

CLAIMS:

1. A composition comprising at least 4 different types of transduction particles, wherein each of said particles comprises a nucleic acid and said particles are capable of contacting *E coli* cells and introducing therein the nucleic acid, wherein

5 (a) said nucleic acid of each particle comprises a nucleotide sequence encoding a product of interest (POI), wherein the nucleic acid is capable of expressing the POI in an *E coli* cell; and wherein the POI comprises:

(i) a Cas nuclease for targeting and cutting the DNA of the *E coli* cell, thereby modifying or killing the cell; and

10 (ii) at least one crRNA or guide RNA each comprising a spacer sequence that is complementary to a protospacer sequence comprised by a gene selected from B2 phylogroup *E coli* genes *fimH*, *bolA*, *rpoH*, *lptA* and *murA* and each of which is operable with the Cas nuclease for DNA targeting in the *E coli* cells;

(b) each particle comprises:

15 (iii) an adhesion moiety for recognising and binding to a cognate moiety selected from a LPS and Tsx displayed on the surface of *E coli* cells; and

(iv) a phage capsid containing the nucleic acid; and

(c) said at least 4 different types of transduction particles comprises

20 A: particles which comprise a LPS adhesion moiety and a LamB adhesion moiety;

B: particles which comprise a LPS adhesion moiety and a Tsx adhesion moiety; and

C: particles which comprise a Tsx adhesion moiety but are devoid of LamB and LPS adhesion moieties;

25 and wherein the particles of the composition target all of *E coli* genes *fimH*, *bolA*, *rpoH*, *lptA* and *murA*.

2. The composition of claim 1, wherein the capsid of each particle comprised by the composition is a T-even phage capsid; optionally a capsid of a T2 phage, or a RB69 phage.

3. The composition of any preceding claim, wherein each particle is a phage (optionally a lytic phage) or packaged phagemid.

4. The composition of any preceding claim, wherein the nucleic acid of each particle comprises at least one nucleotide sequence (N1) encoding said POI, wherein each particle is a synthetic T-even phage comprising an insertion of N1 into a Modification Permissive Region (MPR) of the genome of the phage, wherein the MPR is immediately after *gene 49* and to *gene E* when compared to a

reference wild-type T2 phage; optionally wherein

(a) the nucleic acid comprises a DNA deletion of phage DNA in the MPR,

(b) the insertion comprises up to 8000bp of DNA and/or the deletion comprises up to 8000bp of DNA;

(c) the MPR comprises contiguous DNA between said gene 49 and gene E, wherein the contiguous DNA is at least 1000bp in length; or wherein the MPR comprises at least 100bp of DNA between said gene 49 and gene E; and/or

(d) the synthetic phage genome comprises said insertion between coordinates 9000 and 21000, wherein the coordinates are the nucleotide positions counted from the nucleotide (coordinate number 1) immediately after gene 49 towards gene E when compared to a reference wild-type T2 phage.

5. The composition of any preceding claim, wherein the nuclease is a Type I, II, III, IV, V or VI Cas nuclease, optionally a Cas9 or a Cas3.

6. The composition of any preceding claim, wherein each protospacer sequence is of strain ST131.

7. The composition of any preceding claim, wherein the nucleotide sequence encoding the POI comprises an *E coli bolA* promoter or comprises SEQ ID NO: 13.

8. The composition of any preceding claim, wherein the *E coli* cells comprise a strain of *E coli* that causes sepsis, septicaemia or diarrhoea in humans or animals.

9. The composition of any preceding claim, for use in treating or preventing infection by *E coli* cells in a human or animal subject, wherein the use comprises administering the composition to the subject.

10. The composition of any preceding claim for use in treating or preventing sepsis, septicaemia or diarrhoea in a human or animal subject, the use comprising administering to the subject the composition of any preceding claim, wherein the *E coli* cells comprise a strain of *E coli* that causes sepsis, septicaemia or diarrhoea in humans or animals.

11. The composition for use of claims 9 or 10, wherein the subject is a transplant or cancer patient (optionally a haematological cancer patient), or wherein the patient is suffering from or at risk of a urinary tract infection (UTI); and optionally wherein the transplant is a solid organ or stem cell transplant (optionally a haematopoietic cell transplant) or wherein the transplant is a transplant of a medical device; optionally

wherein the administration is carried out prior to the subject receiving a transplant.

12. The composition for use of any one of claims 9-11 for preventing haemolytic uremic syndrome (HUS), a UTI infection, sepsis, septicaemia or diarrhoea in a human subject.

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13. The composition for use of anyone of claims 9-12, wherein at least 1×10^7 PFU of particles are administered to the subject; or a composition according to any one of claims 1-8 wherein the composition comprises a dose of at least 1×10^7 PFU of said particles.

- 10 14. The composition for use of any one of claims 9-13, wherein the particles are administered to the subject at an MOI (multiplicity of infection) of at least 0.01.

- 15 15. The composition, method or dose of any preceding claim, wherein the *E coli* cells comprise at least one strain that is an antibiotic-resistant or MDR strain; and/or at least one B2-I strain; optionally wherein the antibiotic is fluoroquinolone (optionally levofloxacin), carbapenem or vancomycin; and/or wherein the *E coli* cells comprise beta-lactamase (ESBL)-producing *E coli*.