

CLAIMS

1. A method for determining a mechanism for an antimicrobial susceptibility phenotype, comprising:
 - providing a sample comprising at least one microorganism that is not susceptible
5 to at least one antimicrobial agent;
 - contacting the sample with the antimicrobial agent, wherein the antimicrobial agent can kill, inhibit the growth, or otherwise compromise the viability of one or more microorganisms;
 - contacting the at least one microorganism with at least one compound comprising
10 an oligonucleotide molecule targeting at least one specific nucleic acid sequence that is involved in a non-susceptible phenotype to the antimicrobial agent;
 - contacting the sample with a non-replicative transduction particle (NRTP) comprising a reporter nucleic acid molecule encoding a reporter molecule under conditions such that the NRTP inserts into the microorganism the reporter nucleic
15 acid molecule and such that the reporter molecule provides the detectable indication of viability; and
 - determining the mechanism for the antimicrobial susceptibility phenotype of the microorganism based on the presence or absence of a detectable indication of viability associated with the microorganism when the microorganism is in contact
20 with the antimicrobial agent and the oligonucleotide molecule, wherein the presence of the detectable indication of viability indicates that the specific nucleic acid sequence targeted by the oligonucleotide molecule is not related to the mechanism for the antimicrobial susceptibility phenotype to the antimicrobial agent, and wherein the absence of the detectable indication of viability indicates
25 that the specific nucleic acid sequence targeted by the oligonucleotide molecule is related to the mechanism for the antimicrobial susceptibility phenotype to the antimicrobial agent.
2. The method of claim 1, wherein the reporter nucleic acid molecule is a gene encoding a light-emitting molecule.
- 30 3. The method of any one of claims 1 to 2, wherein the NRTP is produced from a bacterial cell packaging system that comprises a host bacteria cell, a first nucleic acid construct inside the host bacteria cell comprising a bacteriophage genome having a non-functional packaging initiation site sequence, wherein the non-functional

packaging initiation site sequence prevents packaging of the bacteriophage genome into the NRTP, and a second nucleic acid construct inside the host bacteria cell and separate from the first nucleic acid construct comprising the reporter nucleic acid molecule having a reporter gene and a functional packaging initiation site sequence for facilitating packaging of a replicon of the reporter nucleic acid molecule into the NRTP, wherein the functional second packaging initiation site sequence on the second nucleic acid construct complements the non-functional packaging initiation site sequence in the bacteriophage genome on the first nucleic acid construct.

4. The method of any one of claims 1 to 3, wherein the compound is selected from the group consisting of a peptide nucleic acid (PNA), a peptide-PNA, a CRISPR RNA (crRNA), an antisense oligonucleotide, and a double-stranded RNA (dsRNA).

5. The method of any one of claims 1 to 4, wherein the at least one specific nucleic acid sequence that is involved in a non-susceptible phenotype to the antimicrobial agent is selected from the group consisting of a *bla_{KPC-3}* gene, a *bla_{NDM-1}* gene, a *bla_{SHV-18}* gene, and a *vanC* gene.

6. The method of any one of claims 1 to 5, wherein the microorganism is of the family Enterobacteriaceae, the genus *Enterococcus*, or the genus *Candida*.

7. The method of any one of claims 1 to 6, wherein the antimicrobial is a β -lactam or vancomycin.

8. A method for determining a mechanism involved in a non-susceptible phenotype, comprising:

- providing a sample comprising an Enterobacteriaceae that is not susceptible to carbapenem;
- contacting the sample with carbapenem;
- contacting the Enterobacteriaceae with an oligonucleotide molecule that targets a gene associated with carbapenem resistance;
- contacting the sample with a non-replicative transduction particle (NRTP) comprising a reporter nucleic acid molecule encoding a reporter molecule under conditions such that the NRTP inserts into the Enterobacteriaceae the reporter nucleic acid molecule and such that the reporter molecule provides the detectable indication of viability; and
- determining the mechanism of carbapenem non-susceptibility for the Enterobacteriaceae based on the presence or absence of a detectable indication of

