGTAACAGATAATGGCCTTGGAATTGATAAAACAACAG	SEQ ID NO:945	R	dn		
Sa_levo	SA0730	115-214	AAATATCCAACGACTCAAATCGAAGCGAGTGGCTTAGATGTTGGACTACC TGAAGGACAAATGGGTAACTCAGAAGTTGGTCATATGAATATCGGTGCAG	SEQ ID NO:946	R	dn		
Sa_levo	SA1021	288-387	CGCTAATTTAACTAAAGAATGTACAGTAATCGGTGTTTCAAATCGTATTG AGATTTGGGATAGAGAAACTTGGAATGATTTCTATGAAGAATCTGAAGAA	SEQ ID NO:947	R	dn		
Sa_levo	SA1022	294-393	TTACGACTTGGGTGTTTCAAGCCCACAACTCGACATTCCAGAACGAGGAT TCAGTTATCACCATGACGCGAACATTAGACATGCGTATGGACCAAACACAA	SEQ ID NO:948	R	dn		x
Sa_levo	SA1023	326-425	AGAATTCTTCTTATGAACGCATATACGAAAAGGCTAAGAAACAGGGGATG AGCCTTGAGAACGATAATGTAAAGGTAGTGCGTAGTAATGGCGAAGCAAA	SEQ ID NO:949	R	dn		x
Sa_levo	SA1987	541-640	GTGGACCTTTAGGTGGTGCCATTGATGTATTGGCAGTCATAGCTACAGTA ACAGGCGTTGCTGCAACATTAGGTTCGGTGCATTGCAAATAAACGAAGG	SEQ ID NO:950	R	dn		
Sa_levo	SA0128	188-287	TACCGGAAGCGATGAGGATGTCAGTCCGTAATAATGGCGGTGGTCATTTT AACCATTCATTATTCTGGGAAATACTATCACCTAATTCTGAAGAAAAAGG	SEQ ID NO:951	R	up		
Sa_levo	SA0480	150-249	ACACGATTCACTAATGAACATGGTTATGAAATCGAAAGTAAACGTGGTGG TGGTGGTTACATCCGAATCACTAAAATTGAAAATAAAGATGCAACAGGTT	SEQ ID NO:952	R	up		
Sa_levo	SA0481	279-378	TTTGAAAGATATTGCACATGTTGGTAAATTTGGGTGTGCTAATTGTTATG CAACATTTAAGATGACATCATTGATATCGTCCGCAGAGTTCAAGGTGGA	SEQ ID NO:953	R	up		
Sa_levo	SA0482	744-843	CGACAAAAGTTAGACACTTATAATCAATTAGAAACACAAGACCGTGTTTT TCGCTCGCTAGGTATTTTTACAAAACTGTAGAATGATAACTATGGAAGAGG	SEQ ID NO:954	R	up		
Sa_levo	SA0685	274-373	GCGGGTCGCACGATATCAGAAGAGTATAATGTCCCTTTATTAATGAAGTT TGAGTTACATGGAAAAAACAAAGACGTTATTGAATTTAAGAACAAGGTGG	SEQ ID NO:955	R	up		x
Sa_levo	SA0686	559-658	AGCTAGTGTCATGTTCTTATTAGAAGTGGATGACAGCTTAAATTCAATT AACTTTATTGATTCAACTGCAAAACAATTAAGTAAAATTGGGGGCGGCGT	SEQ ID NO:956	R	up		x
Sa_levo	SA0687	18-117	GAACACACAAGAAGATATGACGAATATGTTTTGGAGACAAAATATATCTC AAATGTGGGTTGAAACAGAATTTAAGTATCAAAAGACATTGCAAGTTGG	SEQ ID NO:957	R	up		x
Sa_levo	SA0713	492-591	GGTTTAGGTAATCCTGAAGAATATAAAGATTTAGTAGTAAGTGTTCGAGT TGGTATGGAAATGGATAGAAGTGAATTACTTAGAAAACTTGTAGATGTGC	SEQ ID NO:958	R	up		x

Sa_levo	SA0714	2434-2533	TGGTCTTGGATACGTCACATTAGGTCAACAAGCTACAACGTTATCAGGTG GTGAGGCTCAACGTGTGAAACTTGCATCTGAACTTCATAAACGTTCAACT	SEQ ID NO:959	R	up	
Sa_levo	SA0835	1313-1412	AAAGCGCACTTAAAAATGAATCTGACAATGCGAGCAAACAGAGATTACAA GAACTACAAGAAGAGCTTGCCAATGAAAAAGAGAAACAAGCAGCACTTCA	SEQ ID NO:960	R	up	
Sa_levo	SA1128	605-704	TCGGTAATCCAGAGACTACACCAGGTGGACGTGCATTAAAATTCTATAGT TCAGTAAGACTAGAAGTACGTCGTGCAGAACAGCTTAAACAAGGACAAGA	SEQ ID NO:961	R	up	x
Sa_levo	SA1174	321-420	TCCATTACCTGAACACTTAACATCGACACATAATAGCGACATATTCATAT TAAACGTCGTAGGCGACAGTATGATTGAGGCTGGTATATTAGACGGAGAC	SEQ ID NO:962	R	up	
Sa_levo	SA1175	178-277	GCTCACTCGGAACAAGTGTACGAAATGACTGACCATCAAATTAAGAACAA TACGATAAATAAAGCATACGAACATAAAGACCCTACACAAACAATAGCGAAC	SEQ ID NO:963	R	up	
Sa_levo	SA1180	499-598	ATTGATGAAGATGCCGTCAATATTTTAATTAGTCATCTGACTGTTCAAGG TGGAAAGACATCTGATTCTGAAAGACCATTAACTATTGGAACGGTTGAAT	SEQ ID NO:964	R	up	x
Sa_levo	SA1181	133-232	GATGCAATGACTTATGCCTTGTTTGGTAAAGCATCAACTGAACAAAGAGA AGAAAATGATTTGAGAAGTCATTTCGCTGATGGTAAACAGCCGATGTCAG	SEQ ID NO:965	R	up	x
Sa_levo	SA1196	864-963	AGCAGAGTTCGAGCAAGAAAAAAAGTGGCAAGAACGATACATTTTGCCTT TGGCTATAGTGATGAAGGCGGTGTACATAAGCAATATACTTTGAAGATC	SEQ ID NO:966	R	up	
Sa_levo	SA1198	144-243	AATAACAGTGCCAGGCAAAAATGATGAAGTACAACGCTGTATTACTGCTC ATGTTGATACTTTAGGTGCAATGGTTAAAGAAATTAAGAAGATGGTCGC	SEQ ID NO:967	R	up	x
Sa_levo	SA1221	3-102	GAAAAAATGGCAATTTGTTGGTACTACAGCTTTAGGTGCAACACTATTAT TAGGTGCTTGTGGTGGCGGTAATGGTGGCAGTGGTAATAGTGATTTAAAA	SEQ ID NO:968	R	up	
Sa_levo	SA1315	49-148	GCATGCGGTGCAGCAGCGCCAGATATATATGATTACGACGACGAAGGTAT TGCTTTCGTAATCCTTGACGATAACCAAGGTACTGCAGAAGTACCTGAGG	SEQ ID NO:969	R	up	
Sa_levo	SA1411	8-107	CAGATAGGCAATTGAGTATATTAAACGCAATTGTTGAGGATTATGTTGAT TTTGGACAACCCGTTGGTTCTAAAACACTAATTGAGCGACATAACTTGAA	SEQ ID NO:970	R	up	
Sa_levo	SA1738	209-308	GGCTACACGAGGCGCTACAATATGCCCAACCTGTAGAAGTTAAATTTTAT AATAATGGCTTTGTAGATTCAGTACGCTTAACCATTTATCGTATTGATGC	SEQ ID NO:971	R	up	
Sa_levo	SA1759	134-233	TGTGGGGAAATGCAAAAGATGCAATCAATAACGATTTTAAAAACATGGCA ACAGTATATGAAAACACACCATCGTTTGTTCCACAAATAGGTGATGTGGC	SEQ ID NO:972	R	up	
Sa_levo	SA1764	1165-1264	AGTGATACACCGCCAGAAAATCCAGTCAATGATATGCTTTGGTATGATAC AAGTAACCCTGATGTTGCTGTCTTGCGTAGATATTGGAATGGTCGATGGA	SEQ ID NO:973	R	up	

Sa_levo	SA1765	686-785	GTCGGCGGTGACTTTGTGATATCCAATCTTGGCGAAGGATATAAAGCAAC TAATTTTCCTGATGCAAAAGGTTGGGTTGGTGCTGGCACGAAACGAGGGC	SEQ ID NO:974	R	up	
Sa_levo	SA1811	696-795	AAAGGCACTCCAGAGTTCAAAGATATGCTTAAAAACTTGAATGTAAATGA TGTTCTATATGCAGGTCATAATAGCACATGGGACCCTCAATCAAATTCAA	SEQ ID NO:975	R	up	
Sa_levo	SA1898	25-124	TCATTAGCAGTAGGTTTAGGAATCGTAGCAGGAAATGCAGGTCACGAAGC CCATGCAAGTGAAGCGGACTTAAATAAAGCATCTTTAGCGCAAATGGCGC	SEQ ID NO:976	R	up	
Sa_levo	SA2097	268-367	GCTAATAATTGGGCTGCTGCTGCACAAGGTGCTGGATTCACAGTAAATCA TACACCTTCTAAAGGCGCTATCCTACAATCTTCTGAAGGACCATTTGGTC	SEQ ID NO:977	R	up	
Sa_levo	SA2420	962-1061	GTCGTTGCAACAGCAGATCACTCTACTGGTGGTCTAACAATTGGTAAAGA TAAAGGATACGAATGGAATCCTCAACCGATTAAATCGATGAAACACTCTG	SEQ ID NO:978	R	up	
Sa_levo	SAS009	34-133	CAAGAATTCCAAGAGATACTTAATAGTGGCATTCATCCTGAATGGCTTTA TTGTGCAAAGGCTAATCTTGTTTTAGAGCCTGCTTATACTGGCGAAGGCA	SEQ ID NO:979	R	up	
Sa_levo	SAS016	6-105	TATTTATCGACAGTATCACCATGAAGGCGCACCAGTTTATGAAATTATAA CCAAACGTTTCAGCATGTTTCAATTAAATGTGACGATTCATTTAGTGAT	SEQ ID NO:980	R	up	
Cpase_ES BL	KPC	314-413	ACCCATCTCGGAAAAATATCTGACACAACAGGCATGACGGTGGCGGAGCTGT CCGCGGCCGCCGTGCAATACAGTGATAACGCCGCCGCCAATTTGTTGCTG	SEQ ID NO:981	R	carbapenemase	
Cpase_ES BL	NDM	112-211	CAAATGGAAACTGGCGACCAACGGTTTGGCGATCTGGTTTTCCGCCAGCT CGCACCGAATGTCTGGCAGCACACTTCCTATCTCGACATGCCGGGTTTCG	SEQ ID NO:982	R	carbapenemase	
Cpase_ES BL	OXA48	413-512	TGCTACATGCTTTCGATTATGGTAATGAGGACATTTCGGGCAATGTAGAC AGTTTCTGGCTCGACGGTGGTATTCGAATTTCGGCCACGGAGCAAATCAG	SEQ ID NO:983	R	carbapenemase	
Cpase_ES BL	IMP_A	37-136	GAAGAAGGTGTTTATGTTCATACATCGTTCGAAGAAGTTAACGGTTGGGG TGTTGTTTCTAAACACGGTTTGGTGGTTCTTGTAAACACTGACGCCTATC	SEQ ID NO:984	R	carbapenemase	
Cpase_ES BL	IMP_B	45-144	GAAAAGTTAGTCAATTGGTTTGTGGAGCGCGGCTATAAAATCAAAGGCAC TATTTCCTCACATTTCCATAGCGACAGCACAGGGGGAATAGAGTGGCTTA	SEQ ID NO:985	R	carbapenemase	
Cpase_ES BL	IMP_C	45-144	GAAAGTTAGTCACTTGGTTTGTGGAACGTGGCTATAAAATAAAAGGCAG TATTTCCTCTCATTTTCATAGCGACAGCACGGGCGGAATAGAGTGGCTTA	SEQ ID NO:986	R	carbapenemase	

Cpase_ESBL	IMP_D	1-100	TATGCATCTGAATTAACAAATGAACTTCTTAAAAAAGACGGTAAGGTACA AGCTAAAAATTCATTTAGCGGAGTTAGCTATTGGCTAGTTAAGAAAAAGA	SEQ ID NO:987	carbapenemase			
Cpase_ESBL	VIM	477-576	CTCTAGTGGAGATGTGGTGCGCTTCGGTCCCGTAGAGGTTTTCTATCCTG GTGCTGCGCATTCGGGCGACAATCTTGTGGTATACGTGCCGGCCGTGCGC	SEQ ID NO:988	carbapenemase			
Cpase_ESBL	CTXM15	259-358	AGTGAAAGCGAACCGAATCTGTTAAATCAGCGAGTTGAGATCAAAAAATC TGACCTTGTTAACTATAATCCGATTGCGGAAAAGCACGTCAATGGGACGA	SEQ ID NO:989	ESBL			
Cpase_ESBL	OXA10	246-345	CATAAAGAATGAGCATCAGGTTTTCAAATGGGACGGAAAGCCAAGAGCCA TGAAGCAATGGGAAAGAGACTTGACCTTAAGAGGGGCAATACAAGTTTCA	SEQ ID NO:990	ESBL			

Reverse complement sequences of select 100mer target sequences are presented in SEQ ID NOs: 991-1876 of the accompanying Sequence Listing, with SEQ ID NOs: 1877-2762 presenting select "Probe B" sequences (without terminal tag sequences) and SEQ ID NOs: 2763-3648 presenting select "Probe A" sequences (also without terminal tag sequences).

Table 10: every strain, MIC, CLSI class, and GoPhAST-R call, sorted by MIC. For phase 1, separate train and test.

KpMero_Phase 1	Species:	***K. pneumoniae***						
	Drug:	**meropenem**						
	Concentration treated:	2 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	1	mg/L	S				
	I =	2	mg/L	R				
	R ≥	4	mg/L	R				
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	6			

		Broth microdilution		GoPhAST-R				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**Res_prob**	**class**	CPase/select ESBL	**agreement**	
Strains used for phase 1 testing (classifier validation)	RB274	0.5	S	0.026	**S**		concordant	S_concordant
	RB404	0.5	S	0.104	**S**		concordant	S_concordant
	RB419	0.5	S	0.014	**S**		concordant	S_concordant
	RB288	0.5	S	0.114	**S**		concordant	S_concordant
	RB587	1	S	0.066	**S**	CTX-M-15	concordant	S_concordant
	RB411	2	I	0.366	**S**		discordant	I_discordant
	RB400	8	R	0.992	**R**	KPC (unknown type)	concordant	R_concordant
	RB271	16	R	0.722	**R**	KPC-3	concordant	R_concordant
	RB401	32	R	1	**R**	KPC (unknown type)	concordant	R_concordant
	RB408	64	R	1	**R**	VIM-27; CTX-M-15	concordant	R_concordant
	RB579	64	R	0.994	**R**	NDM-1; CTX-M15	concordant	R_concordant
	RB596	64	R	0.895	**R**		concordant	R_concordant
Strains used for phase 1 training (feature selection and	RB039	0.5	S	n/a	n/a			
	RB270	0.5	S	n/a	n/a			
	RB275	0.5	S	n/a	n/a			
	RB405	0.5	S	n/a	n/a			

classifier derivation)	RB410	0.5	S	n/a	n/a	CTX-M15; OXA-10		
	RB417	1	S	n/a	n/a			
	RB268	8	R	n/a	n/a	s		
	RB414	8	R	n/a	n/a	CTX-M15		
	RB290	32	R	n/a	n/a	KPC-3		
	RB285	64	R	n/a	n/a	KPC-2		
	RB402	64	R	n/a	n/a	KPC (unknown type)		
	RB552	64	R	n/a	n/a	OXA-10		
KpMero_Phase2	Species:	***K. pneumoniae***						
	Drug:	**meropenem**						
	Concentration treated:	2 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	1	mg/L	S				
	I =	2	mg/L	R				
	R ≥	4	mg/L	R				
	Aggregate performance:							

	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	6			
		Broth microdilution		**GoPhAST-R**				
PHASE 2 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**	CPase/select ESBL	**agreement**	
Strains used for phase 2 testing (classifier validation)	RB565	0.125	S	0.042	**S**		concordant	S_concordant
	RB483	0.25	S	0.002	**S**		concordant	S_concordant
	RB540	0.25	S	0	**S**		concordant	S_concordant
	RB541	0.25	S	0	**S**		concordant	S_concordant
	RB564	0.25	S	0	**S**		concordant	S_concordant
	RB039	0.5	S	0	**S**		concordant	S_concordant
	RB274	0.5	S	0	**S**		concordant	S_concordant
	RB041	0.5	S	0	**S**		concordant	S_concordant
	RB042	0.5	S	0.012	**S**		concordant	S_concordant
	RB273	0.5	S	0	**S**		concordant	S_concordant
	RB276	0.5	S	0.074	**S**		concordant	S_concordant
	RB280	0.5	S	0	**S**		concordant	S_concordant
	RB284	0.5	S	0	**S**		concordant	S_concordant
	RB554	0.5	S	0.746	**R**	OXA-48	discordant	S_discordant
	AR0034	2	I	0.682	**R**	IMP-4	concordant	I_concordant
	RB543	2	I	0.93	**R**	CTX-M-15	concordant	I_concordant
	RB780	2	I	0.656	**R**	KPC-3	concordant	I_concordant

AR0044	4	R	0.72	R	CTX-M-15	concordant	R_concordant
RB584	4	R	0.774	R	CTX-M-15	concordant	R_concordant
AR0047	4	R	0.992	R		concordant	R_concordant
AR0135	8	R	0.79	R	VIM-1	concordant	R_concordant
RB291	8	R	0.968	R		concordant	R_concordant
RB289	16	R	0.76	R	KPC-3	concordant	R_concordant
RB551	16	R	0.762	R	CTX-M-15; OXA-48	concordant	R_concordant
RB826	16	R	0.996	R	NDM-1; CTX-M-15; OXA-10	concordant	R_concordant
RB401	32	R	0.998	R	KPC (unknown type)	concordant	R_concordant
AR0139	32	R	0.728	R	NDM-1; CTX-M-15; OXA-10	concordant	R_concordant
RB462	32	R	0.858	R	KPC-2; OXA-10	concordant	R_concordant
RB480	32	R	0.772	R	KPC-2	concordant	R_concordant
RB285	64	R	0.978	R	KPC-2	concordant	R_concordant
Strains used for phase 2 training (feature selection and classifier derivation)							
RB274	0.5	S	n/a	n/a			
RB404	0.5	S	n/a	n/a			
RB419	0.5	S	n/a	n/a			
RB288	0.5	S	n/a	n/a			
RB039	0.5	S	n/a	n/a			
RB270	0.5	S	n/a	n/a			

	RB275	0.5	S	n/a	n/a			
	RB405	0.5	S	n/a	n/a			
	RB410	0.5	S	n/a	n/a	CTX-M15; OXA-10		
	RB587	1	S	n/a	n/a	CTX-M-15		
	RB417	1	S	n/a	n/a			
	RB411	2	I	n/a	n/a			
	RB400	8	R	n/a	n/a	KPC (unknown type)		
	RB268	8	R	n/a	n/a	KPC-4		
	RB414	8	R	n/a	n/a	CTX-M15		
	RB271	16	R	n/a	n/a	KPC-3		
	RB401	32	R	n/a	n/a	KPC (unknown type)		
	RB290	32	R	n/a	n/a	KPC-3		
	RB408	64	R	n/a	n/a	VIM-27; CTX-M-15		
	RB579	64	R	n/a	n/a	NDM-1; CTX-M15		
	RB596	64	R	n/a	n/a			
	RB285	64	R	n/a	n/a	KPC-2		
	RB402	64	R	n/a	n/a	KPC (unknown type)		
	RB552	64	R	n/a	n/a	OXA-10		

KpCip_phase1	Species:	***K. pneumoniae***						
	Drug:	**ciprofloxacin**						
	Concentration treated:	1 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	1	mg/L	S				
	I =	2	mg/L	R				
	R ≥	4	mg/L	R				
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	0			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**		**agreement**	
	RB041	0.03	S	0.004	**S**		concordant	S_concordant

Strains used for phase 1 testing (classifier validation)	RB416	0.03	S	0.138	**S**		concordant	S_concorda
	RB268	0.125	S	0.042	**S**		concordant	S_concorda
	RB405	0.5	S	0.012	**S**		concordant	S_concorda
	RB418	1	S	0.074	**S**		concordant	S_concorda
	RB122	2	I	0.48	**S**		discordant	I_discordar
	RB400	32	R	0.868	**R**		concordant	R_concordant
	RB595	64	R	0.786	**R**		concordant	R_concordant
	RB039	128	R	0.906	**R**		concordant	R_concordant
Strains used for phase 1 training (feature selection and classifier derivation)	RB040	0.03	S	n/a	n/a			
	RB123	0.03	S	n/a	n/a			
	RB403	0.06	S	n/a	n/a			
	RB592	0.25	S	n/a	n/a			
	RB415	0.5	S	n/a	n/a			
	RB401	16	R	n/a	n/a			
	RB578	64	R	n/a	n/a			
	RB013	128	R	n/a	n/a			
	RB402	128	R	n/a	n/a			
KpCip_phase2	Species:	***K. pneumoniae***						
	Drug:	**ciprofloxacin**						
	Concentration treated:	1 mg/L						

	CLSI breakpoints (2018 M100)			GoPhAST-R class								
	S ≤	1	mg/L	S								
	I =	2	mg/L	R								
	R ≥	4	mg/L	R								
	Aggregate performance:											
	Confusion matrix											
					Reference (MIC by CLSI)							
					SPD	S	I	R				
	Prediction				S	5	1	0				
					NS (I or R)	0	0	6				
					Broth microdilution		GoPhAST-R					
	PHASE 2 STATUS:	Strain		MIC	class	probR	class					agreement
Strains used for phase 2 testing (classifier validation)		RB040		0.03	S	0.084	S					concordant
		RB041		0.03	S	0.048	S					concordant
		RB572		0.03	S	0.112	S					concordant
		RB564		0.03	S	0.292	S					concordant
		RB568		0.06	S	0.236	S					concordant
		RB780		0.06	S	0.452	S					concordant

	AR0160	0.06	S	0.366	S		concordant	S_concordant
	RB274	0.125	S	0.164	S		concordant	S_concordant
	RB277	0.125	S	0.216	S		concordant	S_concordant
	RB565	0.125	S	0.11	S		concordant	S_concordant
	RB571	0.125	S	0.428	S		concordant	S_concordant
	AR0126	0.125	S	0.73	R		discordant	S_discordant
	AR0034	1	S	0.58	R		discordant	S_discordant
	RB419	16	R	0.866	R		concordant	R_concordant
	RB583	16	R	0.784	R		concordant	R_concordant
	RB287	64	R	0.994	R		concordant	R_concordant
	RB290	64	R	0.993	R		concordant	R_concordant
	RB543	64	R	0.848	R		concordant	R_concordant
	RB563	64	R	0.994	R		concordant	R_concordant
	RB569	64	R	0.872	R		concordant	R_concordant
	RB579	64	R	0.88	R		concordant	R_concordant
	RB582	64	R	0.98	R		concordant	R_concordant
	RB013	128	R	0.994	R		concordant	R_concordant
	RB039	128	R	0.995	R		concordant	R_concordant
	RB408	128	R	0.993	R		concordant	R_concordant
Strains used for phase 2 training (feature selection and classifier derivation)	RB041	0.03	S	n/a	n/a			
	RB416	0.03	S	n/a	n/a			
	RB040	0.03	S	n/a	n/a			
	RB123	0.03	S	n/a	n/a			
	RB403	0.06	S	n/a	n/a			
	RB268	0.125	S	n/a	n/a			
	RB592	0.25	S	n/a	n/a			

	RB405	0.5	S	n/a	n/a						
	RB415	0.5	S	n/a	n/a						
	RB418	1	S	n/a	n/a						
	RB122	2	I	n/a	n/a						
	RB401	16	R	n/a	n/a						
	RB400	32	R	n/a	n/a						
	RB595	64	R	n/a	n/a						
	RB578	64	R	n/a	n/a						
	RB039	128	R	n/a	n/a						
	RB013	128	R	n/a	n/a						
	RB402	128	R	n/a	n/a						
KpGent_phase1	Species:	***K. pneumoniae***									
	Drug:	**gentamicin**									
	Concentration treated:	4 mg/L									
	CLSI breakpoints (2018 M100)				GoPhAST-R class						
	S ≤	4	mg/L	S							
	I =	8	mg/L	R							
	R ≥	16	mg/L	R							

	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	4			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**		**agreement**	
Strains used for phase 1 testing (classifier validation)	IDR1600039511-01-00	0.5	S	0.004	**S**		concordant	
	UCI_7	0.5	S	0.016	**S**		concordant	
	AR0080	1	S	0.084	**S**		concordant	
	MGH_30	1	S	0.064	**S**		concordant	
	RB042	2	S	0.362	**S**		concordant	
	BIT-10	4	S	0.952	R		discordant	1-dilution error (S called R, i.e. not-S)
	UCI_63	4	S	0.948	R		discordant	1-dilution error (S cal R, i.e. not-S
	UCI_37	16	R	0.916	**R**		concordant	R_concord
	AR0042	32	R	0.728	**R**		concordant	R_concord
	BIDMC_34	32	R	0.94	**R**		concordant	R_concord
	MGH_63	32	R	0.95	**R**		concordant	R_concord
	ATCC 700721	64	R	0.816	**R**		concordant	R_concordant

	RB122	128	R	0.932	R		concordant	R_concorda
Strains used for phase 1 training (feature selection and classifier derivation)	RB040	0.5	S	n/a	n/a			
	UCI_13	0.5	S	n/a	n/a			
	BAC0800007138	0.5	S	n/a	n/a			
	RB121	1	S	n/a	n/a			
	AR0043	1	S	n/a	n/a			
	BWH_15	4	S	n/a	n/a			
	BIDMC_2A	4	S	n/a	n/a			
	UCI_67	8	I	n/a	n/a			"I" called "R" for training
	RB012	32	R	n/a	n/a			
	AR0076	32	R	n/a	n/a			
	MGH_35	32	R	n/a	n/a			
	RB826	64	R	n/a	n/a			
	IDR1600031102-01-00	64	R	n/a	n/a			
EcMero_phase1	Species:	***E. coli***						
	Drug:	**meropenem**						
	Concentration treated:	2 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	1	mg/L	S				
	I =	2	mg/L	R				

	R ≥	4	mg/L	R				
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	3			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**	CPase/select ESBL	**agreement**	
Strains used for phase 1 testing (classifier validation)	AR0058	0.25	S	0.078	**S**		concordant	S_concordant
	BAA2523*	0.5	S	0.702	**R**	OXA-48	discordant	*large inoculum effect (MIC 0.5 --> 32); called R; +CPase
	AR0089	0.5	S	0.204	**S**		concordant	S_concordant
	AR0104*	1	S	0.904	**R**	KPC-4	discordant	*large inoculum effect (MIC --> >32); S

								called R; +CPase
	IDR1300027657	1	S	0.116	S		concordant	S_concorda
	IDR1600043633	2	I	0.874	R	CTX-M-15	concordant	I_concorda
	UCI_51	4	R	0.168	S	CTX-M-15	discordant	R called S, 1 dilution fro int'd breakpoint, 2 from susc
	IDR1600029769	8	R	1	R	OXA-48	concordant	R_concordant
	BAA2469	16	R	1	R	NDM-1	concordant	R_concordant
	AR0048	32	R	0.822	R	NDM-1; CTX-M-15	concordant	R_concordant
	RB767	64	R	0.91	R	NDM	concordant	R_concordant
	RB765	64	R	1	R	NDM; KPC	concordant	R_concordant
	* = large inoculum effect							
Strains used for phase 1 training (feature selection and classifier derivation)	RB001	0.25	S	n/a	n/a			
	RB002	0.25	S	n/a	n/a			
	AR0077	0.5	S	n/a	n/a			
	BIDMC_77	0.5	S	n/a	n/a	CTX-M-15		
	RB076	0.5	S	n/a	n/a			
	IDR1600035372	0.5	S	n/a	n/a	CTX-M-15		
	RB156	1	S	n/a	n/a			
	MGH_57	4	R	n/a	n/a	CTX-M-15		
	AR0055	8	R	n/a	n/a	NDM-1		
	AR0061	8	R	n/a	n/a	KPC-3		
	AR0069	16	R	n/a	n/a	NDM-1		

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	IDR1200024571	64	R	n/a	n/a			
	IDR1200039757	64	R	n/a	n/a			
EcCip_phase1	Species:	***E. coli***						
	Drug:	**ciprofloxacin**						
	Concentration treated:	1 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	1	mg/L	S				
	I =	2	mg/L	R				
	R ≥	4	mg/L	R				
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	0			
		Broth microdilution		**GoPhAST-R**				

PHASE 1 STATUS:	Strain	MIC	class	probR	class		agreement	
Strains used for phase 1 testing (classifier validation)	RB001	0.03	S	0.002	**S**		concordant	S_concorda
	RB025	0.25	S	0.156	**S**		concordant	S_concorda
	AR0089	0.25	S	0.088	**S**		concordant	S_concorda
	IDR1200024571	0.5	S	0.034	**S**		concordant	S_concorda
	RB110	8	R	1	**R**		concordant	R_concordant
	AR0085	16	R	0.972	**R**		concordant	R_concordant
	RB086	64	R	1	**R**		concordant	R_concordant
	BAA2469	64	R	0.9	**R**		concordant	R_concordant
	BAC0800005647	64	R	1	**R**		concordant	R_concordant
Strains used for phase 1 training (feature selection and classifier derivation)	RB075	0.03	S	n/a	n/a			
	IDR1300034680	0.03	S	n/a	n/a			
	AR0061	0.25	S	n/a	n/a			
	BAA2523	0.5	S	n/a	n/a			
	RB077	1	S	n/a	n/a			
	AR0081	16	R	n/a	n/a			
	AR0104	32	R	n/a	n/a			
	RB051	64	R	n/a	n/a			
	RB057	64	R	n/a	n/a			
EcGent_phase1	Species:	***E. coli***						
	Drug:	**gentamicin**						
	Concentration treated:	4 mg/L						

	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	4	mg/L	S				
	I =	8	mg/L	R				
	R ≥	16	mg/L	R				
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	0	0			
		NS (I or R)	0	0	0			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**		**agreement**	
Strains used for phase 1 testing (classifier validation)	RB075	0.5	S	0.106	**S**		concordant	S_concorda
	MGH_57	0.5	S	0.474	**S**		concordant	S_concorda
	IDR1300034680	1	S	0.002	**S**		concordant	S_concorda
	BAC0800005647	1	S	0	**S**		concordant	S_concorda
	AR0061	32	R	1	**R**		concordant	R_concorda
	AR0055	64	R	1	**R**		concordant	R_concordant

	IDR1600047120	64	R	0.928	R		concordant	R_concordi
	RB051	256	R	0.916	R		concordant	R_concordi
Strains used for phase 1 training (feature selection and classifier derivation)	AR0081	0.5	S	n/a	n/a			
	AR0084	0.5	S	n/a	n/a			
	RB001	1	S	n/a	n/a			
	RB076	1	S	n/a	n/a			
	AR0085	2	S	n/a	n/a			
	BAA2469	64	R	n/a	n/a			
	IDR1300027657	64	R	n/a	n/a			
	RB765	64	R	n/a	n/a			
	RB057	256	R	n/a	n/a			
AbMero_phase1	Species:	***A. baumanii***						
	Drug:	**meropenem**						
	Concentration treated:	2 mg/L						
	CLSI breakpoints (2018 M100)							
	S ≤	2	mg/L					
	I =	4-8	mg/L					
	R ≥	16	mg/L					

	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	2			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**	CPase/select ESBL	**agreement**	
Strains used for phase 1 testing (classifier validation)	RB197	0.5	S	0.042	**S**		concordant	S_concordant
	RB197s	0.5	S	0.19	**S**		concordant	S_concordant
	RB206	1	S	0.6	R		discordant	S misclassified as R, 1 dilution from breakpoint, 2-dilution error
	AR0063	4	I	0.702	**R**		concordant	R_concordant
	RB204	16	R	0.754	**R**		concordant	R_concordant
	AR0036	16	R	0.668	**R**		concordant	R_concordant
	AR0045	32	R	0.948	**R**		concordant	R_concordant
	AR0101	64	R	0.882	**R**		concordant	R_concordant
	RB203	64	R	0.998	**R**		concordant	R_concordant

	AR0078	64	R	0.88	R		concordant	R_concord
	AR0035	64	R	0.834	R		concordant	R_concord
Strains used for phase 1 training (feature selection and classifier derivation)	RB201	0.25	S	n/a	n/a			
	ATCC 17978	0.5	S	n/a	n/a			
	RB205	1	S	n/a	n/a			
	AR0052	2	S	n/a	n/a			
	AR0102	4	I	n/a	n/a			"I" called "R" for training
	RB198	8	I	n/a	n/a			"I" called "R" for training
	AR0070	16	R	n/a	n/a			
	RB202	32	R	n/a	n/a			
	RB200	64	R	n/a	n/a			
	AR0033	64	R	n/a	n/a	NDM-1		
	AR0037	64	R	n/a	n/a	NDM-1		
	AR0056	64	R	n/a	n/a			
	NOTE: "s" modifier to strain name denotes small colony morphotype of RB197							

AbCip_phase1	Species:	***A. baumanii***						
	Drug:	**ciprofloxacin**						
	Concentration treated:	1 mg/L						
	CLSI breakpoints (2018 M100)							
	S ≤	1	mg/L					
	I =	2	mg/L					
	R ≥	4	mg/L					
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	5	1	0			
		NS (I or R)	0	0	3			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**		**agreement**	
	RB201	0.25	S	0.308	**S**		concordant	S_concordant

Strains used for phase 1 testing (classifier validation)	RB201a	0.25	S	0.136	**S**		concordant	S_concorda
	RB197s	0.25	S	0.114	**S**		concordant	S_concorda
	RB205	1	S	0.012	**S**		concordant	S_concorda
	AR0063	8	R	1	**R**		concordant	R_concorda
	RB198	64	R	0.942	**R**		concordant	R_concorda
	RB203	64	R	1	**R**		concordant	R_concordant
	RB206	64	R	1	**R**		concordant	R_concordant
	AR0035	64	R	1	**R**		concordant	R_concordant
	AR0045	64	R	1	**R**		concordant	R_concordant
	AR0078	64	R	1	**R**		concordant	R_concordant
	AR0102	64	R	1	**R**		concordant	R_concordant
Strains used for phase 1 training (feature selection and classifier derivation)	RB197	0.25	S	n/a	n/a			
	RB197b	0.25	S	n/a	n/a			
	RB197a	0.25	S	n/a	n/a			
	ATCC 17978	0.5	S	n/a	n/a			
	AR0052	4	R	n/a	n/a			
	AR0070	8	R	n/a	n/a			
	RB202	64	R	n/a	n/a			
	RB204	64	R	n/a	n/a			
	AR0033	64	R	n/a	n/a			
	AR0037	64	R	n/a	n/a			
	AR0056	64	R	n/a	n/a			
	AR0101	64	R	n/a	n/a			
	AR0036	64	R	n/a	n/a			

	NOTE: "a", "b", and "c" modifiers to strain names denote biological replicates:							
	separate colonies of each isolate, grown and treated separately							
	(done because of paucity of cip-S *A. baumanii* strains in the collection)							
AbGent_phase1	Species:	***A. baumanii***						
	Drug:	**gentamicin**						
	Concentration treated:	4 mg/L						
	CLSI breakpoints (2018 M100)							
	S ≤	4	mg/L					
	I =	8	mg/L					
	R ≥	16	mg/L					

Aggregate performance:

Confusion matrix

		Reference (MIC by CLSI)		
	SPD	S	I	R
Prediction	S	5	1	0
	NS (I or R)	0	0	1

		Broth microdilution		GoPhAST-R		
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**	**agreement**
Strains used for phase 1 testing (classifier validation)	ATCC 17978	0.5	S	0.162	S	concordant
	RB205	2	S	0.248	S	concordant
	AR0063	4	S	0.088	S	concordant
	AR0035	16	R	0.953	R	concordant
	AR0052	32	R	1	R	concordant
	RB200	64	R	1	R	concordant
	RB204	64	R	0.958	R	concordant
	AR0037	64	R	1	R	concordant
	AR0056	64	R	1	R	concordant
	AR0078	64	R	1	R	concordant

Strains used for phase 1 training (feature selection and classifier derivation)	RB197	0.5	S	n/a	n/a			
	RB201	1	S	n/a	n/a			
	RB203	4	S	n/a	n/a			
	AR0101	8	I	n/a	n/a			"I" called " for training
	AR0033	32	R	n/a	n/a			
	RB198	64	R	n/a	n/a			
	RB202	64	R	n/a	n/a			
	RB206	64	R	n/a	n/a			
	AR0045	64	R	n/a	n/a			
	AR0070	64	R	n/a	n/a			
	AR0102	64	R	n/a	n/a			
PaCip_phase1	Species:	***P. aeruginosa***						
	Drug:	**ciprofloxacin**						
	Concentration treated:	1 mg/L						
	CLSI breakpoints (2018 M100)			GoPhAST-R class				
	S ≤	0.5	mg/L	S				
	I =	1	mg/L	R				
	R ≥	2	mg/L	R				

	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					
		SPD	S	I	R			
	Prediction	S	6	0	0			
		NS (I or R)	0	1	5			
		Broth microdilution		**GoPhAST-R**				
PHASE 1 STATUS:	**Strain**	**MIC**	**class**	**probR**	**class**		**agreement**	
Strains used for phase 1 testing (classifier validation)	BL08	0.06	S	0.242	**S**		concordant	
	BWHPSA043	0.06	S	0.024	**S**		concordant	
	CF18	0.06	S	0.198	**S**		concordant	
	BL11	0.125	S	0.394	**S**		concordant	
	UDL	0.125	S	0.332	**S**		concordant	
	BL22	0.5	S	0.498	**S**		concordant	
	CF27	1	I	0.86	**R**		concordant	
	BWHPSA048	8	R	0.678	**R**		concordant	
	X13273	8	R	0.896	**R**		concordant	
	BL17	16	R	0.994	**R**		concordant	
	BWHPSA006	16	R	1	**R**		concordant	
	BWH053	16	R	1	**R**		concordant	
	BWH029	0.03	S	n/a	n/a			

Strains used for phase 1 training (feature selection and classifier derivation)	BWH033	0.06	S	n/a	n/a			
	BWHPSA046	0.06	S	n/a	n/a			
	BL01	0.125	S	n/a	n/a			"I" called " for training
	BWH055	0.125	S	n/a	n/a			
	BWH050	0.25	S	n/a	n/a			
	BWHPSA041	2	R	n/a	n/a			
	CF5	8	R	n/a	n/a			
	BL03	16	R	n/a	n/a			
	BWHPSA003	16	R	n/a	n/a			
	BWH049	16	R	n/a	n/a			
	X24509	64	R	n/a	n/a			
Sa_Levo_phase1								
	Species:	***S. aureus***						
	Drug:	**levofloxacin**						
	Concentration treated:	1 mg/L						
	CLSI breakpoints (2018 M100)				GoPhAST-R class			
	S ≤	1	mg/L		S			
	I =	2	mg/L		R			
	Aggregate performance:							
	Confusion matrix							
			Reference (MIC by CLSI)					

		SPD	S	I	R
	Prediction	S	6	0	0
		NS (I or R)	0	0	6

PHASE 1 STATUS:	Strain	Broth microdilution MIC	class	GoPhAST R probR	class	agreement	Comments
Strains used for phase 1 testing (classifier validation)	RB065	0.06	S	0.002	S	concordant	
	RB067	0.13	S	0.012	S	concordant	
	RB069	0.13	S	0	S	concordant	
	RB098	0.13	S	0	S	concordant	
	RB223	0.13	S	0.002	S	concordant	
	RB247	0.5	S	0.006	S	concordant	
	RB064	8	R	1	R	concordant	
	RB211	16	R	1	R	concordant	
	RB045	32	R	1	R	concordant	
	RB090	32	R	1	R	concordant	
	RB219	32	R	1	R	concordant	
	RB047	64	R	1	R	concordant	

Strains used for phase 1 training (feature selection and classifier derivation)						
	RB006	0.06	S	n/a	n/a	
	RB066	0.06	S	n/a	n/a	
	RB003	0.125	S	n/a	n/a	
	RB096	0.13	S	n/a	n/a	
	RB221	0.13	S	n/a	n/a	
	RB245	0.25	S	n/a	n/a	
	RB072	4	R	n/a	n/a	

RB007	16	R	n/a		n/a
RB004	32	R	n/a		n/a
RB074	32	R	n/a		n/a
RB095	32	R	n/a		n/a
RB010	64	R	n/a		n/a

One skilled in the art would readily appreciate that the present disclosure is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the disclosure. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the disclosure, are defined by the scope of the claims.

In addition, where features or aspects of the disclosure are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the disclosure is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

The use of the terms "a" and "an" and "the" and similar referents in the context of describing the disclosure (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms "comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein.

All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the disclosure and does not pose a limitation on the scope of the disclosure unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the disclosure.

Embodiments of this disclosure are described herein, including the best mode known to the inventors for carrying out the disclosed disclosure. Variations of those embodiments may become apparent to those of ordinary skill in the art upon reading the foregoing description.

The disclosure illustratively described herein suitably can be practiced in the absence of any element or elements, limitation or limitations that are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of", and "consisting of" may be replaced with either of the other two terms. The terms and expressions which

have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the disclosure claimed. Thus, it should be understood that although the present disclosure provides preferred embodiments, optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this disclosure as defined by the description and the appended claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications can be made to the disclosure disclosed herein without departing from the scope and spirit of the disclosure. Thus, such additional embodiments are within the scope of the present disclosure and the following claims. The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the disclosure to be practiced otherwise than as specifically described herein. Accordingly, this disclosure includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the disclosure unless otherwise indicated herein or otherwise clearly contradicted by context. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure described herein. Such equivalents are intended to be encompassed by the following claims.

REFERENCES

Abeel, T., T. Van Parys, Y. Saeys, J. Galagan, and Y. Van de Peer. 2012. 'GenomeView: a next-generation genome browser', Nucleic Acids Res, 40: e12.

Adams-Sapper, S., S. Nolen, G. F. Donzelli, M. Lal, K. Chen, L. H. Justo da Silva, B. M. Moreira, and L. W. Riley. 2015. 'Rapid induction of high-level carbapenem resistance in heteroresistant KPC-producing Klebsiella pneumoniae', Antimicrob Agents Chemother, 59: 3281-9.

Adler, A., M. Ben-Dalak, I. Chmelnitsky, and Y. Carmeli. 2015. 'Effect of Resistance Mechanisms on the Inoculum Effect of Carbapenem in Klebsiella pneumoniae Isolates with Borderline Carbapenem Resistance', Antimicrob Agents Chemother, 59: 5014-7.

Allcock, R. J. N., A. V. Jennison, and D. Warrilow. 2017. 'Towards a Universal Molecular Microbiological Test', J Clin Microbiol, 55: 3175-82.

Anderson, K. F., D. R. Lonsway, J. K. Rasheed, J. Biddle, B. Jensen, L. K. McDougal, R. B. Carey, A. Thompson, S. Stocker, B. Limbago, and J. B. Patel. 2007. 'Evaluation of methods to identify the Klebsiella pneumoniae carbapenemase in Enterobacteriaceae', J Clin Microbiol, 45: 2723-5.

Arnold, R. S., K. A. Thom, S. Sharma, M. Phillips, J. Kristie Johnson, and D. J. Morgan. 2011. 'Emergence of Klebsiella pneumoniae carbapenemase-producing bacteria', South Med J, 104: 40-5.

Arzanlou, M., Chai, W. C. & Venter, H. Intrinsic, adaptive and acquired antimicrobial resistance in Gram-negative bacteria. Essays Biochem 61, 49-59, doi:10.1042/EBC20160063 (2017).

Barczak, A. K., J. E. Gomez, B. B. Kaufmann, E. R. Hinson, L. Cosimi, M. L. Borowsky, A. B. Onderdonk, S. A. Stanley, D. Kaur, K. F. Bryant, D. M. Knipe, A. Sloutsky, and D. T. Hung. 2012. 'RNA signatures allow rapid identification of pathogens and antibiotic susceptibilities', Proc Natl Acad Sci U S A, 109: 6217-22.

Bhattacharyya, R. P., M. Walker, R. Boykin, S. S. Son, J. Liu, A. C. Hachey, P. Ma, L. Wu, K. Choi, K. C. Cummins, M. Benson, J. Skerry, H. Ryu, S. Y. Wong, M. B. Goldberg, J. Han, V. M. Pierce, L. A. Cosimi, N. Shoresh, J. Livny, J. Beechem, and D. T. Hung. 2019. 'Rapid identification and phylogenetic classification of diverse bacterial pathogens in a multiplexed hybridization assay targeting ribosomal RNA', Sci Rep.

Bhattacharyya, R. P., Grad, Y. H. & Hung, D. T. in Harrison's Principles of Internal Medicine (eds J.L. Jameson et al.) Ch. 474, 3491-3504 (McGraw-Hill Education, 2018).

Boehme, C. C. et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 363, 1005-1015, doi:10.1056/NEJMoa0907847 (2010).Bradley, P., H. C. den Bakker, E. P. C. Rocha, G. McVean, and Z. Iqbal. 2019. 'Ultrafast search of all deposited bacterial and viral genomic data', Nat Biotechnol, 37: 152-59.

Bradley, P., N. C. Gordon, T. M. Walker, L. Dunn, S. Heys, B. Huang, S. Earle, L. J. Pankhurst, L. Anson, M. de Cesare, P. Piazza, A. A. Votintseva, T. Golubchik, D. J. Wilson, D. H. Wyllie, R. Diel, S. Niemann, S. Feuerriegel, T. A. Kohl, N. Ismail, S. V. Omar, E. G. Smith, D. Buck, G. McVean, A. S. Walker, T. E. Peto, D. W. Crook, and Z. Iqbal. 2015. 'Rapid antibiotic-resistance

predictions from genome sequence data for Staphylococcus aureus and Mycobacterium tuberculosis', Nat Commun, 6: 10063.

Bradley, P., den Bakker, H. C., Rocha, E. P. C., McVean, G. & Iqbal, Z. Ultrafast search of all deposited bacterial and viral genomic data. Nat Biotechnol 37, 152-159, doi:10.1038/s41587-018-0010-1 (2019).

Brown, L. D., Cai, T. T. & DasGupta, A. Interval Estimation for a Binomial Proportion. Statist Sci 16, 101-133, doi:10.1214/ss/1009213286 (2001).

Burnham, C. D., Leeds, J., Nordmann, P., O'Grady, J. & Patel, J. Diagnosing antimicrobial resistance. Nat Rev Microbiol 15, 697-703, doi:10.1038/nrmicro.2017.103 (2017).

Caniaux, I., A. van Belkum, G. Zambardi, L. Poirel, and M. F. Gros. 2017. 'MCR: modern colistin resistance', Eur J Clin Microbiol Infect Dis, 36: 415-20.

Canton, R., Gonzalez-Alba, J. M. & Galan, J. C. CTX-M Enzymes: Origin and Diffusion. Front Microbiol 3, 110, doi:10.3389/fmicb.2012.00110 (2012).

Centers for Disease, Control, and Prevention. 2009. 'Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities', MMWR Morb Mortal Wkly Rep, 58: 256-60.

Cermak, N., S. Olcum, F. F. Delgado, S. C. Wasserman, K. R. Payer, A. Murakami M, S. M. Knudsen, R. J. Kimmerling, M. M. Stevens, Y. Kikuchi, A. Sandikci, M. Ogawa, V. Agache, F. Baleras, D. M. Weinstock, and S. R. Manalis. 2016. 'High-throughput measurement of single-cell growth rates using serial microfluidic mass sensor arrays', Nat Biotechnol, 34: 1052-59.

Cerqueira, G. C., A. M. Earl, C. M. Ernst, Y. H. Grad, J. P. Dekker, M. Feldgarden, S. B. Chapman, J. L. Reis-Cunha, T. P. Shea, S. Young, Q. Zeng, M. L. Delaney, D. Kim, E. M. Peterson, T. F. O'Brien, M. J. Ferraro, D. C. Hooper, S. S. Huang, J. E. Kirby, A. B. Onderdonk, B. W. Birren, D. T. Hung, L. A. Cosimi, J. R. Wortman, C. I. Murphy, and W. P. Hanage. 2017. 'Multi-institute analysis of carbapenem resistance reveals remarkable diversity, unexplained mechanisms, and limited clonal outbreaks', Proc Natl Acad Sci U S A, 114: 1135-40.

Charnot-Katsikas, A., V. Tesic, N. Love, B. Hill, C. Bethel, S. Boonlayangoor, and K. G. Beavis. 2018. 'Use of the Accelerate Pheno System for Identification and Antimicrobial Susceptibility

Testing of Pathogens in Positive Blood Cultures and Impact on Time to Results and Workflow', J Clin Microbiol, 56.

Chea, N., S. N. Bulens, T. Kongphet-Tran, R. Lynfield, K. M. Shaw, P. S. Vagnone, M. A. Kainer, D. B. Muleta, L. Wilson, E. Vaeth, G. Dumyati, C. Concannon, E. C. Phipps, K. Culbreath, S. J. Janelle, W. M. Bamberg, A. Y. Guh, B. Limbago, and A. J. Kallen. 2015. 'Improved Phenotype-Based Definition for Identifying Carbapenemase Producers among Carbapenem-Resistant Enterobacteriaceae', Emerg Infect Dis, 21: 1611-6.

Choi, J., H. Y. Jeong, G. Y. Lee, S. Han, S. Han, B. Jin, T. Lim, S. Kim, D. Y. Kim, H. C. Kim, E. C. Kim, S. H. Song, T. S. Kim, and S. Kwon. 2017. 'Direct, rapid antimicrobial susceptibility test from positive blood cultures based on microscopic imaging analysis', Sci Rep, 7: 1148.

Clark, R. B., Lewinski, M. A., Loeffelholz, M. J. & Tibbetts, R. J. Cumitech 31A, Verification and validation of procedures in the clinical microbiology laboratory. (ASM Press, 2009).

CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th edn. CLSI Supplement M07. Wayne, PA: Clinical and Laboratory Standards Institute (2018).

CLSI. 2018. Performance Standards for Antimicrobial Susceptibility Testing.

Consortium, C. RyPTIC, Genomes Project the, C. Allix-Beguec, I. Arandjelovic, L. Bi, P. Beckert, M. Bonnet, P. Bradley, A. M. Cabibbe, I. Cancino-Munoz, M. J. Caulfield, A. Chaiprasert, D. M. Cirillo, D. A. Clifton, I. Comas, D. W. Crook, M. R. De Filippo, H. de Neeling, R. Diel, F. A. Drobniewski, K. Faksri, M. R. Farhat, J. Fleming, P. Fowler, T. A. Fowler, Q. Gao, J. Gardy, D. Gascoyne-Binzi, A. L. Gibertoni-Cruz, A. Gil-Brusola, T. Golubchik, X. Gonzalo, L. Grandjean, G. He, J. L. Guthrie, S. Hoosdally, M. Hunt, Z. Iqbal, N. Ismail, J. Johnston, F. M. Khanzada, C. C. Khor, T. A. Kohl, C. Kong, S. Lipworth, Q. Liu, G. Maphalala, E. Martinez, V. Mathys, M. Merker, P. Miotto, N. Mistry, D. A. J. Moore, M. Murray, S. Niemann, S. V. Omar, R. T. Ong, T. E. A. Peto, J. E. Posey, T. Prammananan, A. Pym, C. Rodrigues, M. Rodrigues, T. Rodwell, G. M. Rossolini, E. Sanchez Padilla, M. Schito, X. Shen, J. Shendure, V. Sintchenko, A. Sloutsky, E. G. Smith, M. Snyder, K. Soetaert, A. M. Starks, P. Supply, P. Suriyapol, S. Tahseen, P. Tang, Y. Y. Teo, T. N. T. Thuong, G. Thwaites, E. Tortoli, D. van Soolingen, A. S. Walker, T. M. Walker, M. Wilcox, D. J. Wilson, D. Wyllie, Y. Yang, H. Zhang, Y. Zhao, and B. Zhu. 2018. 'Prediction of Susceptibility to First-Line Tuberculosis Drugs by DNA Sequencing', N Engl J Med, 379: 1403-15.