- viability associated with the Enterobacteriaceae when the Enterobacteriaceae is in contact with the carbapenem and the oligonucleotide molecule, wherein the presence of the detectable indication of viability indicates that the gene targeted by the oligonucleotide molecule is not related to the mechanism of carbapenem non-susceptibility, and wherein the absence of the detectable indication of viability indicates that the gene targeted by the oligonucleotide molecule is related to the mechanism of carbapenem non-susceptibility.
9. The method of claim 8, wherein the reporter nucleic acid molecule is a gene encoding a light-emitting molecule.
 10. The method of any one of claims 8 to 9, wherein the NRTP is produced from a bacterial cell packaging system that comprises a host bacteria cell, a first nucleic acid construct inside the host bacteria cell comprising a bacteriophage genome having a non-functional packaging initiation site sequence, wherein the non-functional packaging initiation site sequence prevents packaging of the bacteriophage genome into the NRTP, and a second nucleic acid construct inside the host bacteria cell and separate from the first nucleic acid construct comprising the reporter nucleic acid molecule having a reporter gene and a functional packaging initiation site sequence for facilitating packaging of a replicon of the reporter nucleic acid molecule into the NRTP, wherein the functional second packaging initiation site sequence on the second nucleic acid construct complements the non-functional packaging initiation site sequence in the bacteriophage genome on the first nucleic acid construct.
 11. The method of any one of claims 8 to 10, wherein the oligonucleotide molecule is selected from the group consisting of a peptide nucleic acid (PNA), a peptide-PNA, a CRISPR RNA (crRNA), an antisense oligonucleotide, and a double-stranded RNA (dsRNA).
 12. The method of claim 11 wherein the oligonucleotide molecule is selected from the group consisting of SEQ ID NO 2 or SEQ ID NO 3, or wherein the oligonucleotide molecule is a CRISPR/Cas9 System comprising SEQ ID NO 4 or SEQ ID NO 5.
 13. A method for reducing the amount of potentially cross-reactive or interfering organisms in an assay designed to detect a target organism comprising:
 - providing a sample comprising at least one organism that is potentially cross-reactive or interfering in an assay designed to detect a target organism;

- contacting the cross-reactive or interfering organism with at least one compound comprising an oligonucleotide molecule targeting at least one specific nucleic acid sequence that is involved with the viability of the potentially cross-reactive or interfering organism, wherein the specific nucleic acid sequence is unique to the potentially cross-reactive or interfering organism; and causing the potentially cross-reactive or interfering organism to lose viability; and
 - contacting the sample with a non-replicative transduction particle (NRTP) comprising a reporter nucleic acid molecule encoding a reporter molecule under conditions such that the NRTP inserts into the target organism the reporter nucleic acid molecule and such that the reporter molecule provides a detectable indication of viability of the target organism.
14. The method of claim 13, wherein the reporter nucleic acid molecule is a gene encoding a light-emitting molecule.
 15. The method of any one of claims 13 to 14, wherein the compound is selected from the group consisting of a peptide nucleic acid (PNA), a peptide-PNA, a CRISPR RNA (crRNA), an antisense oligonucleotide, and a double-stranded RNA (dsRNA).
 16. The method of any one of claims 13 to 15, wherein the NRTP is produced from a bacterial cell packaging system that comprises a host bacteria cell, a first nucleic acid construct inside the host bacteria cell, comprising of a bacteriophage genome having a non-functional packaging initiation site sequence, wherein the non-functional packaging initiation site sequence prevents packaging of the bacteriophage genome into the NRTP, and a second nucleic acid construct inside the host bacteria cell and separate from the first nucleic acid construct, comprising of the reporter nucleic acid molecule having a reporter gene and a functional packaging initiation site sequence for facilitating packaging of a replicon of the reporter nucleic acid molecule into the NRTP, wherein the functional second packaging initiation site sequence on the second nucleic acid construct complements the non-functional packaging initiation site sequence in the bacteriophage genome on the first nucleic acid construct.
 17. The method of any one of claims 13 to 16, wherein the target organism is of the family Enterobacteriaceae.
 18. The method of any one of claims 13 to 17, wherein the at least one specific nucleic acid sequence that is involved with the viability of the potentially cross-reactive or interfering organism is the *murA* gene.