Cubero, M. et al. Carbapenem-resistant and carbapenem-susceptible isogenic isolates of Klebsiella pneumoniae ST101 causing infection in a tertiary hospital. BMC Microbiol 15, 177, doi:10.1186/s12866-015-0510-9 (2015).

Didelot, X., R. Bowden, D. J. Wilson, T. E. A. Peto, and D. W. Crook. 2012. 'Transforming clinical microbiology with bacterial genome sequencing', Nat Rev Genet, 13: 601-12.

Efron, B. & Gong, G. A Leisurely Look at the Bootstrap, the Jackknife, and Cross-Validation. American Statistician 37, 36-48, doi:Doi 10.2307/2685844 (1983).

Ellington, M. J., O. Ekelund, F. M. Aarestrup, R. Canton, M. Doumith, C. Giske, H. Grundman, H. Hasman, M. T. G. Holden, K. L. Hopkins, J. Iredell, G. Kahlmeter, C. U. Koser, A. MacGowan, D. Mevius, M. Mulvey, T. Naas, T. Peto, J. M. Rolain, O. Samuelsen, and N. Woodford. 2017. 'The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST Subcommittee', Clin Microbiol Infect, 23: 2-22.

Evans, S. R., A. M. Hujer, H. Jiang, K. M. Hujer, T. Hall, C. Marzan, M. R. Jacobs, R. Sampath, D. J. Ecker, C. Manca, K. Chavda, P. Zhang, H. Fernandez, L. Chen, J. R. Mediavilla, C. B. Hill, F. Perez, A. M. Caliendo, V. G. Fowler, Jr., H. F. Chambers, B. N. Kreiswirth, R. A. Bonomo, and Group Antibacterial Resistance Leadership. 2016. 'Rapid Molecular Diagnostics, Antibiotic Treatment Decisions, and Developing Approaches to Inform Empiric Therapy: PRIMERS I and II', Clin Infect Dis, 62: 181-9.

Fauci, A. S. & Morens, D. M. The perpetual challenge of infectious diseases. N Engl J Med 366, 454-461, doi:10.1056/NEJMra1108296 (2012).

Florio, W., Tavanti, A., Barnini, S., Ghelardi, E. & Lupetti, A. Recent Advances and Ongoing Challenges in the Diagnosis of Microbial Infections by MALDI-TOF Mass Spectrometry. Front Microbiol 9, 1097, doi:10.3389/fmicb.2018.01097 (2018).

Ford, B. A. 2018. 'mecC-Harboring Methicillin-Resistant Staphylococcus aureus: Hiding in Plain Sight', J Clin Microbiol, 56.

Garcia-Alvarez, L., M. T. Holden, H. Lindsay, C. R. Webb, D. F. Brown, M. D. Curran, E. Walpole, K. Brooks, D. J. Pickard, C. Teale, J. Parkhill, S. D. Bentley, G. F. Edwards, E. K. Girvan, A. M. Kearns, B. Pichon, R. L. Hill, A. R. Larsen, R. L. Skov, S. J. Peacock, D. J. Maskell, and M. A. Holmes. 2011. 'Meticillin-resistant Staphylococcus aureus with a novel mecA homologue in human

and bovine populations in the UK and Denmark: a descriptive study', Lancet Infect Dis, 11: 595-603.

Geiss, G. K., R. E. Bumgarner, B. Birditt, T. Dahl, N. Dowidar, D. L. Dunaway, H. P. Fell, S. Ferree, R. D. George, T. Grogan, J. J. James, M. Maysuria, J. D. Mitton, P. Oliveri, J. L. Osborn, T. Peng, A. L. Ratcliffe, P. J. Webster, E. H. Davidson, L. Hood, and K. Dimitrov. 2008. 'Direct multiplexed measurement of gene expression with color-coded probe pairs', Nat Biotechnol, 26: 317-25.

Gotz, S. et al. High-throughput functional annotation and data mining with the Blast2GO suite. Nucleic Acids Res 36, 3420-3435, doi:10.1093/nar/gkn176 (2008).

Gupta, N., Limbago, B. M., Patel, J. B. & Kallen, A. J. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis 53, 60-67, doi:10.1093/cid/cir202 (2011).

Gupta, S. K. et al. ARG-ANNOT, a new bioinformatic tool to discover antibiotic resistance genes in bacterial genomes. Antimicrob Agents Chemother 58, 212-220, doi:10.1128/AAC.01310-13 (2014).

Gupta, V., R. Garg, K. Kumaraswamy, P. Datta, G. K. Mohi, and J. Chander. 2018. 'Phenotypic and genotypic characterization of carbapenem resistance mechanisms in Klebsiella pneumoniae from blood culture specimens: A study from North India', J Lab Physicians, 10: 125-29.

Holdren, J. P. et al. President's Council of Advisors on Science and Technology: Report to the President on Combating Antibiotic Resistance. (2014).

Hooper, D. C. New uses for new and old quinolones and the challenge of resistance. Clin Infect Dis 30, 243-254, doi:10.1086/313677 (2000).

Hou, H. W., R. P. Bhattacharyya, D. T. Hung, and J. Han. 2015. 'Direct detection and drug-resistance profiling of bacteremias using inertial microfluidics', Lab Chip, 15: 2297-307.

Humphries, R., and T. Di Martino. 2019. 'Effective implementation of the Accelerate Pheno system for positive blood cultures', J Antimicrob Chemother, 74: i40-i43.

Humphries, R. M. CIM City: The game continues for a better carbapenemase test. J Clin Microbiol, doi:10.1128/JCM.00353-19 (2019).

Ioannidis, P. et al. Cepheid GeneXpert MTB/RIF assay for Mycobacterium tuberculosis detection and rifampin resistance identification in patients with substantial clinical indications of tuberculosis

and smear-negative microscopy results. J Clin Microbiol 49, 3068-3070, doi:10.1128/JCM.00718-11 (2011).

Iovleva, A. & Doi, Y. Carbapenem-Resistant Enterobacteriaceae. Clin Lab Med 37, 303-315, doi:10.1016/j.cll.2017.01.005 (2017).

Jia, B. et al. CARD 2017: expansion and model-centric curation of the comprehensive antibiotic resistance database. Nucleic Acids Res 45, D566-D573, doi:10.1093/nar/gkw1004 (2017).

Kaase, M., F. Szabados, L. Wassill, and S. G. Gatermann. 2012. 'Detection of carbapenemases in Enterobacteriaceae by a commercial multiplex PCR', J Clin Microbiol, 50: 3115-8.

Kadri, S. S. et al. Difficult-to-Treat Resistance in Gram-negative Bacteremia at 173 US Hospitals: Retrospective Cohort Analysis of Prevalence, Predictors, and Outcome of Resistance to All First-line Agents. Clin Infect Dis 67, 1803-1814, doi:10.1093/cid/ciy378 (2018).

Klungthong, C., P. Chinnawirotpisan, K. Hussem, T. Phonpakobsin, W. Manasatienkij, C. Ajariyakhajorn, K. Rungrojcharoenkit, R. V. Gibbons, and R. G. Jarman. 2010. 'The impact of primer and probe-template mismatches on the sensitivity of pandemic influenza A/H1N1/2009 virus detection by real-time RT-PCR', J Clin Virol, 48: 91-5.

Kumar, A., D. Roberts, K. E. Wood, B. Light, J. E. Parrillo, S. Sharma, R. Suppes, D. Feinstein, S. Zanotti, L. Taiberg, D. Gurka, A. Kumar, and M. Cheang. 2006. 'Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock', Crit Care Med, 34: 1589-96.

Letunic, I. & Bork, P. Interactive Tree Of Life (iTOL) v4: recent updates and new developments. Nucleic Acids Res 47, W256-W259, doi:10.1093/nar/gkz239 (2019).

Li, H., and R. Durbin. 2009. 'Fast and accurate short read alignment with Burrows-Wheeler transform', Bioinformatics, 25: 1754-60.

Li, Y. et al. Penicillin-Binding Protein Transpeptidase Signatures for Tracking and Predicting beta-Lactam Resistance Levels in Streptococcus pneumoniae. MBio 7, doi:10.1128/mBio.00756-16 (2016).

Liakopoulos, A., D. J. Mevius, B. Olsen, and J. Bonnedahl. 2016. 'The colistin resistance mcr-1 gene is going wild', J Antimicrob Chemother, 71: 2335-6.

Liaw, A. & Wiener, M. Classification and Regression by RandomForest. Vol. 23 (2001).

Liu, B., and M. Pop. 2009. 'ARDB--Antibiotic Resistance Genes Database', Nucleic Acids Res, 37: D443-7.

Liu, Y. Y., Y. Wang, T. R. Walsh, L. X. Yi, R. Zhang, J. Spencer, Y. Doi, G. Tian, B. Dong, X. Huang, L. F. Yu, D. Gu, H. Ren, X. Chen, L. Lv, D. He, H. Zhou, Z. Liang, J. H. Liu, and J. Shen. 2016. 'Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study', Lancet Infect Dis, 16: 161-8.

Lomovskaya, O., D. Sun, D. Rubio-Aparicio, K. Nelson, R. Tsivkovski, D. C. Griffith, and M. N. Dudley. 2017. 'Vaborbactam: Spectrum of Beta-Lactamase Inhibition and Impact of Resistance Mechanisms on Activity in Enterobacteriaceae', Antimicrob Agents Chemother, 61.

Longo, G., L. Alonso-Sarduy, L. M. Rio, A. Bizzini, A. Trampuz, J. Notz, G. Dietler, and S. Kasas. 2013. 'Rapid detection of bacterial resistance to antibiotics using AFM cantilevers as nanomechanical sensors', Nat Nanotechnol, 8: 522-6.

Love, M. I., W. Huber, and S. Anders. 2014. 'Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2', Genome Biol, 15: 550.

Lutgring, J. D., and B. M. Limbago. 2016. 'The Problem of Carbapenemase-Producing-Carbapenem-Resistant-Enterobacteriaceae Detection', J Clin Microbiol, 54: 529-34.

Ma, P., H. H. Laibinis, C. M. Ernst, and D. T. Hung. 2018. 'Carbapenem Resistance Caused by High-Level Expression of OXA-663 beta-Lactamase in an OmpK36-Deficient Klebsiella pneumoniae Clinical Isolate', Antimicrob Agents Chemother, 62.

Marlowe, E. M. et al. Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of Mycobacterium tuberculosis complex in respiratory specimens. J Clin Microbiol 49, 1621-1623, doi:10.1128/JCM.02214-10 (2011).

Marner, E. S. et al. Diagnostic accuracy of the Cepheid GeneXpert vanA/vanB assay ver. 1.0 to detect the vanA and vanB vancomycin resistance genes in Enterococcus from perianal specimens. Diagn Microbiol Infect Dis 69, 382-389, doi:10.1016/j.diagmicrobio.2010.11.005 (2011).

Marschal, M., J. Bachmaier, I. Autenrieth, P. Oberhettinger, M. Willmann, and S. Peter. 2017. 'Evaluation of the Accelerate Pheno System for Fast Identification and Antimicrobial Susceptibility

Testing from Positive Blood Cultures in Bloodstream Infections Caused by Gram-Negative Pathogens', J Clin Microbiol, 55: 2116-26.

Marshall, S., A. M. Hujer, L. J. Rojas, K. M. Papp-Wallace, R. M. Humphries, B. Spellberg, K. M. Hujer, E. K. Marshall, S. D. Rudin, F. Perez, B. M. Wilson, R. B. Wasserman, L. Chikowski, D. L. Paterson, A. J. Vila, D. van Duin, B. N. Kreiswirth, H. F. Chambers, V. G. Fowler, Jr., M. R. Jacobs, M. E. Pulse, W. J. Weiss, and R. A. Bonomo. 2017. 'Can Ceftazidime-Avibactam and Aztreonam Overcome beta-Lactam Resistance Conferred by Metallo-beta-Lactamases in Enterobacteriaceae?', Antimicrob Agents Chemother, 61.

Martinez-Martinez, L., and J. J. Gonzalez-Lopez. 2014. 'Carbapenemases in Enterobacteriaceae: types and molecular epidemiology', Enferm Infecc Microbiol Clin, 32 Suppl 4: 4-9.

Maurer, F. P., Christner, M., Hentschke, M. & Rohde, H. Advances in Rapid Identification and Susceptibility Testing of Bacteria in the Clinical Microbiology Laboratory: Implications for Patient Care and Antimicrobial Stewardship Programs. Infect Dis Rep 9, 6839, doi:10.4081/idr.2017.6839 (2017).

McArthur, A. G. et al. The comprehensive antibiotic resistance database. Antimicrob Agents Chemother 57, 3348-3357, doi:10.1128/AAC.00419-13 (2013).

McMullen, A. R., Yarbrough, M. L., Wallace, M. A., Shupe, A. & Burnham, C. D. Evaluation of Genotypic and Phenotypic Methods to Detect Carbapenemase Production in Gram-Negative Bacilli. Clin Chem 63, 723-730, doi:10.1373/clinchem.2016.264804 (2017).

Milheirico, C., de Lencastre, H. & Tomasz, A. Full-Genome Sequencing Identifies in the Genetic Background Several Determinants That Modulate the Resistance Phenotype in Methicillin-Resistant Staphylococcus aureus Strains Carrying the Novel mecC Gene. Antimicrob Agents Chemother 61, doi:10.1128/AAC.02500-16 (2017).

Miller, S., and R. M. Humphries. 2016. 'Clinical laboratory detection of carbapenem-resistant and carbapenemase-producing Enterobacteriaceae', Expert Rev Anti Infect Ther, 14: 705-17.

Nathan, C. & Cars, O. Antibiotic Resistance - Problems, Progress, and Prospects. N Engl J Med, doi:10.1056/NEJMp1408040 (2014).

Nguyen, M. et al. Developing an in silico minimum inhibitory concentration panel test for Klebsiella pneumoniae. Sci Rep 8, 421, doi:10.1038/s41598-017-18972-w (2018).

Nordmann, P., G. Cuzon, and T. Naas. 2009. 'The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria', Lancet Infect Dis, 9: 228-36.

Nordmann, P., L. Dortet, and L. Poirel. 2012. "Carbapenem resistance in Enterobacteriaceae: here is the storm!" Trends Mol Med, 18: 263-72.

Paterson, D. L., W. C. Ko, A. Von Gottberg, J. M. Casellas, L. Mulazimoglu, K. P. Klugman, R. A. Bonomo, L. B. Rice, J. G. McCormack, and V. L. Yu. 2001. 'Outcome of cephalosporin treatment for serious infections due to apparently susceptible organisms producing extended-spectrum beta-lactamases: implications for the clinical microbiology laboratory', J Clin Microbiol, 39: 2206-12.

Paterson, G. K., E. M. Harrison, and M. A. Holmes. 2014. 'The emergence of mecC methicillin-resistant Staphylococcus aureus', Trends Microbiol, 22: 42-7.

Perez, K. K. et al. Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs. Arch Pathol Lab Med 137, 1247-1254, doi:10.5858/arpa.2012-0651-OA (2013).

Quach, D. T., G. Sakoulas, V. Nizet, J. Pogliano, and K. Pogliano. 2016. 'Bacterial Cytological Profiling (BCP) as a Rapid and Accurate Antimicrobial Susceptibility Testing Method for Staphylococcus aureus', EBioMedicine, 4: 95-103.

Rasko, D. A., D. R. Webster, J. W. Sahl, A. Bashir, N. Boisen, F. Scheutz, E. E. Paxinos, R. Sebra, C. S. Chin, D. Iliopoulos, A. Klammer, P. Peluso, L. Lee, A. O. Kislyuk, J. Bullard, A. Kasarskis, S. Wang, J. Eid, D. Rank, J. C. Redman, S. R. Steyert, J. Frimodt-Moller, C. Struve, A. M. Petersen, K. A. Krogfelt, J. P. Nataro, E. E. Schadt, and M. K. Waldor. 2011. 'Origins of the E. coli strain causing an outbreak of hemolytic-uremic syndrome in Germany', N Engl J Med, 365: 709-17.

Robnik-Šikonja, Marko, and Igor Kononenko. 2003. 'Theoretical and Empirical Analysis of ReliefF and RReliefF', Machine Learning, 53: 23-69.

Rossen, J. W. A., A. W. Friedrich, J. Moran-Gilad, Escmid Study Group for Genomic, and Diagnostics Molecular. 2018. 'Practical issues in implementing whole-genome-sequencing in routine diagnostic microbiology', Clin Microbiol Infect, 24: 355-60.

Salimnia, H. et al. Evaluation of the FilmArray Blood Culture Identification Panel: Results of a Multicenter Controlled Trial. J Clin Microbiol 54, 687-698, doi:10.1128/JCM.01679-15 (2016).

Shishkin, A. A., G. Giannoukos, A. Kucukural, D. Ciulla, M. Busby, C. Surka, J. Chen, R. P. Bhattacharyya, R. F. Rudy, M. M. Patel, N. Novod, D. T. Hung, A. Gnirke, M. Garber, M. Guttman, and J. Livny. 2015. 'Simultaneous generation of many RNA-seq libraries in a single reaction', Nat Methods, 12: 323-5.

Smith, K. P., and J. E. Kirby. 2018. 'The Inoculum Effect in the Era of Multidrug Resistance: Minor Differences in Inoculum Have Dramatic Effect on MIC Determination', Antimicrob Agents Chemother, 62.

Smith, M., B. Diederen, J. Scharringa, M. Leversteijn-van Hall, A. C. Fluit, and J. Cohen Stuart. 2016. 'Rapid and accurate detection of carbapenemase genes in Enterobacteriaceae with the Cepheid Xpert Carba-R assay', J Med Microbiol, 65: 951-3.

Sullivan, K. V., B. Deburger, S. S. Roundtree, C. A. Ventrola, D. L. Blecker-Shelly, and J. E. Mortensen. 2014. 'Pediatric multicenter evaluation of the Verigene gram-negative blood culture test for rapid detection of inpatient bacteremia involving gram-negative organisms, extended-spectrum beta-lactamases, and carbapenemases', J Clin Microbiol, 52: 2416-21.

Sun, J., H. Zhang, Y. H. Liu, and Y. Feng. 2018. 'Towards Understanding MCR-like Colistin Resistance', Trends Microbiol, 26: 794-808.

Tacconelli, E. et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis 18, 318-327, doi:10.1016/S1473-3099(17)30753-3 (2018).

Tagini, F., and G. Greub. 2017. 'Bacterial genome sequencing in clinical microbiology: a pathogen-oriented review', Eur J Clin Microbiol Infect Dis, 36: 2007-20.

Tanner, H., Evans, J. T., Gossain, S. & Hussain, A. Evaluation of three sample preparation methods for the direct identification of bacteria in positive blood cultures by MALDI-TOF. BMC Res Notes 10, 48, doi:10.1186/s13104-016-2366-y (2017).

Traczewski, M. M., Carretto, E., Canton, R., Moore, N. M. & Carba, R. S. T. Multicenter Evaluation of the Xpert Carba-R Assay for Detection of Carbapenemase Genes in Gram-Negative Isolates. J Clin Microbiol 56, doi:10.1128/JCM.00272-18 (2018).

van Belkum, A., M. Welker, D. Pincus, J. P. Charrier, and V. Girard. 2017. 'Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry in Clinical Microbiology: What Are the Current Issues?', Ann Lab Med, 37: 475-83.

van Duin, D., and R. A. Bonomo. 2016. 'Ceftazidime/Avibactam and Ceftolozane/Tazobactam: Second-generation beta-Lactam/beta-Lactamase Inhibitor Combinations', Clin Infect Dis, 63: 234-41.

Vandesompele, J. et al. Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. Genome Biol 3, RESEARCH0034 (2002).

Wadsworth, C. B., Sater, M. R. A., Bhattacharyya, R. P. & Grad, Y. H. Impact of species diversity on the design of RNA-based diagnostics for antibiotic resistance in Neisseria gonorrhoeae. Antimicrob Agents Chemother, doi:10.1128/AAC.00549-19 (2019).

Walker, G. T. et al. Analytical Performance of Multiplexed Screening Test for 10 Antibiotic Resistance Genes from Perianal Swab Samples. Clin Chem 62, 353-359, doi:10.1373/clinchem.2015.246371 (2016).

Walker, T. et al. Clinical Impact of Laboratory Implementation of Verigene BC-GN Microarray-Based Assay for Detection of Gram-Negative Bacteria in Positive Blood Cultures. J Clin Microbiol 54, 1789-1796, doi:10.1128/JCM.00376-16 (2016).

Weisenberg, S. A., D. J. Morgan, R. Espinal-Witter, and D. H. Larone. 2009. 'Clinical outcomes of patients with Klebsiella pneumoniae carbapenemase-producing K. pneumoniae after treatment with imipenem or meropenem', Diagn Microbiol Infect Dis, 64: 233-5.

Wiegand, I., K. Hilpert, and R. E. Hancock. 2008. 'Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances', Nat Protoc, 3: 163-75.

Wolk, D. M. et al. Multicenter evaluation of the Cepheid Xpert methicillin-resistant Staphylococcus aureus (MRSA) test as a rapid screening method for detection of MRSA in nares. J Clin Microbiol 47, 758-764, doi:10.1128/JCM.01714-08 (2009).

Woodworth, K. R., M. S. Walters, L. M. Weiner, J. Edwards, A. C. Brown, J. Y. Huang, S. Malik, R. B. Slayton, P. Paul, C. Capers, M. A. Kainer, N. Wilde, A. Shugart, G. Mahon, A. J. Kallen, J. Patel, L. C. McDonald, A. Srinivasan, M. Craig, and D. M. Cardo. 2018. 'Vital Signs: Containment of Novel Multidrug-Resistant Organisms and Resistance Mechanisms - United States, 2006-2017', MMWR Morb Mortal Wkly Rep, 67: 396-401.

World_Health_Organization. Antimicrobial resistance: global report on surveillance 2014. (2014).

Ye, Y., L. Xu, Y. Han, Z. Chen, C. Liu, and L. Ming. 2018. 'Mechanism for carbapenem resistance of clinical Enterobacteriaceae isolates', Exp Ther Med, 15: 1143-49.

Zankari, E., H. Hasman, S. Cosentino, M. Vestergaard, S. Rasmussen, O. Lund, F. M. Aarestrup, and M. V. Larsen. 2012. 'Identification of acquired antimicrobial resistance genes', J Antimicrob Chemother, 67: 2640-4.

Zhu, Y. Y., E. M. Machleder, A. Chenchik, R. Li, and P. D. Siebert. 2001. 'Reverse transcriptase template switching: a SMART approach for full-length cDNA library construction', Biotechniques, 30: 892-7.

What is claimed is:

1. A method, comprising:

obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a patient or an environmental source;

processing the sample to enrich the one or more bacterial cells;

contacting the sample with one or more antibiotic compounds;

lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells;

hybridizing the released mRNA to at least one set of two nucleic acid probes, wherein each nucleic acid probe includes a unique barcode or tag;

detecting the hybridized nucleic acid probes;

identifying one or more genetic resistance determinants; and

determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells.

2. The method of claim 1, wherein the at least one set of two nucleic acid probes includes one or more probes from **Table 3** and one or more probes from **Table 4**.

3. The method of claim 1, wherein the at least one set of two nucleic acid probes includes one or more probes from **Table 5** and one or more probes from **Table 6**.

4. The method of claim 1, wherein the at least one set of two nucleic acid probes includes a first probe comprising a sequence selected from the group consisting of SEQ ID NOs: 1877-2762 and a second probe comprising a sequence selected from the group consisting of SEQ ID NOs: 2763-3648, optionally wherein the first probe comprises a sequence of SED ID NO: (1877+n) and the second probe comprises a sequence of SEQ ID NO: (2763+n), wherein n = an integer ranging from 0 to 885, optionally wherein one or both probes further comprises a tag sequence.

5. The method of claim 1, wherein the at least one set of two nucleic acid probes binds to one or more Cre2 target sequences listed in **Table 1**.

6. The method of claim 1, wherein the at least one set of two nucleic acid probes binds to one or more KpMero4 target sequences listed in **Table 2**.

7. The method of claim 1, wherein the hybridizing occurs at a temperature between about 64°C and about 69°C.

8. The method of claim 1, wherein the hybridizing occurs at a temperature between about 65°C and about 67°C.

9. The method of claim 1, wherein the hybridizing occurs at about 65°C or about 66°C or about 67°C.

10. A composition comprising a set of nucleic acid probes corresponding to the probes listed in **Table 3** and **Table 4**.

11. A composition comprising a set of nucleic acid probes corresponding to the probes listed in **Table 5** and **Table 6**.

12. A composition comprising a set of nucleic acid probes that includes a first probe comprising a sequence selected from the group consisting of SEQ ID NOs: 1877-2762 and a second probe comprising a sequence selected from the group consisting of SEQ ID NOs: 2763-3648, optionally wherein the first probe comprises a sequence of SED ID NO: (1877+n) and the second probe comprises a sequence of SEQ ID NO: (2763+n), wherein n = an integer ranging from 0 to 885, optionally wherein one or both of the first and second probes further comprises a tag sequence.

13. A method of treating a patient, comprising:

obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a patient or an environmental source;

processing the sample to enrich the one or more bacterial cells;

contacting the sample with one or more antibiotic compounds;

lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells;

hybridizing the released mRNA to at least one set of two nucleic acid probes, wherein each nucleic acid probe includes a unique barcode or tag;

detecting the hybridized nucleic acid probes;

identifying one or more genetic resistance determinants;

determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; and

administering to the patient an appropriate antibiotic based on the determination of the identity and the antibiotic susceptibility of the one or more bacterial cells.

14. The method of claim 1 or 13, wherein processing includes subjecting the sample to centrifugation or differential centrifugation.

15. The method of claim 1 or 13, wherein the one or more antibiotic compounds are at a clinical breakpoint concentration.

16. The method of claim 1 or 13, wherein lysing occurs by a method selected from the group consisting of mechanical lysis, liquid homogenization lysis, sonication, freeze-thaw lysis, and manual grinding.

17. The method of claim 1 or 13, wherein the at least one set of two nucleic acid probes includes one control set and one responsive set, 3-5 control sets and 3-5 responsive sets, or 8-10 control sets and 8-10 responsive sets.

18. The method of claim 13, wherein the hybridizing occurs at a temperature between about 64°C and about 69°C.

19. The method of claim 13, wherein the hybridizing occurs at a temperature between about 65°C and about 67°C.

20. The method of claim 13, wherein the hybridizing occurs at about 65°C or about 66°C or about 67°C.

21. A kit, comprising a set of nucleic acid probes corresponding to the probes listed in **Table 3** and **Table 4**.

22. A kit, comprising a set of nucleic acid probes corresponding to the probes listed in **Table 5** and **Table 6**.

23. A kit, comprising a set of nucleic acid probes that includes a first probe comprising a sequence selected from the group consisting of SEQ ID NOs: 1877-2762 and a second probe comprising a sequence selected from the group consisting of SEQ ID NOs: 2763-3648, optionally wherein the first probe comprises a sequence of SED ID NO: (1877+n) and the second probe comprises a sequence of SEQ ID NO: (2763+n), wherein n = an integer ranging from 0 to 885, optionally wherein one or both of the first and second probes further comprises a tag sequence.

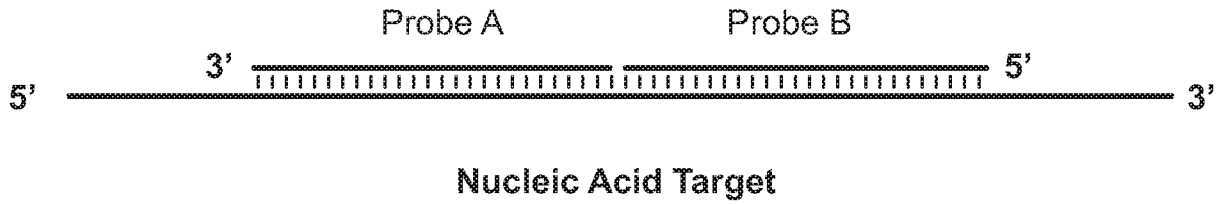


FIG. 1A

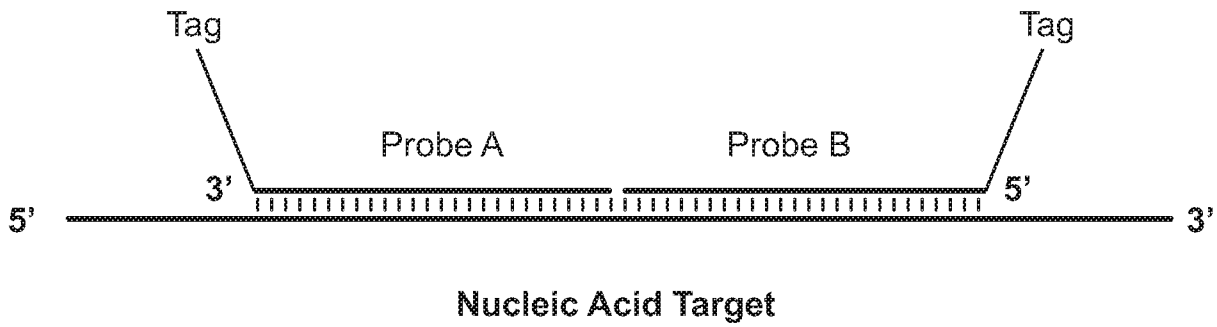


FIG. 1B

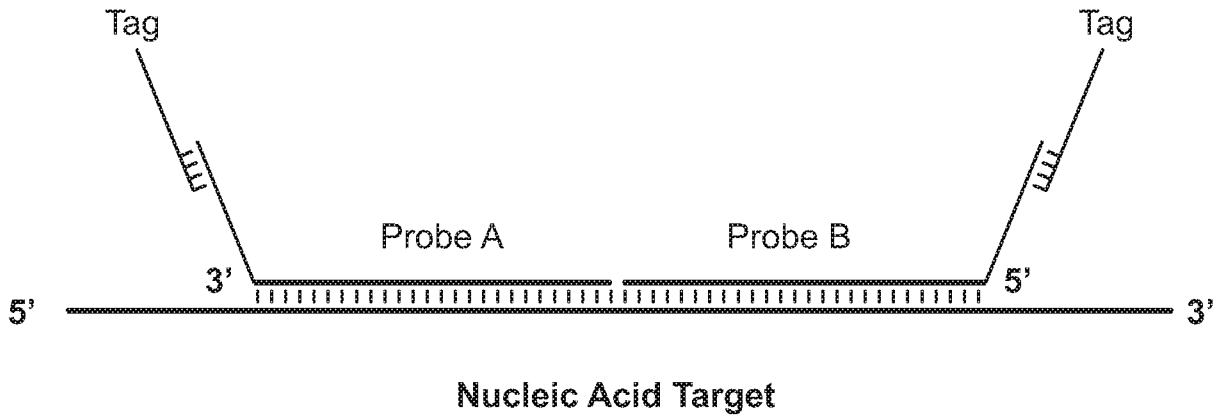


FIG. 1C

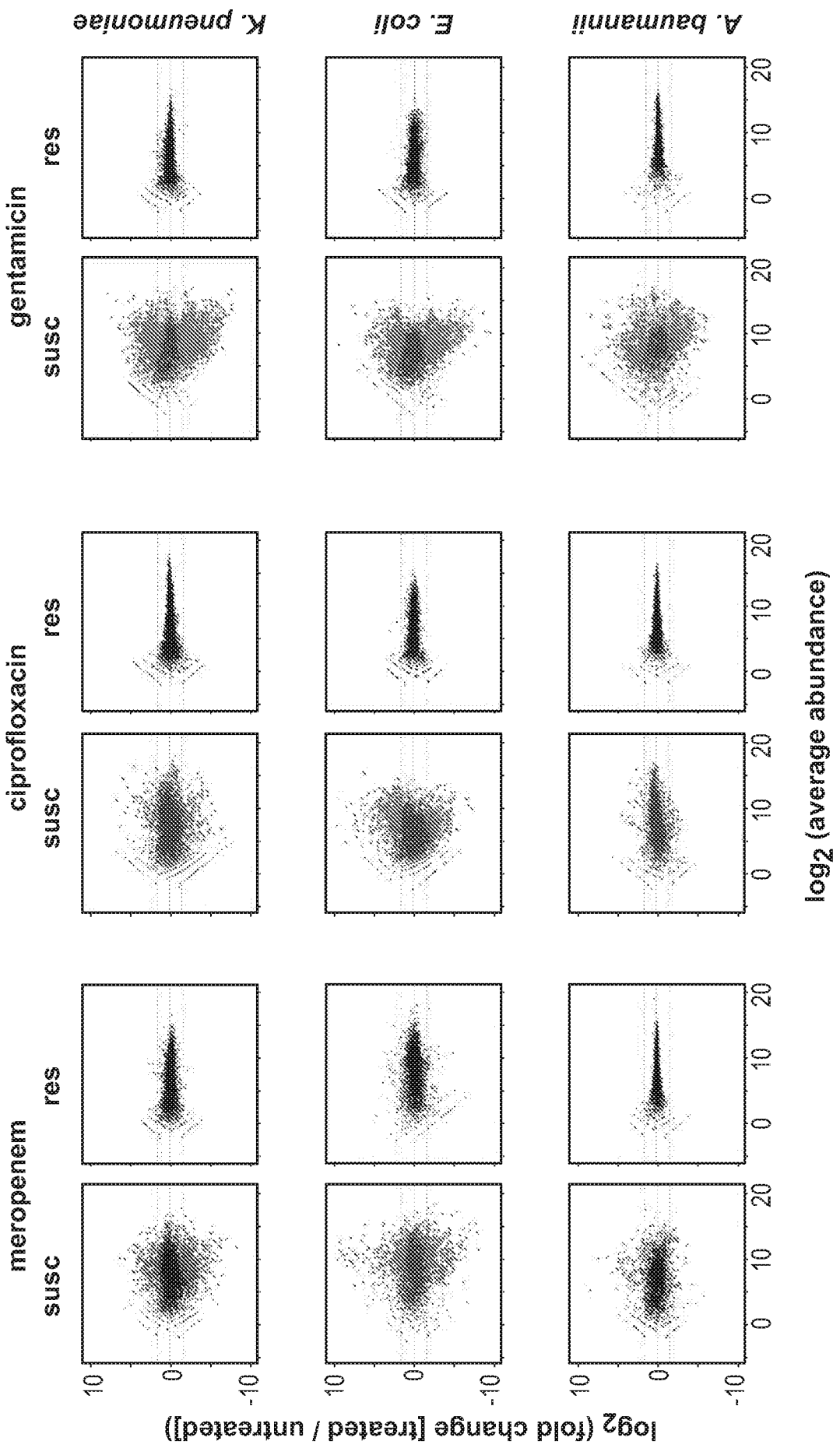

meropenem
ciprofloxacin
gentamicin
susc
res
A. baumannii
E. coli
K. pneumoniae
log2 (fold change [treated / untreated])
log2 (average abundance)
10
0
-10
0
10
20

FIG. 2A

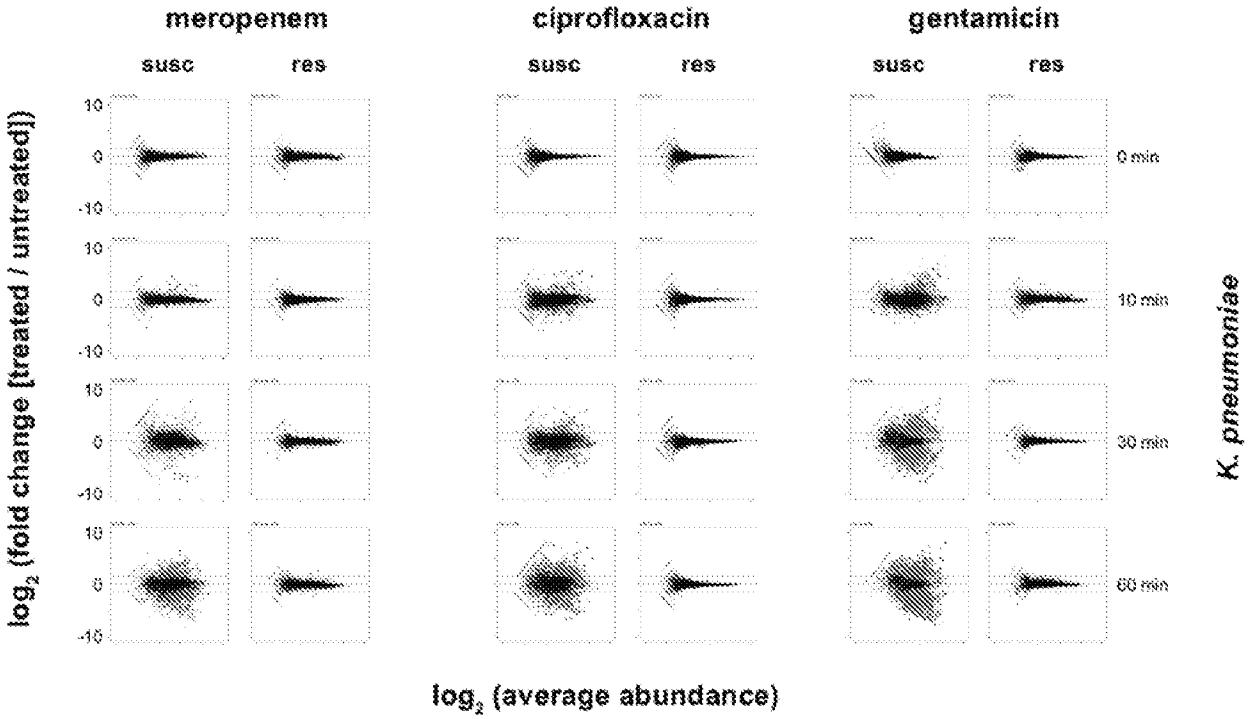

meropenem
ciprofloxacin
gentamicin
susc
res
0 min
10 min
30 min
60 min
K. pneumoniae
log2 (fold change [treated / untreated])
log2 (average abundance)

FIG. 2B

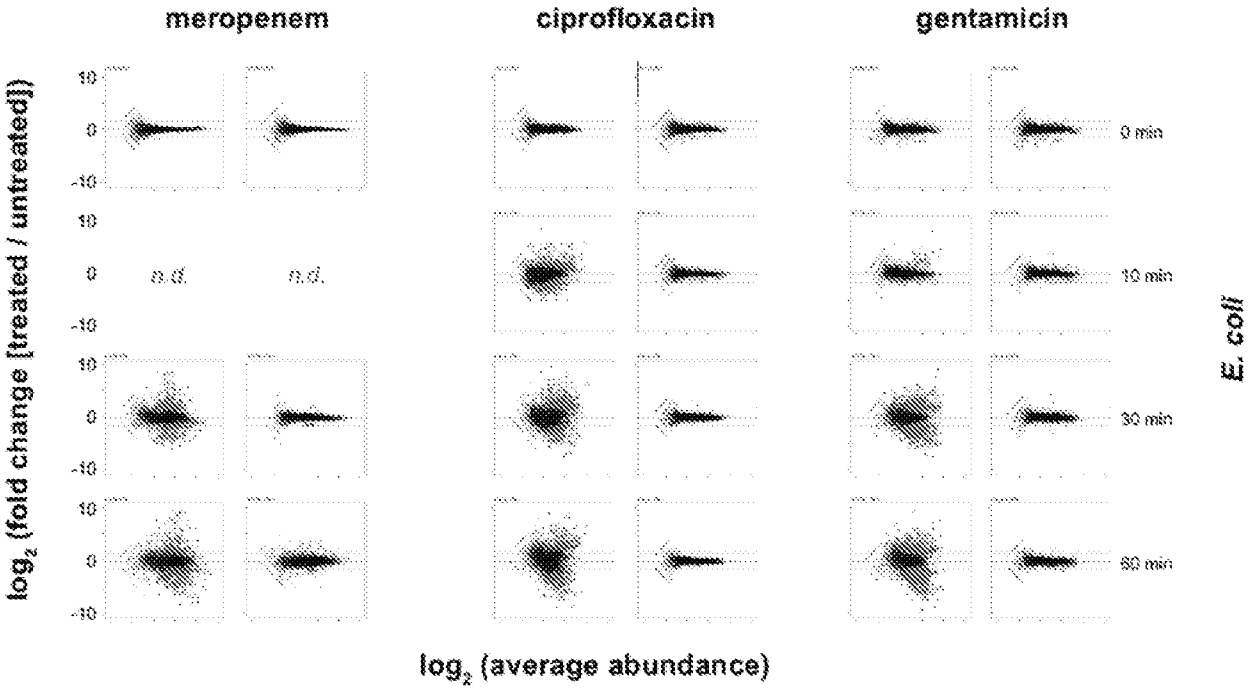

meropenem
ciprofloxacin
gentamicin
n.d.
0 min
10 min
30 min
60 min
E. coli
log2 (fold change [treated / untreated])
log2 (average abundance)

FIG. 2C

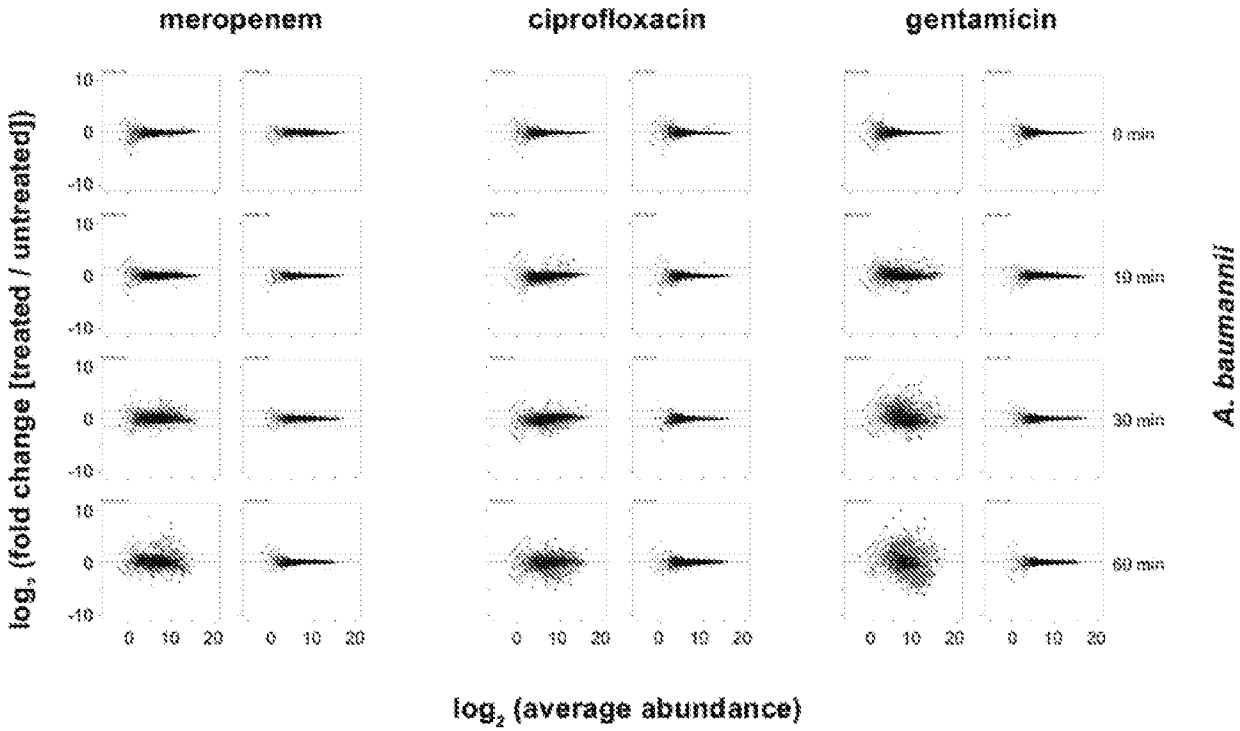

meropenem
ciprofloxacin
gentamicin
log2 (fold change [treated / untreated])
10
0
-10
0 10 20
0 min
10 min
30 min
60 min
A. baumannii
log2 (average abundance)

FIG. 2D


A. baumannii
E. coli
K. pneumoniae
gentamicin
++
ciprofloxacin
+
meropenem
+
S
R
**
x
strains (ordered by MIC)
antibiotic-responsive transcripts (ln [fold-induction])

FIG. 3

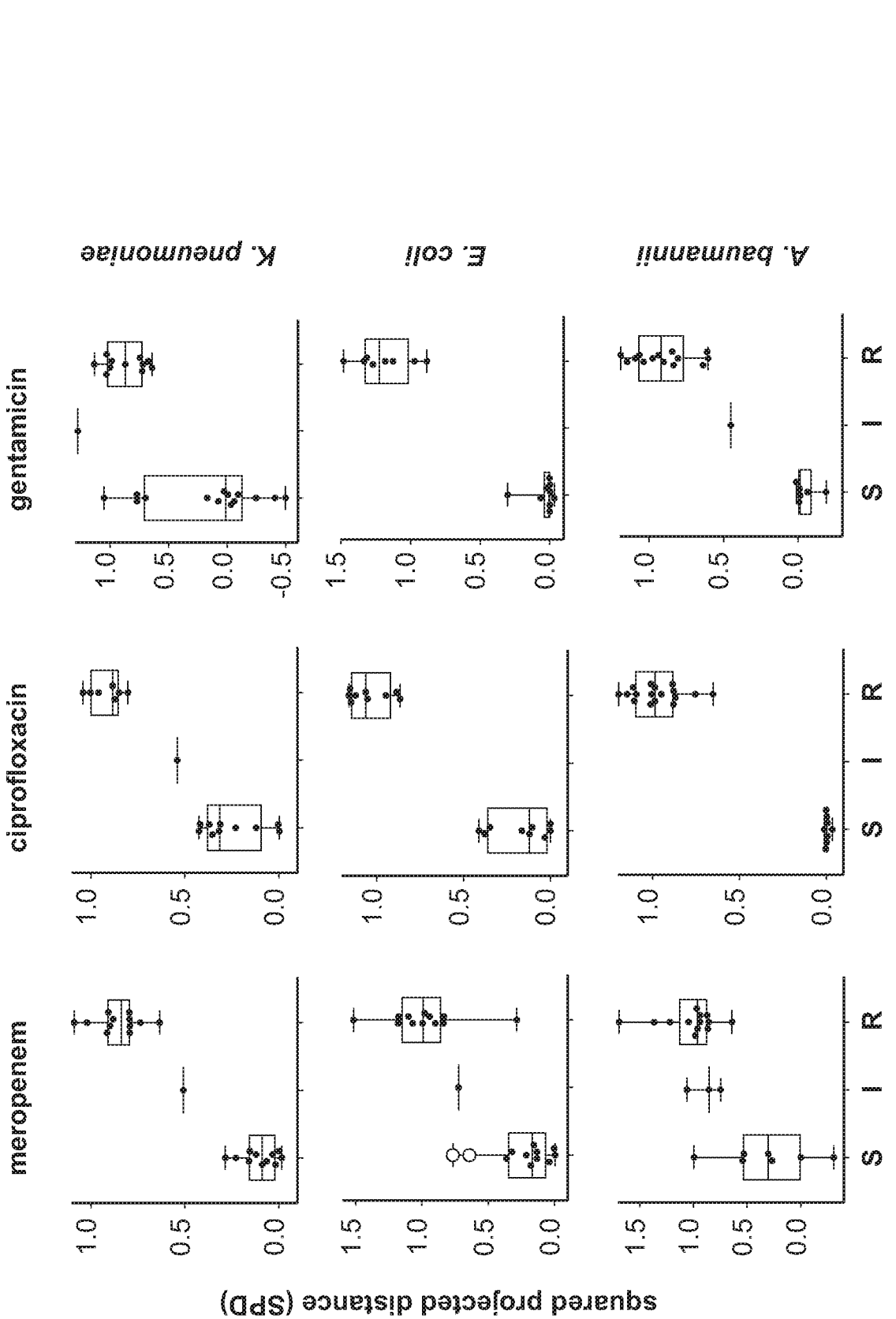

meropenem
ciprofloxacin
gentamicin
A. baumannii
E. coli
K. pneumoniae
squared projected distance (SPD)
CLSI classification
S
I
R

FIG. 4A

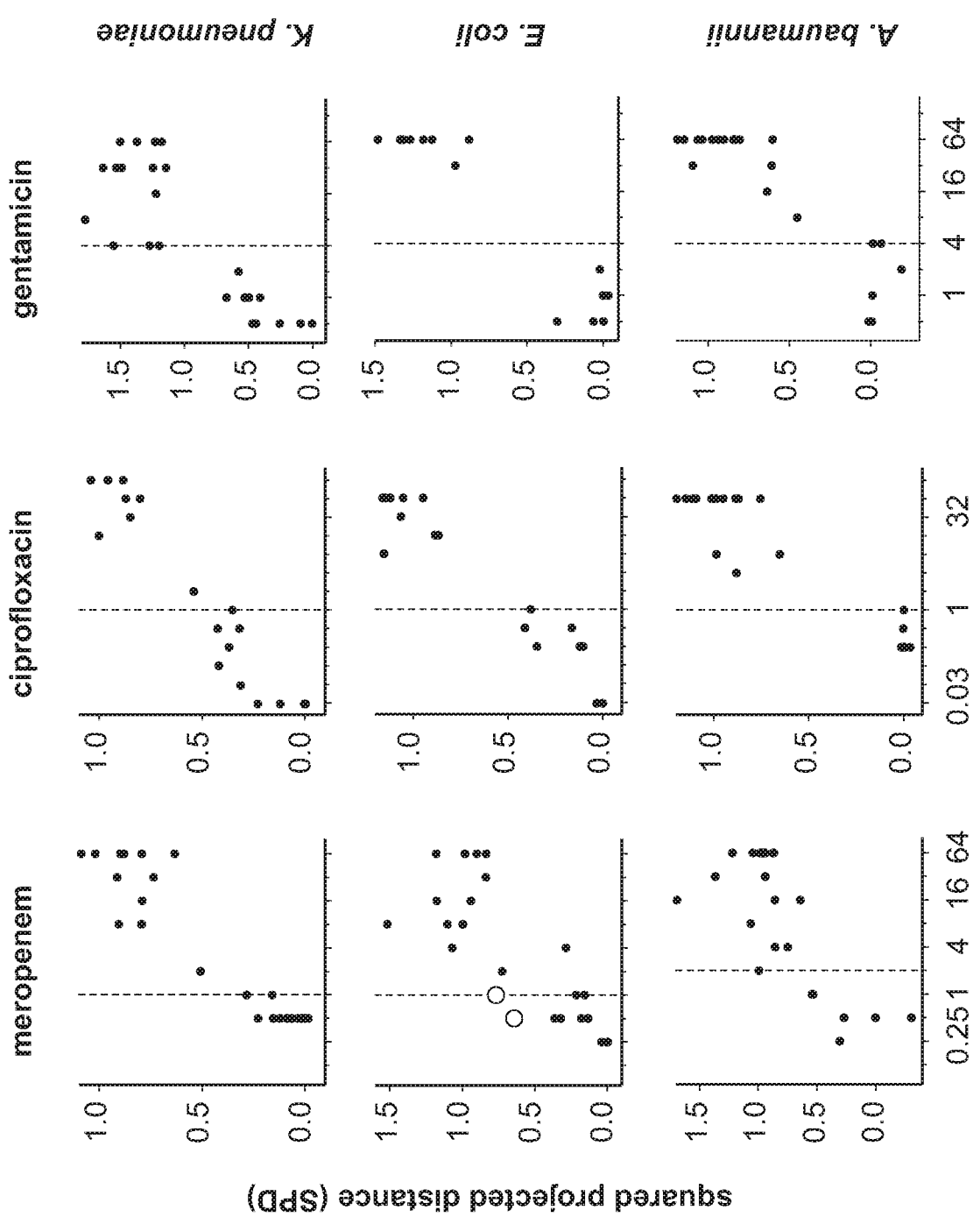

meropenem
ciprofloxacin
gentamicin
A. baumannii
E. coli
K. pneumoniae
squared projected distance (SPD)
minimal inhibitory concentration (mg/L)
0.25 1 4 16 64
0.03 1 32
1 4 16 64

FIG. 4B

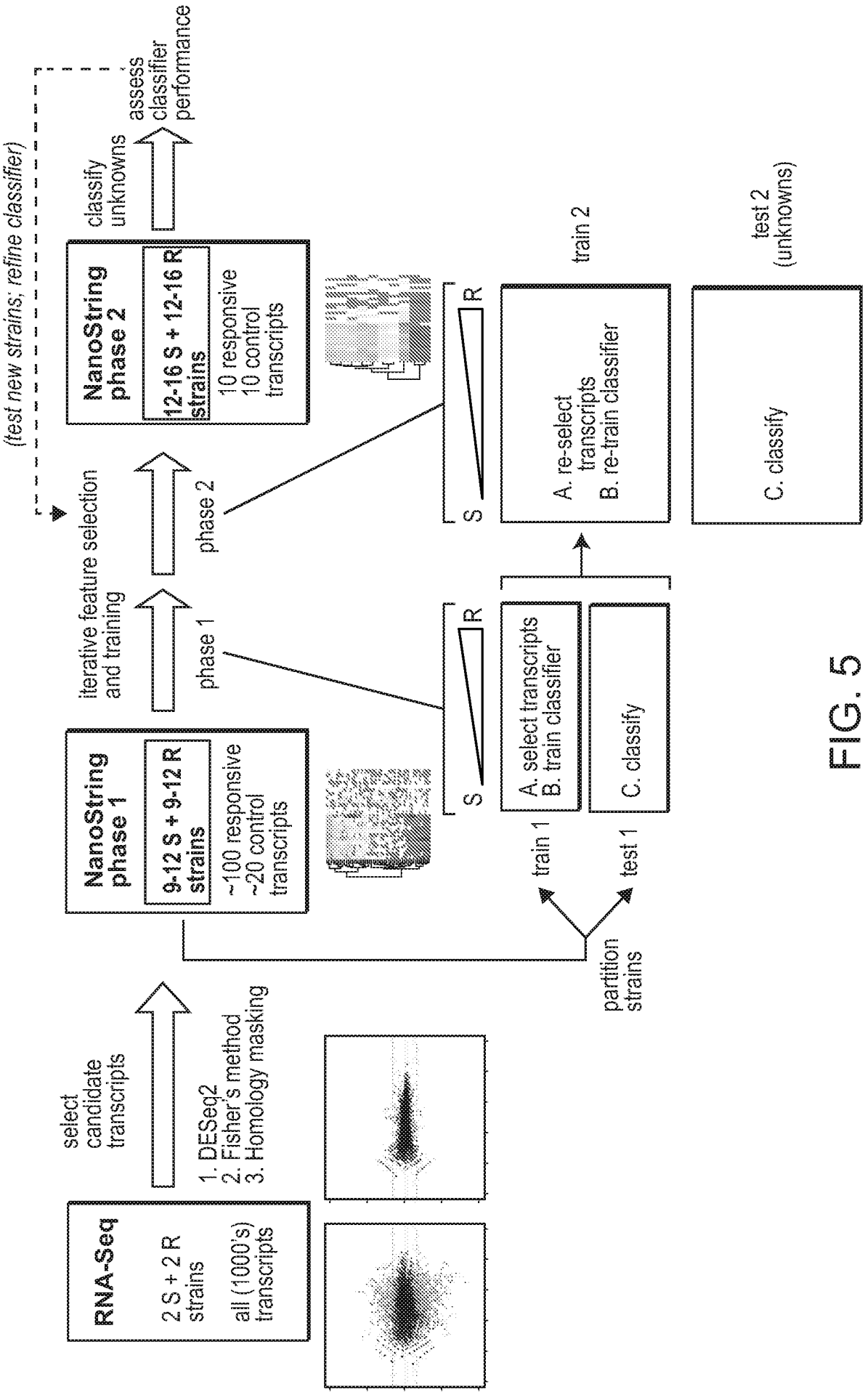

RNA-Seq
2 S + 2 R strains
all (1000's) transcripts
select candidate transcripts
1. DESeq2
2. Fisher's method
3. Homology masking
NanoString phase 1
9-12 S + 9-12 R strains
~100 responsive
~20 control transcripts
iterative feature selection and training
phase 1
phase 2
NanoString phase 2
12-16 S + 12-16 R strains
10 responsive
10 control transcripts
classify unknowns
assess classifier performance
(test new strains; refine classifier)
partition strains
train 1
test 1
A. select transcripts
B. train classifier
C. classify
S
R
train 2
A. re-select transcripts
B. re-train classifier
test 2 (unknowns)
C. classify

FIG. 5

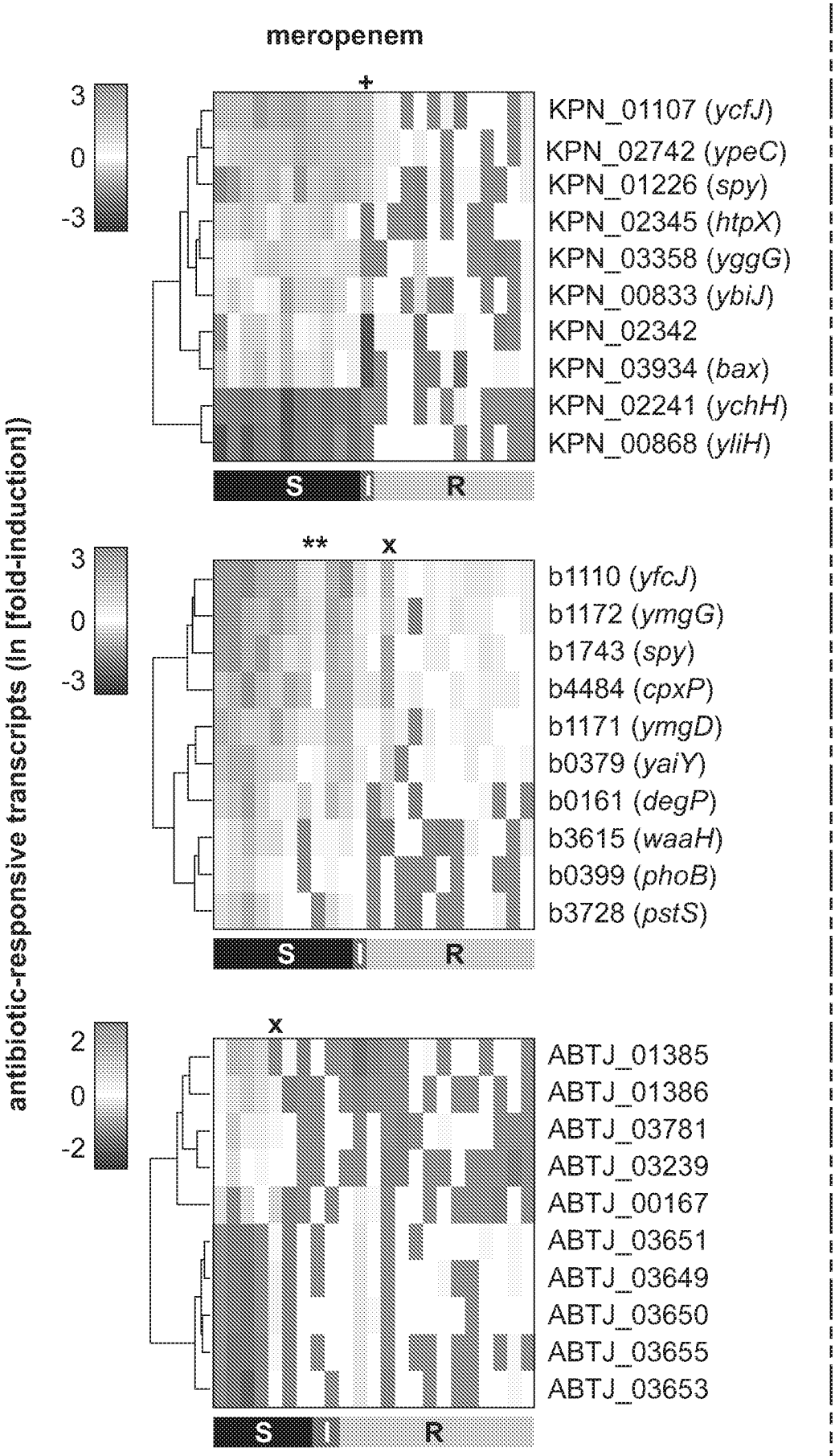

meropenem
antibiotic-responsive transcripts (ln [fold-induction])
3
0
-3
+
KPN_01107 (ycfJ)
KPN_02742 (ypeC)
KPN_01226 (spy)
KPN_02345 (htpX)
KPN_03358 (yggG)
KPN_00833 (ybiJ)
KPN_02342
KPN_03934 (bax)
KPN_02241 (ychH)
KPN_00868 (yliH)
S
R
3
0
-3
**
x
b1110 (yfcJ)
b1172 (ymgG)
b1743 (spy)
b4484 (cpxP)
b1171 (ymgD)
b0379 (yaiY)
b0161 (degP)
b3615 (waaH)
b0399 (phoB)
b3728 (pstS)
S
R
2
0
-2
x
ABTJ_01385
ABTJ_01386
ABTJ_03781
ABTJ_03239
ABTJ_00167
ABTJ_03651
ABTJ_03649
ABTJ_03650
ABTJ_03655
ABTJ_03653
S
R

FIG. 6

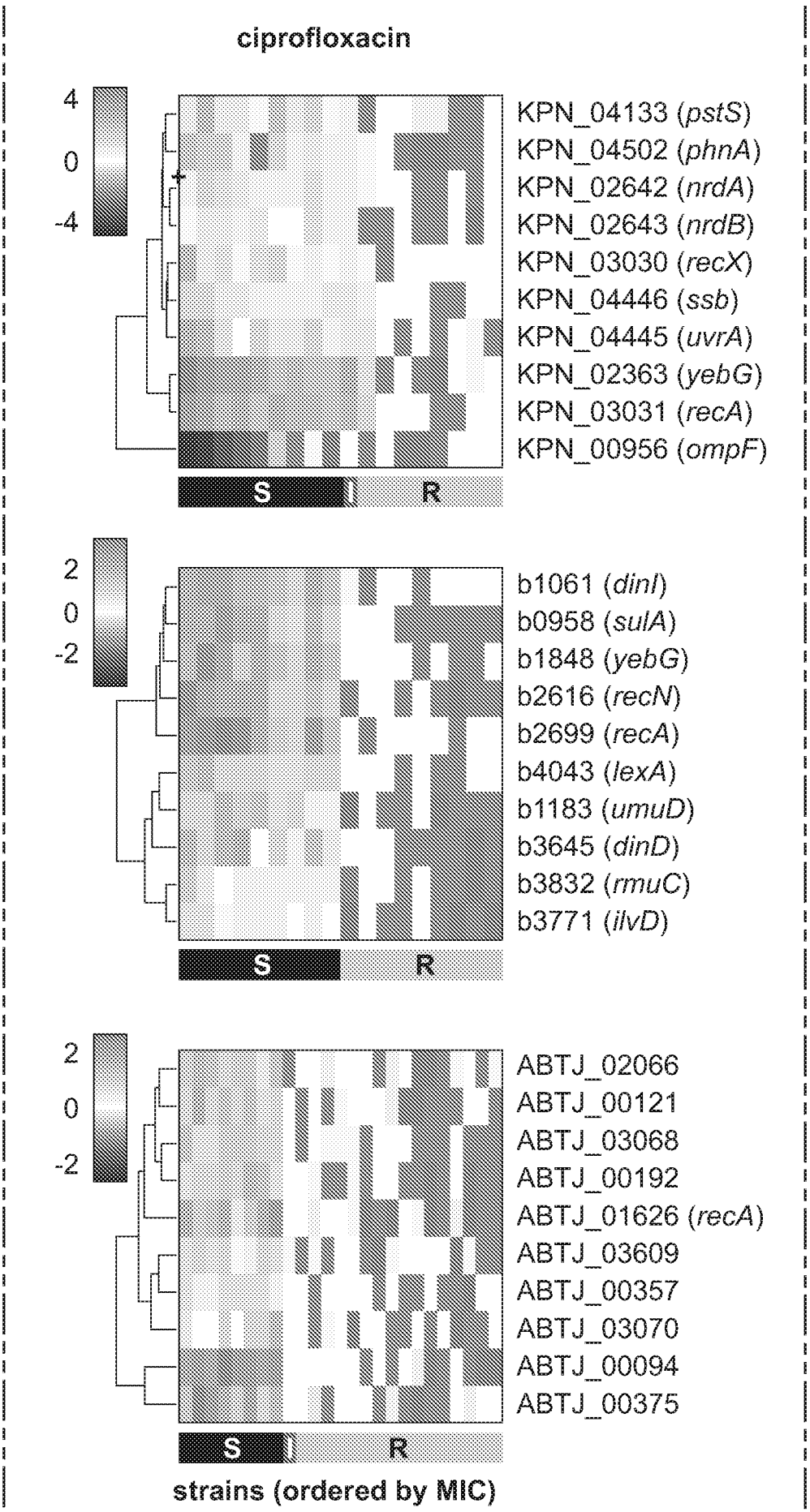

ciprofloxacin
4
0
-4
KPN_04133 (pstS)
KPN_04502 (phnA)
KPN_02642 (nrdA)
KPN_02643 (nrdB)
KPN_03030 (recX)
KPN_04446 (ssb)
KPN_04445 (uvrA)
KPN_02363 (yebG)
KPN_03031 (recA)
KPN_00956 (ompF)
S
R
2
0
-2
b1061 (dinI)
b0958 (sulA)
b1848 (yebG)
b2616 (recN)
b2699 (recA)
b4043 (lexA)
b1183 (umuD)
b3645 (dinD)
b3832 (rmuC)
b3771 (ilvD)
S
R
2
0
-2
ABTJ_02066
ABTJ_00121
ABTJ_03068
ABTJ_00192
ABTJ_01626 (recA)
ABTJ_03609
ABTJ_00357
ABTJ_03070
ABTJ_00094
ABTJ_00375
S
R
strains (ordered by MIC)

FIG. 6 (cont.)

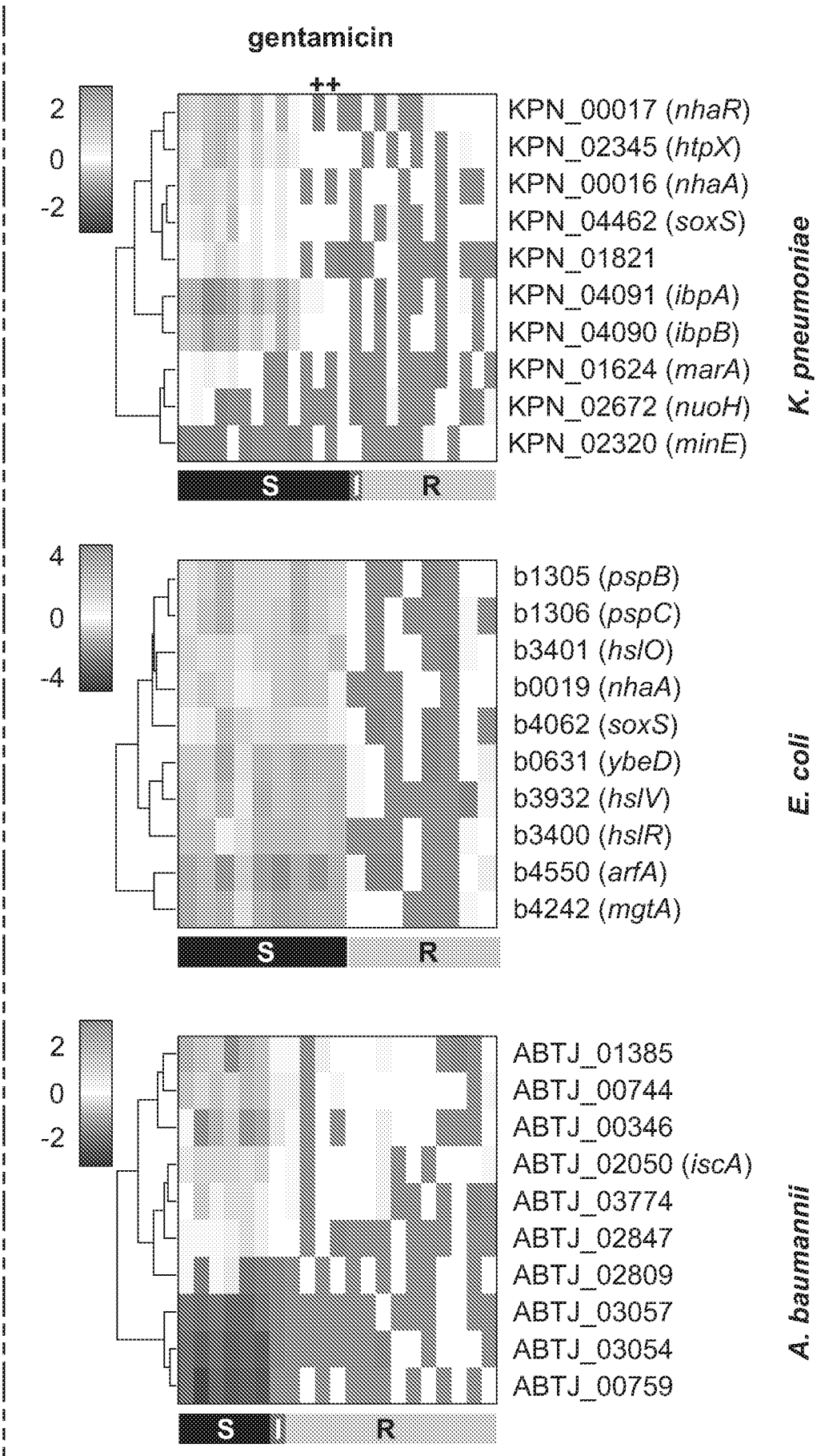

gentamicin
++
2
0
-2
KPN_00017 (nhaR)
KPN_02345 (htpX)
KPN_00016 (nhaA)
KPN_04462 (soxS)
KPN_01821
KPN_04091 (ibpA)
KPN_04090 (ibpB)
KPN_01624 (marA)
KPN_02672 (nuoH)
KPN_02320 (minE)
S
R
K. pneumoniae
4
0
-4
b1305 (pspB)
b1306 (pspC)
b3401 (hslO)
b0019 (nhaA)
b4062 (soxS)
b0631 (ybeD)
b3932 (hslV)
b3400 (hslR)
b4550 (arfA)
b4242 (mgtA)
S
R
E. coli
2
0
-2
ABTJ_01385
ABTJ_00744
ABTJ_00346
ABTJ_02050 (iscA)
ABTJ_03774
ABTJ_02847
ABTJ_02809
ABTJ_03057
ABTJ_03054
ABTJ_00759
S
R
A. baumannii

FIG. 6 (cont.)

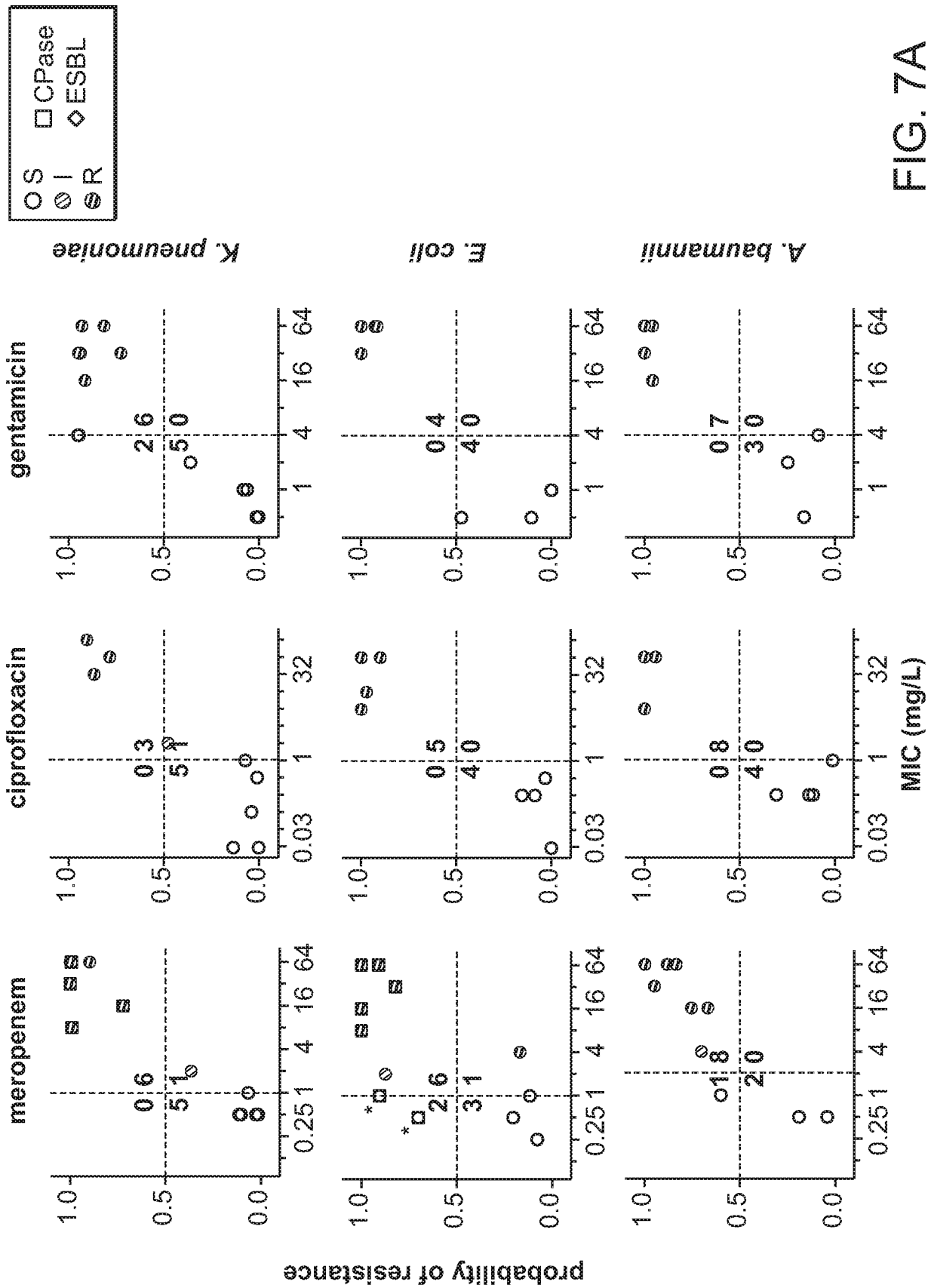

S
I
R
CPase
ESBL
meropenem
ciprofloxacin
gentamicin
K. pneumoniae
E. coli
A. baumannii
probability of resistance
MIC (mg/L)
0.25
1
4
16
64
0.03
32

FIG. 7A

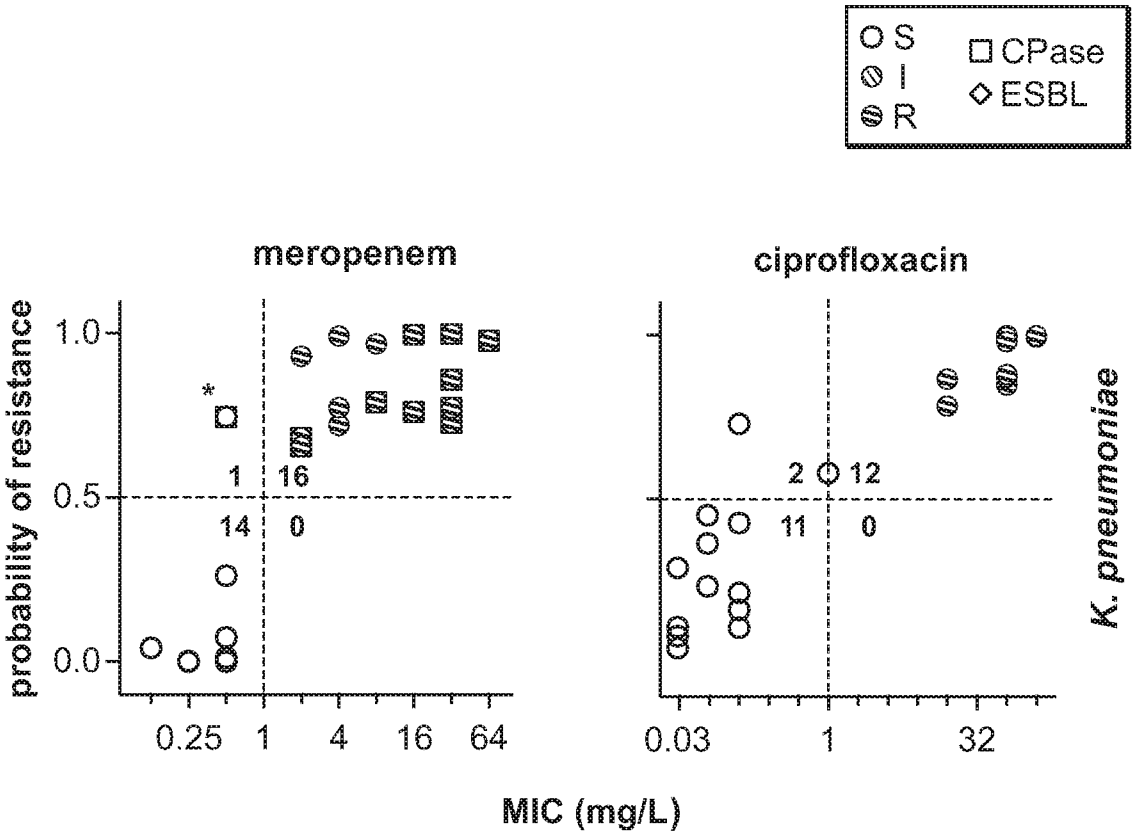

S
I
R
CPase
ESBL
meropenem
ciprofloxacin
probability of resistance
1.0
0.5
0.0
0.25
1
4
16
64
0.03
1
32
1
16
14
0
2
12
11
0
*
K. pneumoniae
MIC (mg/L)

FIG. 7B

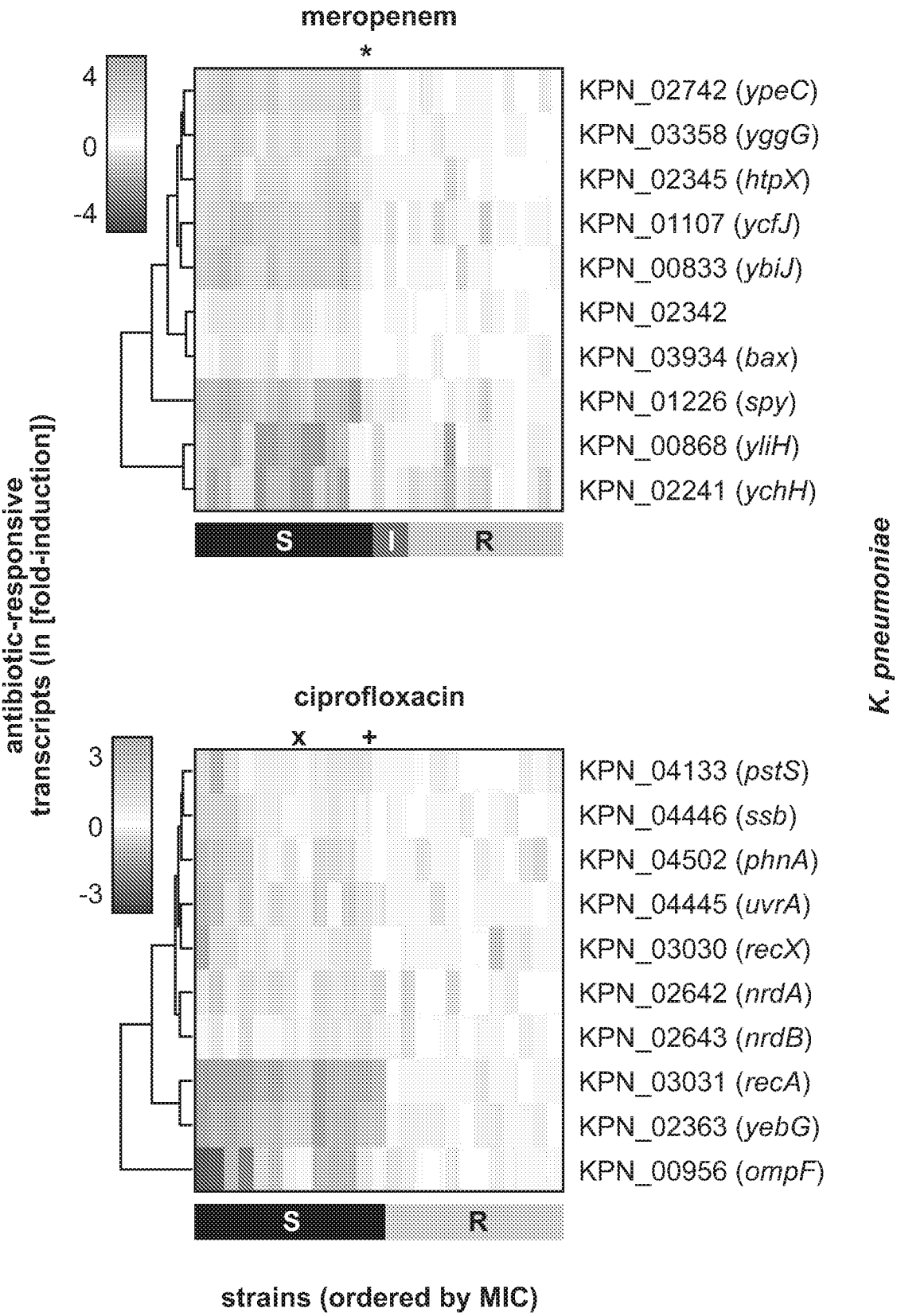

meropenem
*
4
0
-4
KPN_02742 (ypeC)
KPN_03358 (yggG)
KPN_02345 (htpX)
KPN_01107 (ycfJ)
KPN_00833 (ybiJ)
KPN_02342
KPN_03934 (bax)
KPN_01226 (spy)
KPN_00868 (yliH)
KPN_02241 (ychH)
S
I
R
ciprofloxacin
x
+
3
0
-3
KPN_04133 (pstS)
KPN_04446 (ssb)
KPN_04502 (phnA)
KPN_04445 (uvrA)
KPN_03030 (recX)
KPN_02642 (nrdA)
KPN_02643 (nrdB)
KPN_03031 (recA)
KPN_02363 (yebG)
KPN_00956 (ompF)
S
R
antibiotic-responsive transcripts (ln [fold-induction])
K. pneumoniae
strains (ordered by MIC)

FIG. 8

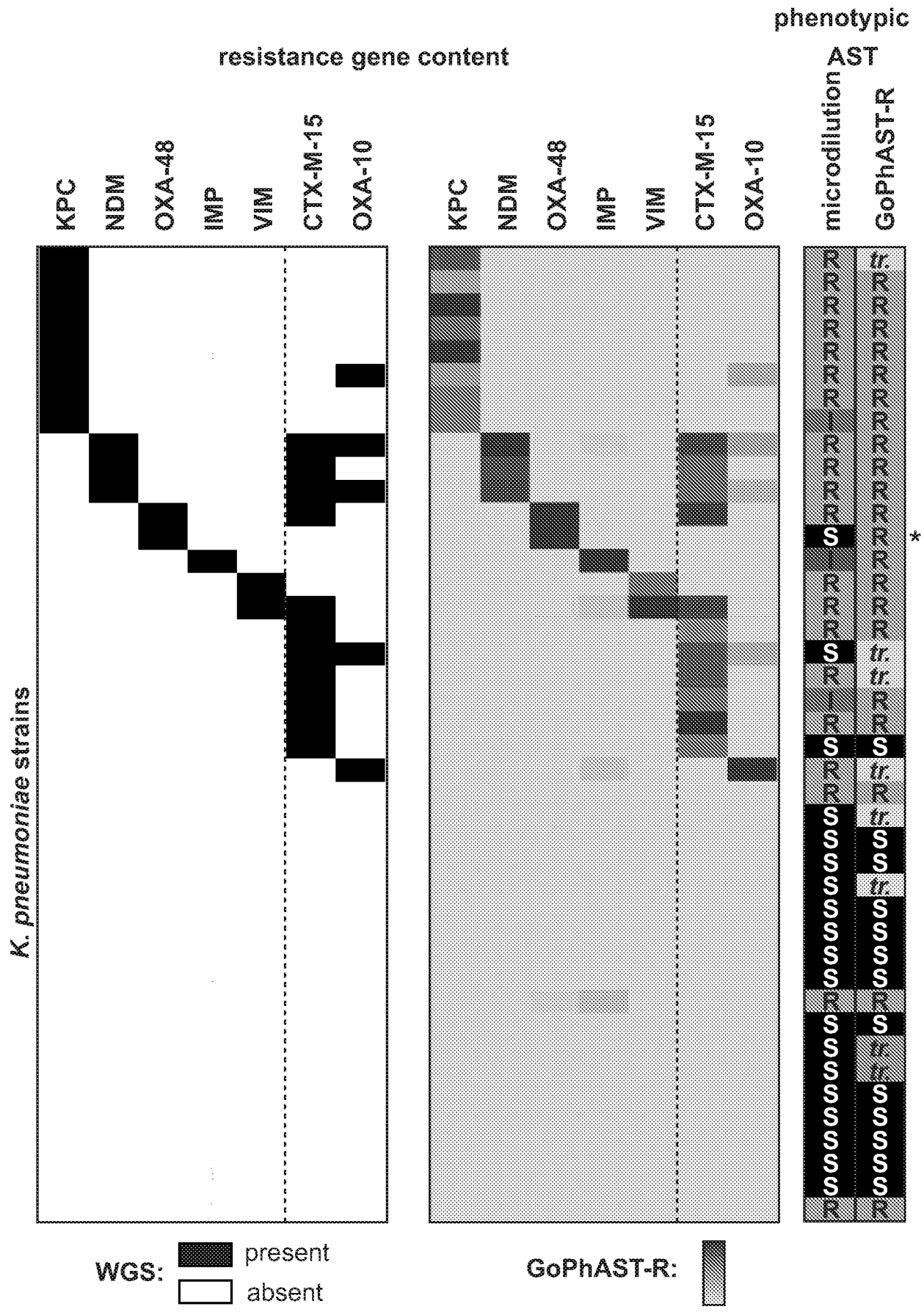

resistance gene content
phenotypic AST
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10
microdilution
GoPhAST-R
K. pneumoniae strains
*
WGS:
present
absent
GoPhAST-R:

FIG. 9A

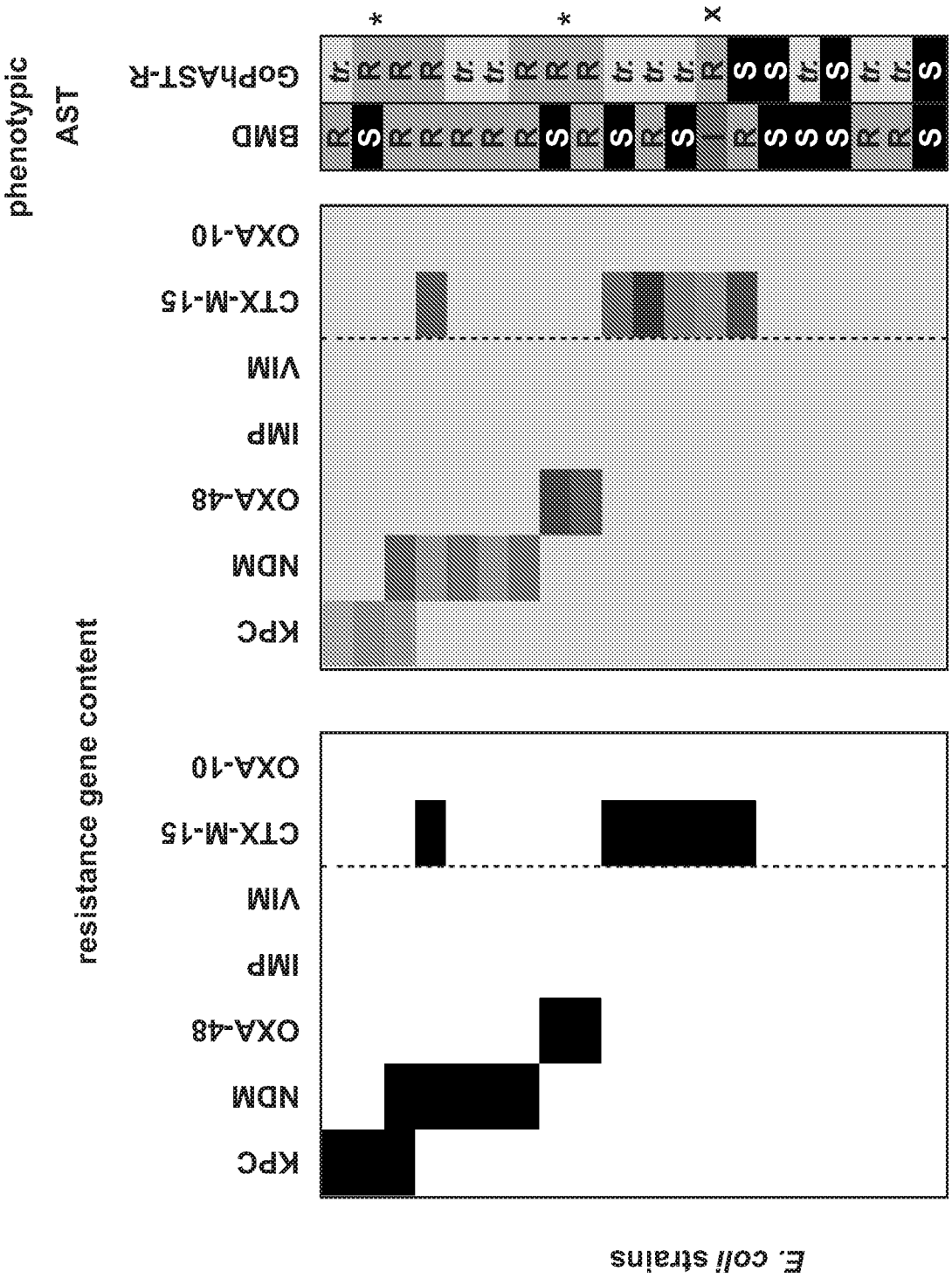

phenotypic AST
BMD
GoPhAST-R
resistance gene content
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10
E. coli strains

FIG. 9B

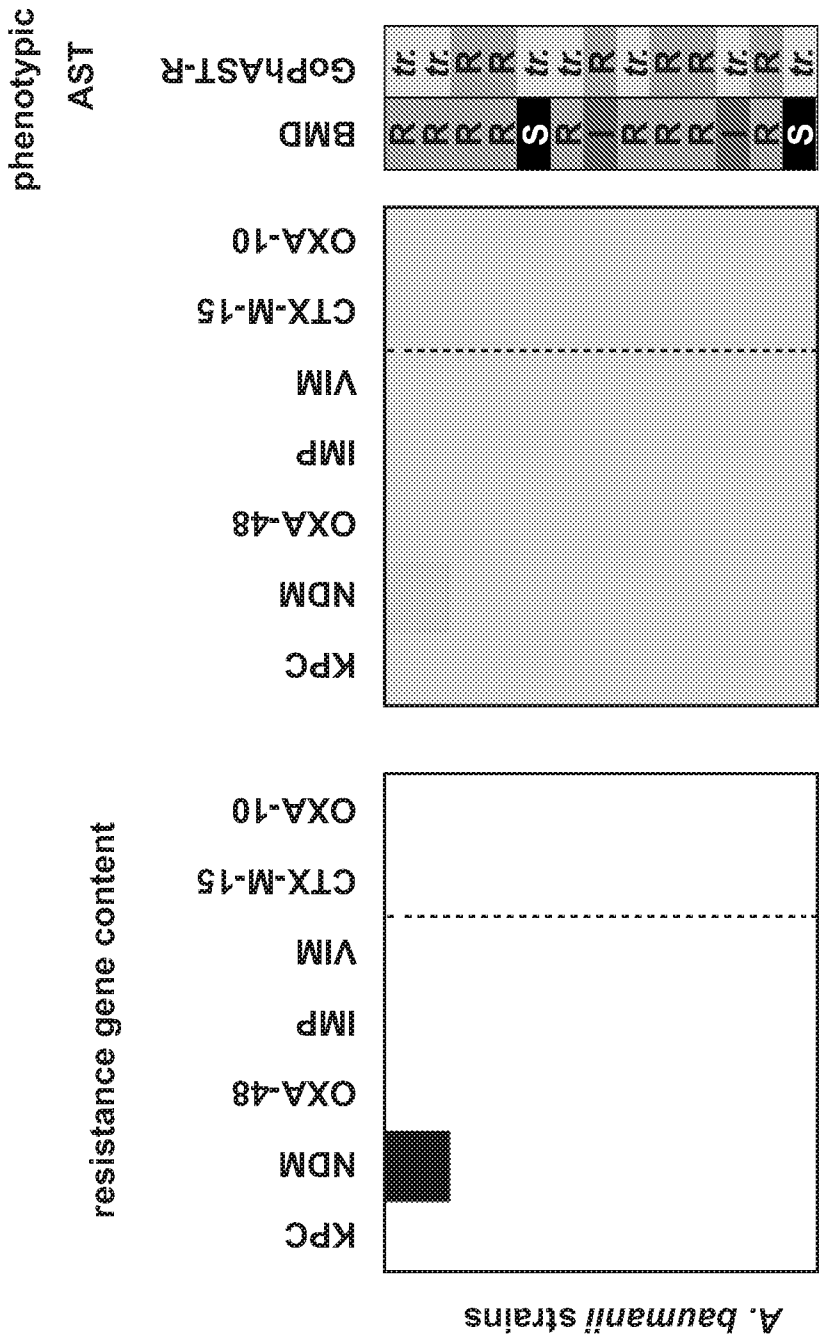

A. baumanii strains
resistance gene content
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10
phenotypic AST
BMD
GoPhAST-R

FIG. 9C

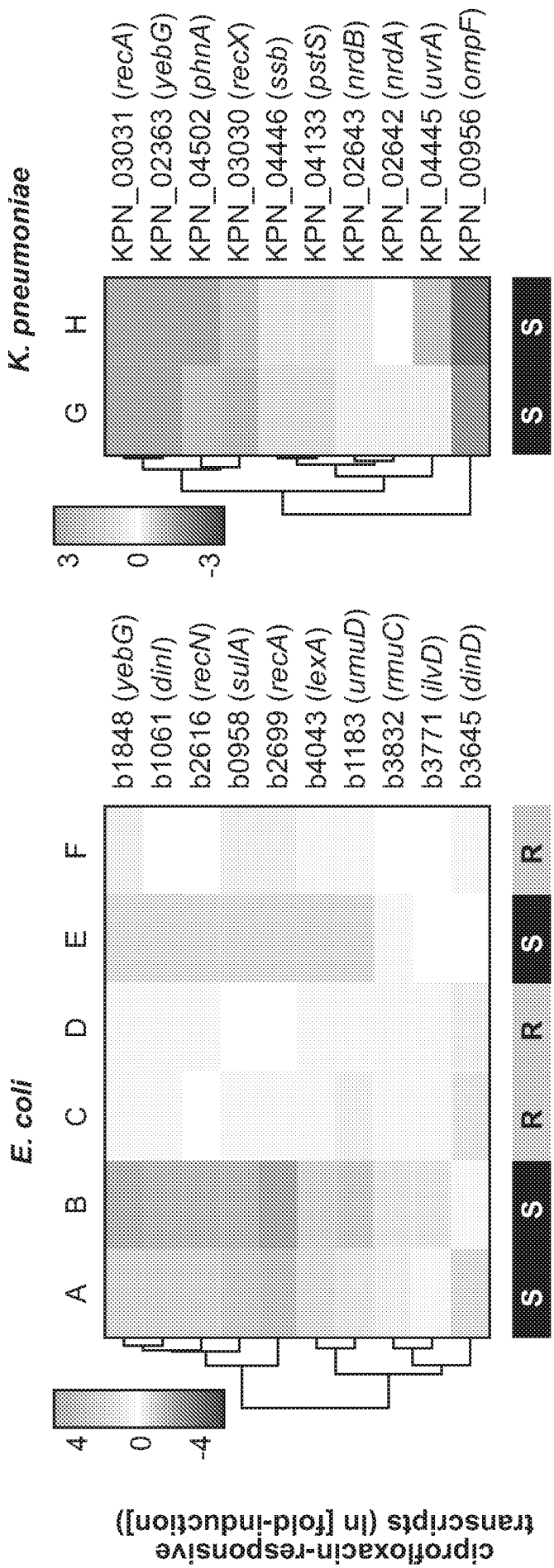

E. coli
A
B
C
D
E
F
b1848 (yebG)
b1061 (dinI)
b2616 (recN)
b0958 (sulA)
b2699 (recA)
b4043 (lexA)
b1183 (umuD)
b3832 (rmuC)
b3771 (ilvD)
b3645 (dinD)
4
0
-4
S S R R S R
K. pneumoniae
G
H
KPN_03031 (recA)
KPN_02363 (yebG)
KPN_04502 (phnA)
KPN_03030 (recX)
KPN_04446 (ssb)
KPN_04133 (pstS)
KPN_02643 (nrdB)
KPN_02642 (nrdA)
KPN_04445 (uvrA)
KPN_00956 (ompF)
3
0
-3
S S
blood culture isolates
ciprofloxacin-responsive
transcripts (in [fold-induction])

FIG. 10

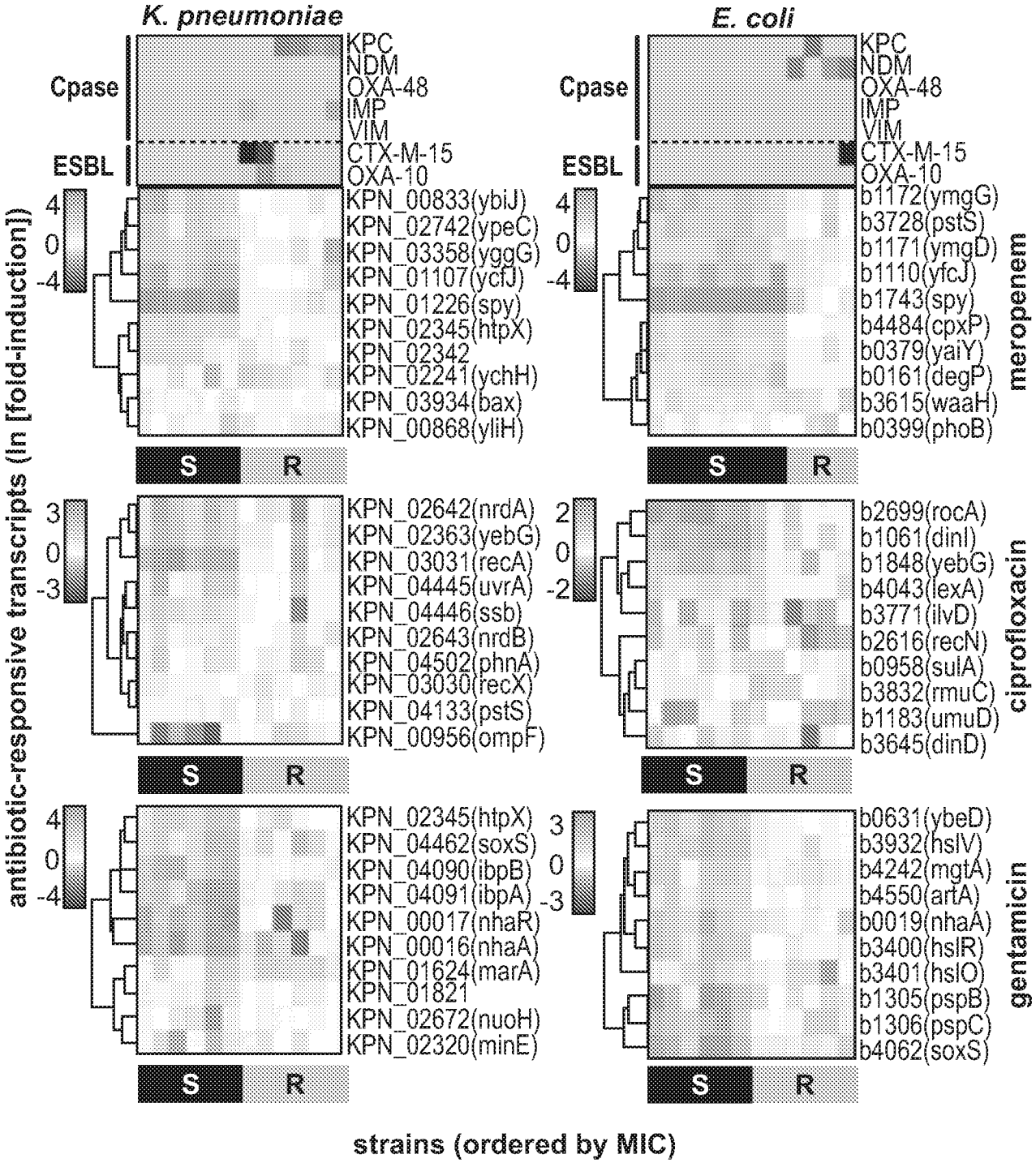

K. pneumoniae
E. coli
Cpase
ESBL
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10
antibiotic-responsive transcripts (ln [fold-induction])
KPN_00833(ybiJ)
KPN_02742(ypeC)
KPN_03358(yggG)
KPN_01107(ycfJ)
KPN_01226(spy)
KPN_02345(htpX)
KPN_02342
KPN_02241(ychH)
KPN_03934(bax)
KPN_00868(yliH)
b1172(ymgG)
b3728(pstS)
b1171(ymgD)
b1110(yfcJ)
b1743(spy)
b4484(cpxP)
b0379(yaiY)
b0161(degP)
b3615(waaH)
b0399(phoB)
meropenem
KPN_02642(nrdA)
KPN_02363(yebG)
KPN_03031(recA)
KPN_04445(uvrA)
KPN_04446(ssb)
KPN_02643(nrdB)
KPN_04502(phnA)
KPN_03030(recX)
KPN_04133(pstS)
KPN_00956(ompF)
b2699(rocA)
b1061(dinI)
b1848(yebG)
b4043(lexA)
b3771(ilvD)
b2616(recN)
b0958(sulA)
b3832(rmuC)
b1183(umuD)
b3645(dinD)
ciprofloxacin
KPN_02345(htpX)
KPN_04462(soxS)
KPN_04090(ibpB)
KPN_04091(ibpA)
KPN_00017(nhaR)
KPN_00016(nhaA)
KPN_01624(marA)
KPN_01821
KPN_02672(nuoH)
KPN_02320(minE)
b0631(ybeD)
b3932(hslV)
b4242(mgtA)
b4550(artA)
b0019(nhaA)
b3400(hslR)
b3401(hslO)
b1305(pspB)
b1306(pspC)
b4062(soxS)
gentamicin
S
R
strains (ordered by MIC)

FIG. 11A

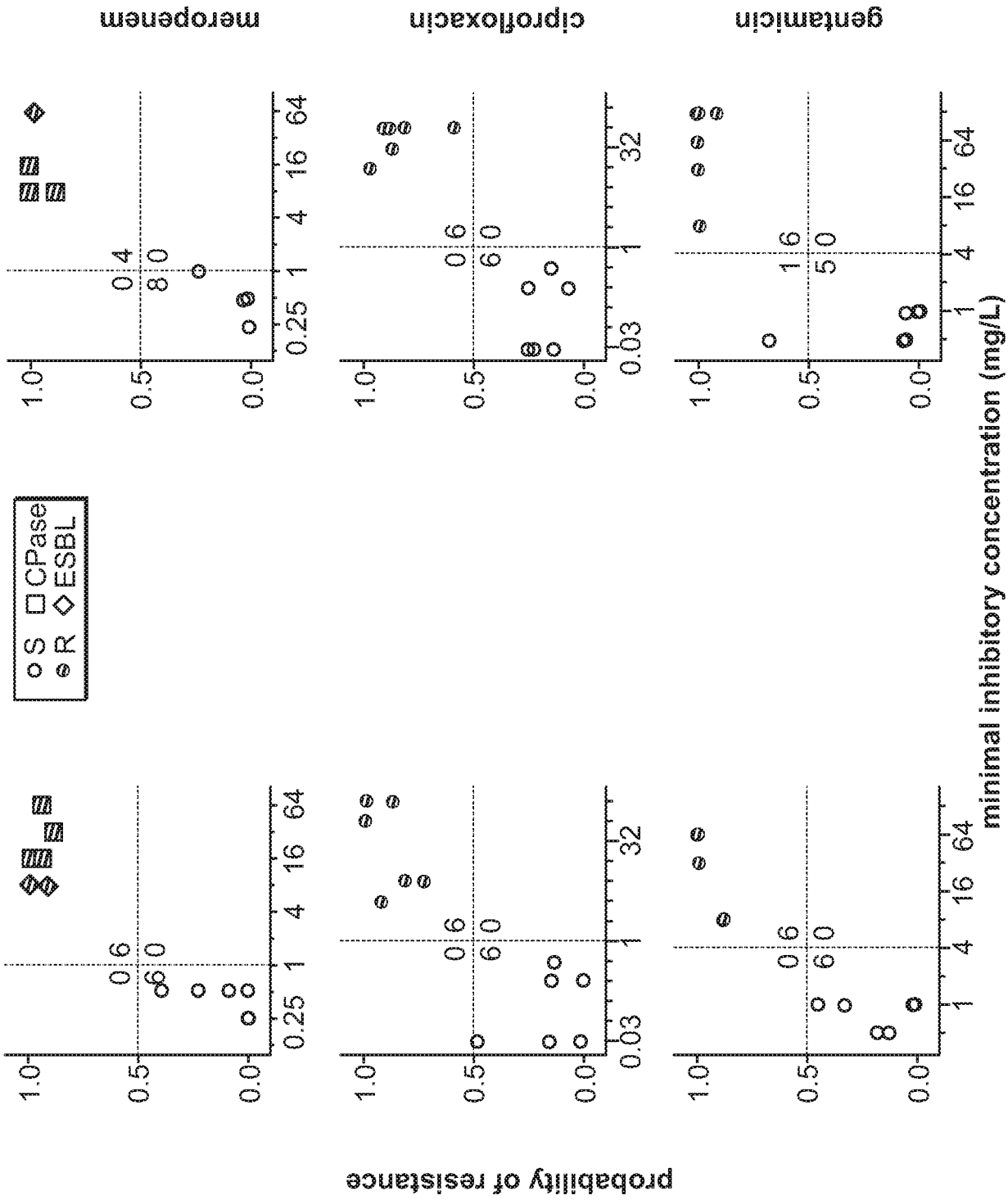

meropenem
ciprofloxacin
gentamicin
S
R
CPase
ESBL
probability of resistance
minimal inhibitory concentration (mg/L)

FIG. 11B

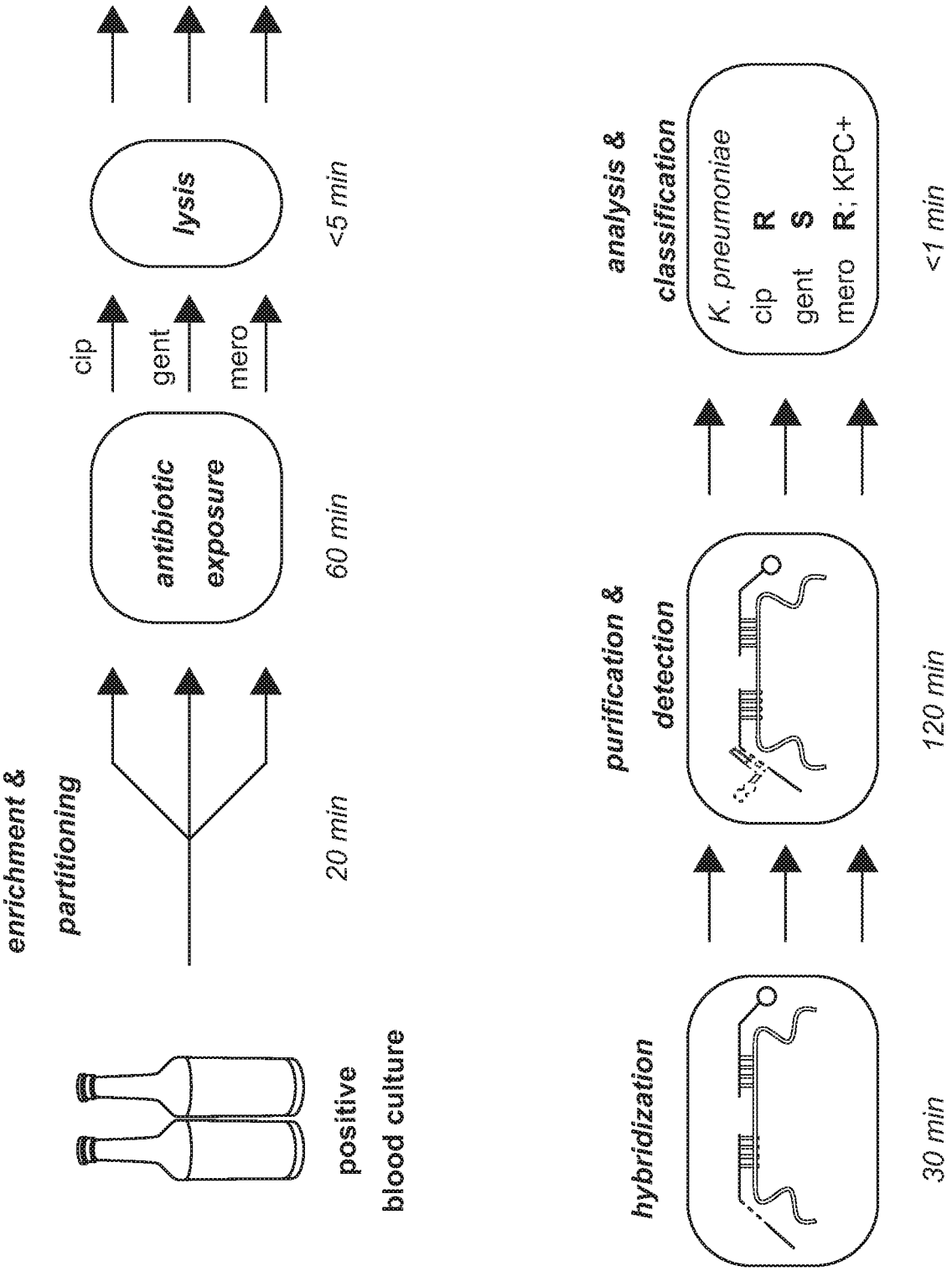

positive blood culture
enrichment & partitioning
20 min
antibiotic exposure
60 min
cip
gent
mero
lysis
<5 min
hybridization
30 min
purification & detection
120 min
analysis & classification
K. pneumoniae
cip R
gent S
mero R; KPC+
<1 min

FIG. 12A

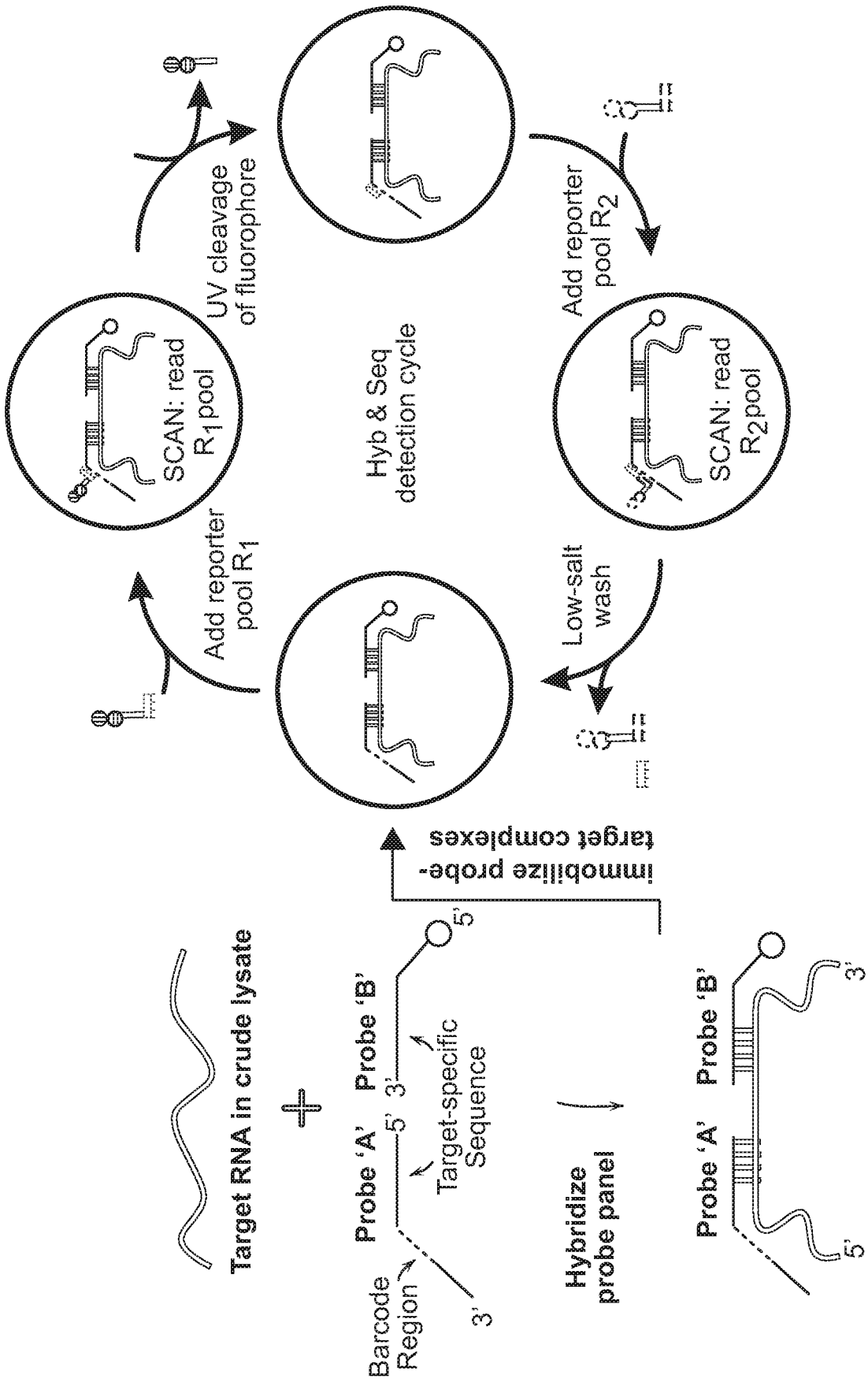

Target RNA in crude lysate
Probe 'A'
Probe 'B'
5'
3'
Barcode Region
Target-specific Sequence
Hybridize probe panel
Immobilize probe-target complexes
Low-salt wash
Add reporter pool R_1
SCAN: read R_1 pool
UV cleavage of fluorophore
Hyb & Seq detection cycle
Add reporter pool R_2
SCAN: read R_2 pool

FIG. 12B

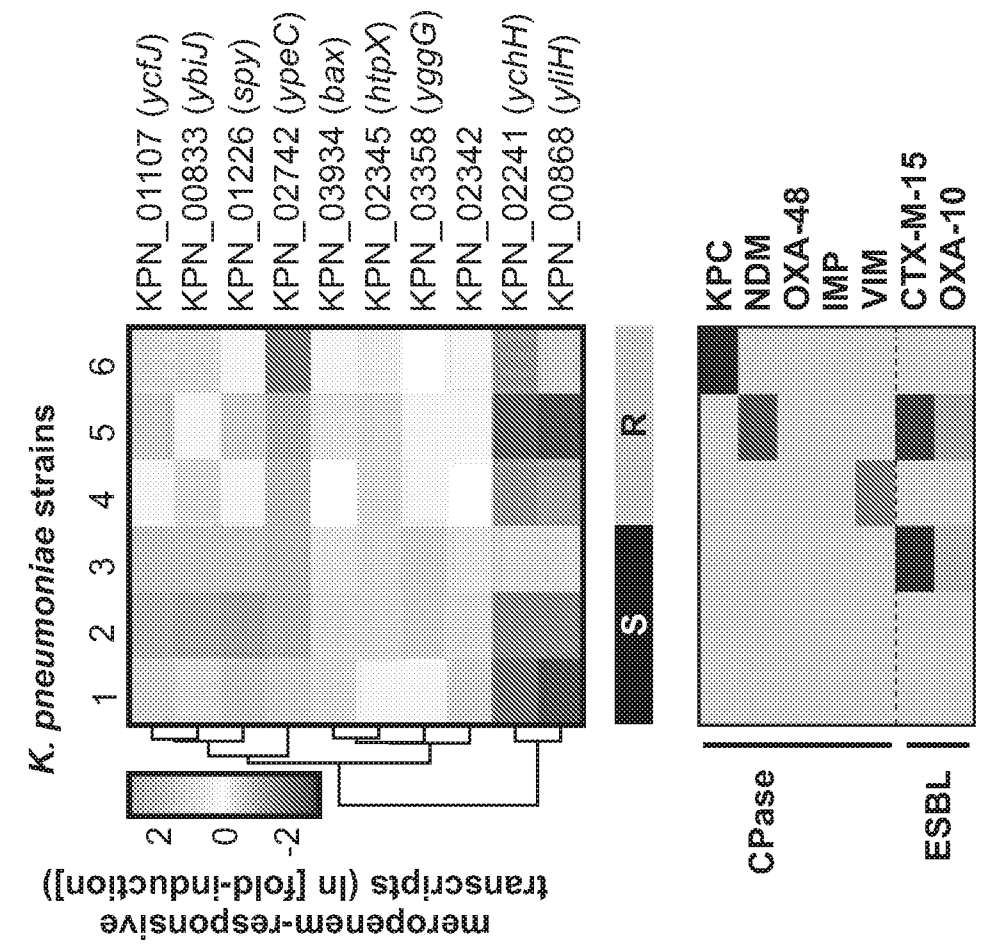

meropenem-responsive
transcripts (ln [fold-induction])
2
0
-2
K. pneumoniae strains
1
2
3
4
5
6
KPN_01107 (ycfJ)
KPN_00833 (ybiJ)
KPN_01226 (spy)
KPN_02742 (ypeC)
KPN_03934 (bax)
KPN_02345 (htpX)
KPN_03358 (yggG)
KPN_02342
KPN_02241 (ychH)
KPN_00868 (yliH)
S
R
CPase
ESBL
KPC
NDM
OXA-48
IMP
VIM
CTX-M-15
OXA-10

FIG. 12B (cont.)

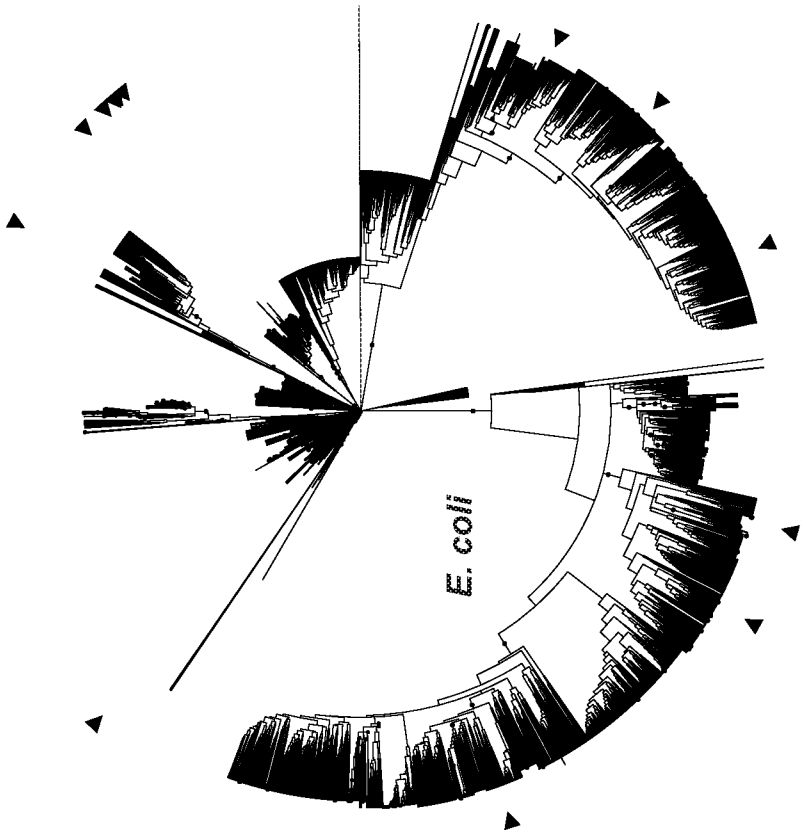


FIG. 13B

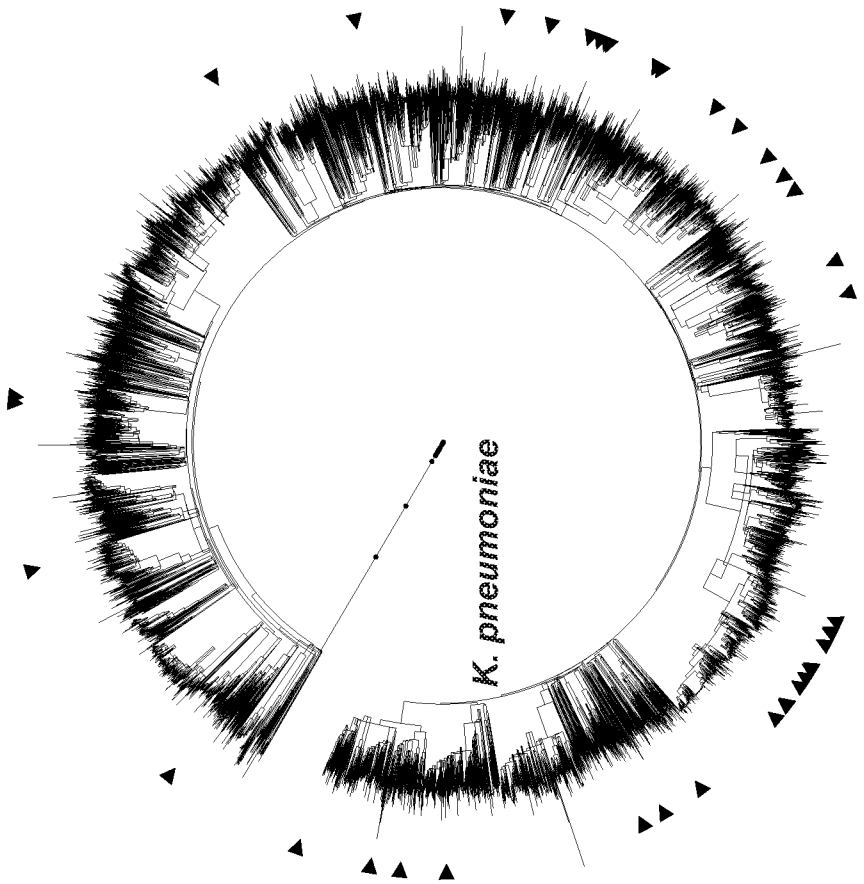


FIG. 13A

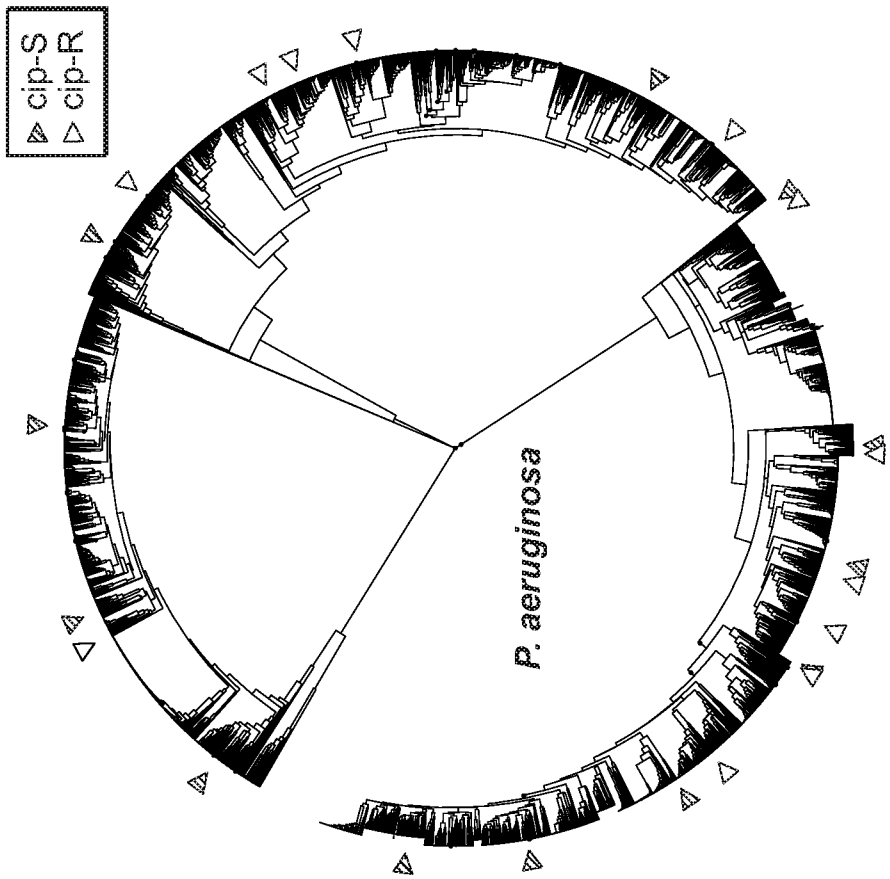


FIG. 13D

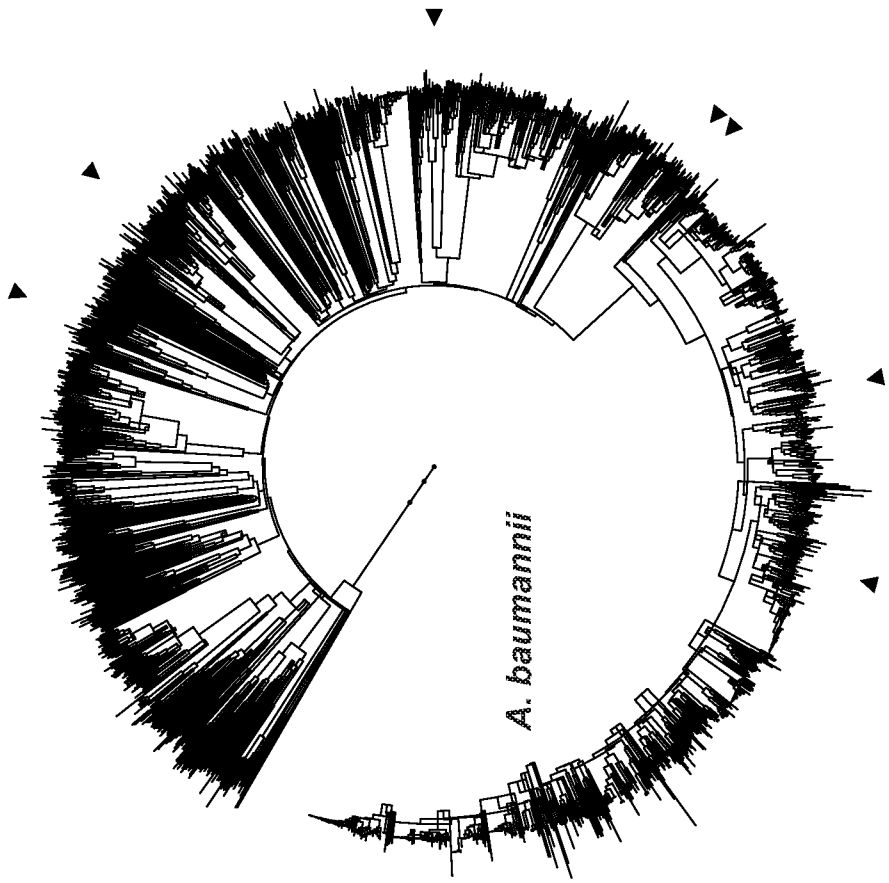


FIG. 13C

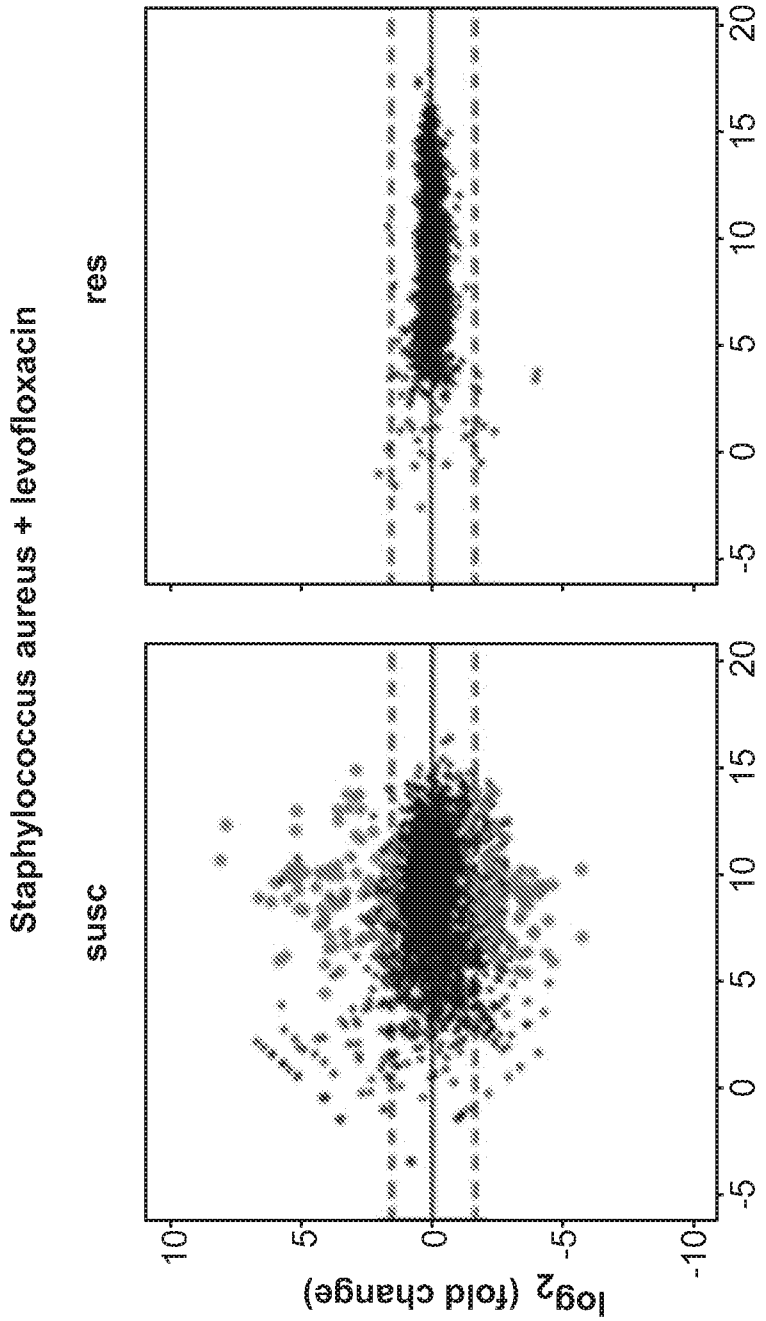

Staphylococcus aureus + levofloxacin
susc
res
log2 (fold change)
log2 (average abundance)
10
5
0
-5
-10
-5
0
5
10
15
20

FIG. 14A

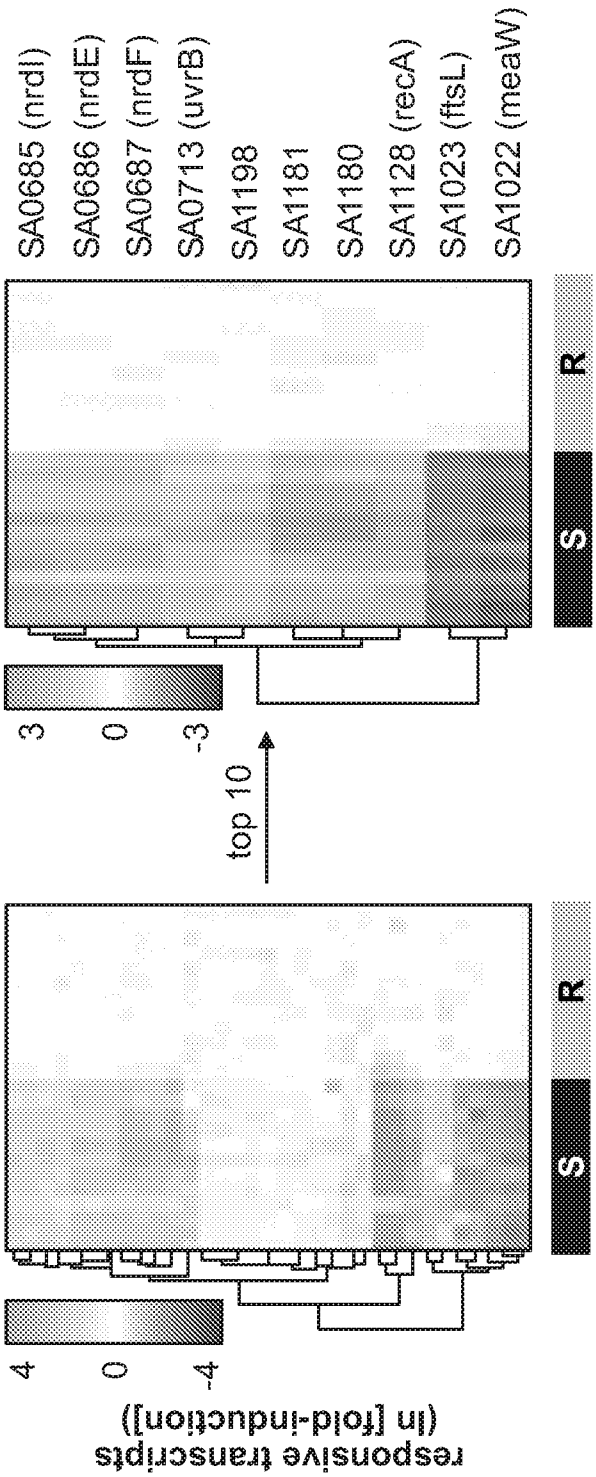

responsive transcripts
(ln [fold-induction])
4
0
-4
top 10
3
0
-3
SA0685 (nrdI)
SA0686 (nrdE)
SA0687 (nrdF)
SA0713 (uvrB)
SA1198
SA1181
SA1180
SA1128 (recA)
SA1023 (ftsL)
SA1022 (meaW)
S
R
S
R
strains (ordered by MIC)

FIG. 14B

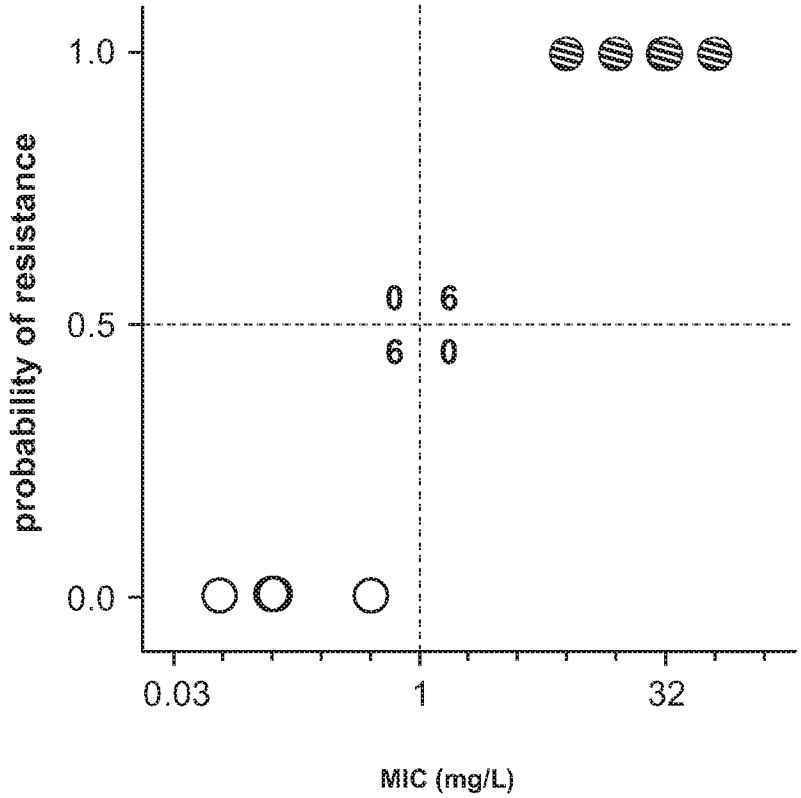


FIG. 14C

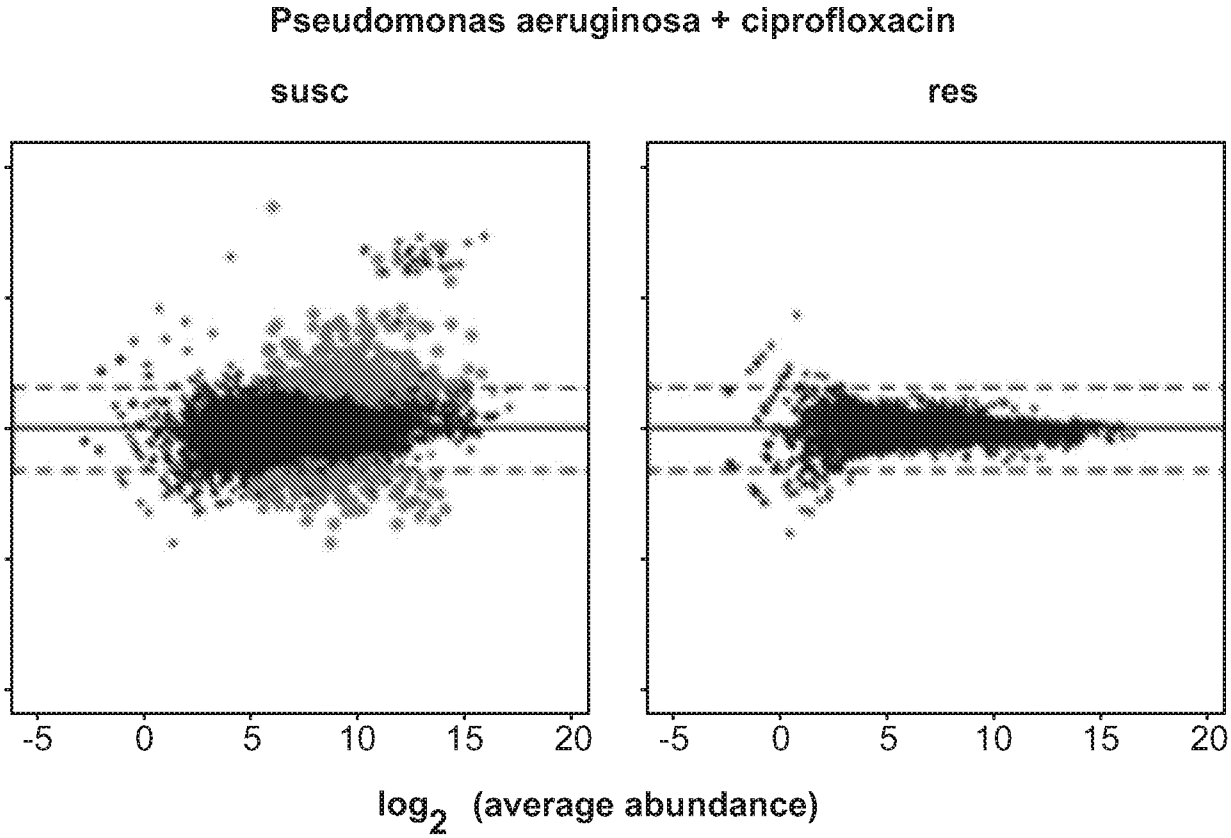


FIG. 14D

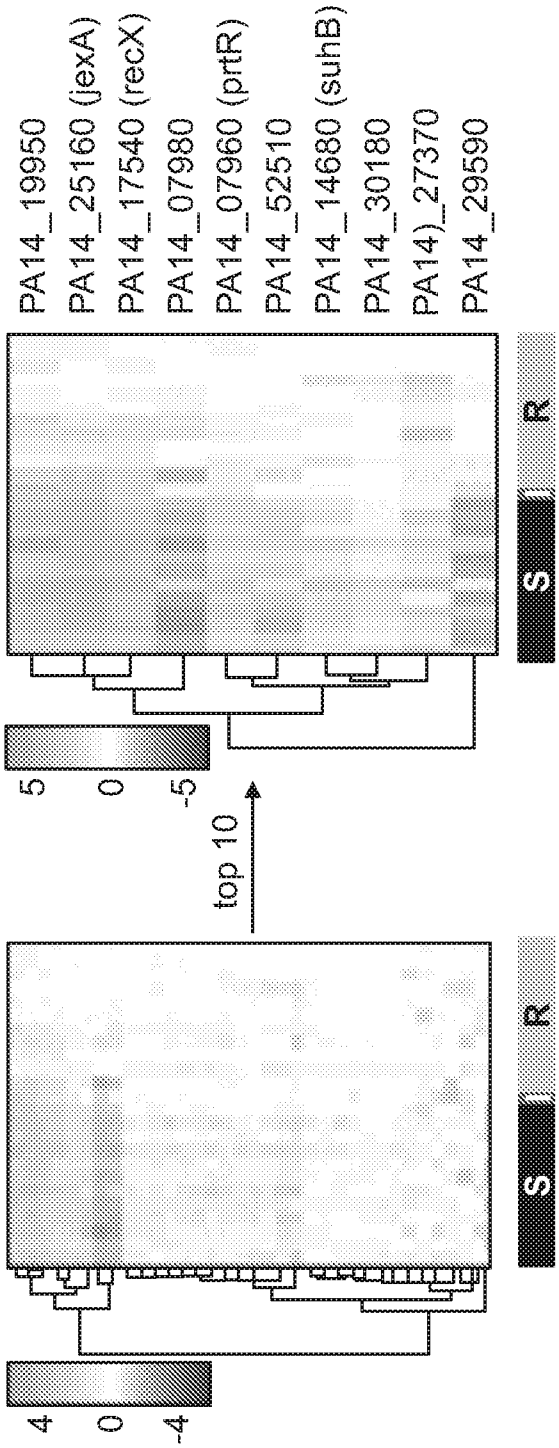

PA14_19950
PA14_25160 (jexA)
PA14_17540 (recX)
PA14_07980
PA14_07960 (prtR)
PA14_52510
PA14_14680 (suhB)
PA14_30180
PA14)_27370
PA14_29590
5
0
-5
top 10
4
0
-4
S
R
S
R
strains (ordered by MIC)

FIG. 14E

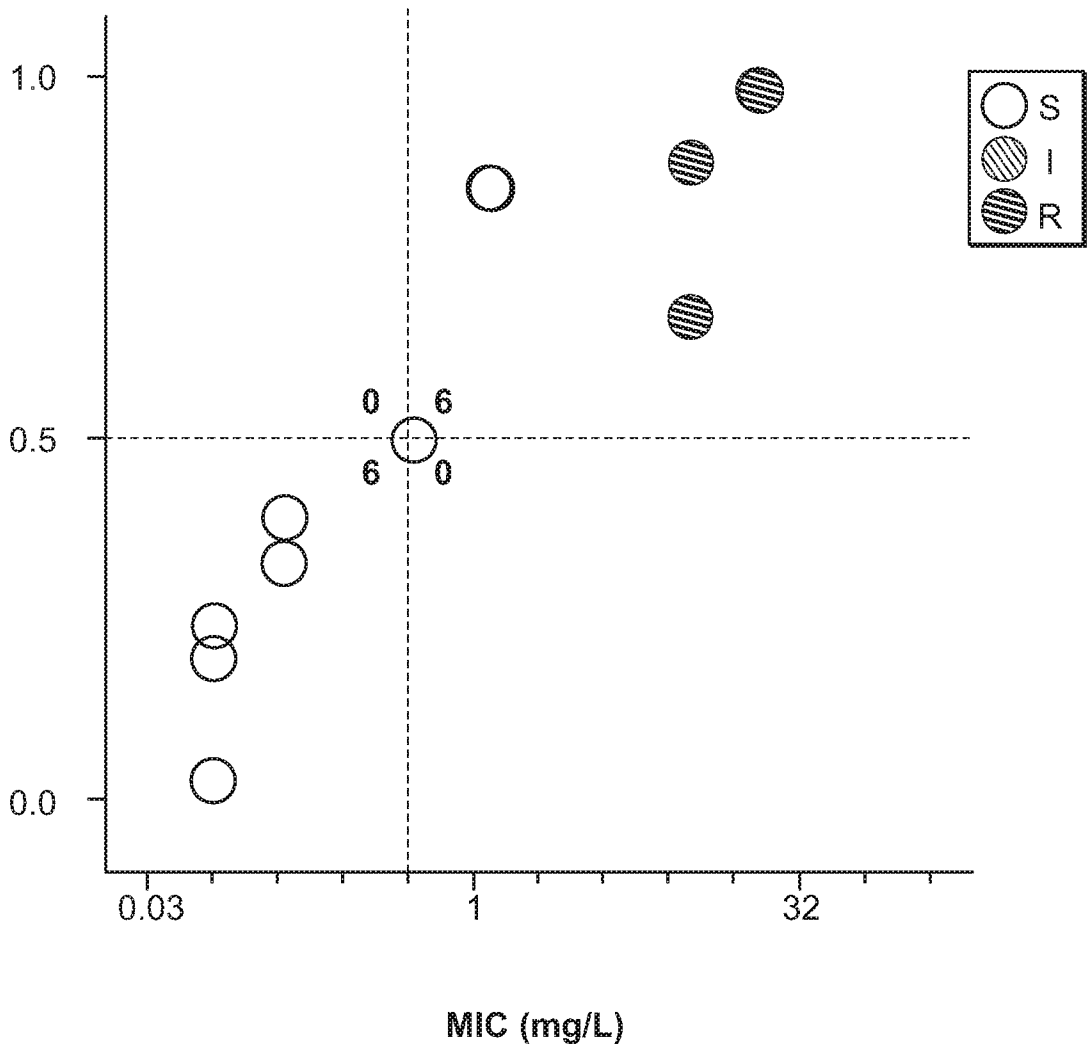


FIG. 14F

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/48114

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12Q 1/04, 1/68; G01N 33/15 (2019.01)

CPC - C12Q 1/025, 1/689; G01N 33/15

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	US 9,885,088 B2 (Hung et al.) 6 February 2018; abstract; figure 2; table 3; column 2, lines 41-67; column 3, lines 1-3, 8-12, 52-56; column 4, lines 1-14, 20-21, 35-38; column 6, lines 3-5, 25-30, 57-64; column 12, lines 49-56; column 15, lines 54-56; column 16, lines 4-6; column 20, lines 1-8; column 23, lines 51-55; column 25, lines 64-66; claim 1	1, 13, 14/1, 14/13, 16/1, 16/13, 17/1, 17/13 -- 7-9, 15/1, 15/13, 18-20 -- 2, 5, 10, 21
Y	WO 2011/094514 A1 (QIAGEN GAITHERSBURG, INC.) 4 August 2011; paragraph [0096]	7-9, 18-20
Y	WO 2018/144918 A1 (SELUX DIAGNOSTICS, INC.) 09 August 2018; paragraphs [0164]-[0165]	15/1, 15/13
A	EP 3231874 A1 (CURETIS GMBH) 18 October 2017; paragraph [0127]; SEQ ID NO: 3	2, 10, 21
A	US 2010/0136534 A1 (Wang et al.) 3 June 2010; paragraph [0008]; SEQ ID NO: 44	2, 10, 21
A	Klebsiella pneumoniae capsular polysaccharide biosynthesis gene cluster, type: KL106-1: GENBANK ACCESSION LT174576.1; Publication [online]. 13 June 2013 [retrieved 17 December 2019]. Retrieved from the internet: <https://www.ncbi.nlm.nih.gov/nucleotide/LT174576.1?report=genbank&log$=nuclalign&blast_rank=14&RID=ZJ5BK3RD016>; pp 1-10	5

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 December 2019 (17.12.2019)	09 JAN 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/48114

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Klebsiella pneumoniae strain KpMDU1 cpsC capsular synthesis gene cluster, complete sequence: GENBANK ACCESSION KR007677.1; Publication [online]. 08 June 2015 [retrieved 17 December 2017]. Retrieved from the internet: <https://www.ncbi.nlm.nih.gov/nucleotide/KR007677.1?report=genbank&log $=nuclalign&blast_rank=19&RID=ZJ5BK3RD016>; pp 1-10	5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US19/48114

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

-***-Please See Supplemental Page-***-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 2 (in-part), 5 (in-part), 7-9, 10 (in-part), 13-20, and 21 (in-part); SEQ ID NO: 35 (CRE2 probe target); SEQ ID NO: 70 (CRE2 probe A sequence); SEQ ID NO: 87 (CRE2 probe B sequence)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US19/48114

-***-Continued from Box No. III Observations where unity of invention is lacking: -***-

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+, Claims 1-23, SEQ ID NO: 35 (CRE2 probe target), SEQ ID NO: 70 (CRE2 probe A sequence), and SEQ ID NO: 87 (CRE2 probe B sequence) are directed toward compositions, methods, and kits for rapid phenotypic detection of antibiotic resistance/susceptibility.

The compositions, methods, and kits will be searched to the extent that they encompass SEQ ID NO: 35 (first exemplary CRE2 probe target); SEQ ID NO: 70 (first exemplary CRE2 probe A sequence) and SEQ ID NO: 87 (first exemplary CRE2 probe B sequence). Applicant is invited to elect additional probe target(s) and/or sequence(s), with specified SEQ ID NO: for each, or with specified substitution(s) at specified site(s) of a SEQ ID NO:, such that the sequence of each elected species is fully specified (i.e. no optional or variable bases or substituents), and available as an option within at least one searchable claim, to be searched. Additional probe target(s) and/or sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1, 2 (in-part), 5 (in-part), 7-9, 10 (in-part), 13-20, and 21 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 35 (CRE2 probe target), SEQ ID NO: 70 (CRE2 probe A sequence), and SEQ ID NO: 87 (CRE2 probe B sequence). Applicants must specify the claims that encompass any additionally elected probe target(s) and/or sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be SEQ ID NO: 36 (CRE2 probe target); SEQ ID NO: 71 (CRE2 probe A sequence); SEQ ID NO: 88 (CRE2 probe B sequence).

No technical features are shared between the probe targets and/or sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features including: a method, comprising: obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a patient or an environmental source; processing the sample to enrich the one or more bacterial cells; contacting the sample with one or more antibiotic compounds; lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; hybridizing the released mRNA to at least one set of two nucleic acid probes, wherein each nucleic acid probe includes a unique barcode or tag; detecting the hybridized nucleic acid probes; identifying one or more genetic resistance determinants; and determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; a composition comprising a set of nucleic acid probes; a composition comprising a set of nucleic acid probes that includes a first probe comprising a sequence and a second probe comprising a sequence; a method of treating a patient, comprising: obtaining a sample including one or more bacterial cells, wherein the sample is obtained from a patient or an environmental source; processing the sample to enrich the one or more bacterial cells; contacting the sample with one or more antibiotic compounds; lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; hybridizing the released mRNA to at least one set of two nucleic acid probes, wherein each nucleic acid probe includes a unique barcode or tag; detecting the hybridized nucleic acid probes; identifying one or more genetic resistance determinants; determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; and administering to the patient an appropriate antibiotic based on the determination of the identity and the antibiotic susceptibility of the one or more bacterial cells; a kit, comprising a set of nucleic acid probes; a kit, comprising a set of nucleic acid probes that includes a first probe comprising a sequence and a second probe comprising a sequence; these shared technical features are previously disclosed by US 9,885,088 B2 to Hung, et al. (hereinafter 'Hung').

-***-Continued on Next Supplemental Page-***-

-***-Continued from Previous Supplemental Page-***-:

Hung discloses a method (abstract), comprising: obtaining a sample including one or more bacterial cells (comprising: obtaining a sample including one or more bacterial cells; column 4, lines 52-53; claim 1), wherein the sample is obtained from a patient (column 4, lines 6-14) or an environmental source; processing the sample to enrich the one or more bacterial cells (centrifuging the sample (processing the sample to enrich the one or more bacterial cells); column 18, lines 35-36; column 25, lines 64-66); contacting the sample with one or more antibiotic compounds (contacting the sample with one or more antibiotic compounds; claim 1); lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells (lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; column 4, lines 20-21; claim 1); hybridizing the released mRNA to at least one set of two nucleic acid probes (hybridizing the released mRNA to at least one set of two nucleic acid probes; figure 1A; column 2, lines 54-62; column 6, lines 25-37; claim 1), wherein each nucleic acid probe includes a unique barcode (column 6, lines 57-58) or tag; detecting the hybridized nucleic acid probes (complexes are imaged and counted (detecting the hybridized nucleic acid probes); figure 2; column 6, lines 60-61); identifying one or more genetic resistance determinants (figure 2; column 6, lines 61-64); and determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells (determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; abstract; column 2, lines 38-45; column 28, lines 10-13); a composition comprising a set of nucleic acid probes (column 2, lines 52-61); a composition comprising a set of nucleic acid probes that includes a first probe comprising a sequence and a second probe comprising a sequence (a composition comprising a set of nucleic acid probes that includes a first probe comprising a sequence and a second probe comprising a sequence; column 2, lines 52-61); a method of treating a patient (optimizing treatment based on detection of mRNA; column 2, lines 38-41), comprising: obtaining a sample including one or more bacterial cells (comprising: obtaining a sample including one or more bacterial cells; column 4, lines 52-53; claim 1), wherein the sample is obtained from a patient (column 4, lines 6-14) or an environmental source; processing the sample to enrich the one or more bacterial cells (centrifuging the sample (processing the sample to enrich the one or more bacterial cells); column 18, lines 35-36; column 25, lines 64-66); contacting the sample with one or more antibiotic compounds (contacting the sample with one or more antibiotic compounds; claim 1); lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells (lysing the sample to release messenger ribonucleic acid (mRNA) from the one or more bacterial cells; column 4, lines 20-21; claim 1); hybridizing the released mRNA to at least one set of two nucleic acid probes (hybridizing the released mRNA to at least one set of two nucleic acid probes; figure 1A; column 2, lines 54-62; column 6, lines 25-37; claim 1), wherein each nucleic acid probe includes a unique barcode (column 6, lines 57-58) or tag; detecting the hybridized nucleic acid probes (complexes are imaged and counted (detecting the hybridized nucleic acid probes); figure 2; column 6, lines 60-61); identifying one or more genetic resistance determinants (figure 2; column 6, lines 61-64); determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells (determining the identity of the one or more bacterial cells and the antibiotic susceptibility of each of the identified one or more bacterial cells; abstract; column 2, lines 38-45; column 28, lines 10-13); and administering to the patient an appropriate antibiotic based on the determination of the identity and the antibiotic susceptibility of the one or more bacterial cells (administering to the patient an appropriate antibiotic based on the determination of the identity and the antibiotic susceptibility of the one or more bacterial cells; column 4, lines 35-38); a kit (column 16, lines 1-13), comprising a set of nucleic acid probes (column 16, lines 1-13); a kit (column 16, lines 1-13), comprising a set of nucleic acid probes that includes a first probe comprising a sequence and a second probe comprising a sequence (column 2, lines 54-62; column 16, lines 1-13).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Hung, unity of invention is lacking.